โลหะคลอไรด์อิมเพรกเนตพิลลาร์เคลย์สำหรับการสังเคราะห์คูมารินและตัวเร่งปฏิกิริยาแอนไอออนอินเทอร์คาเลตเทต Ni/Zn สำหรับปฏิกิริยาการเติมแบบไมเคิล

นางสาวลัดดาวรรณ เจริญศิริวัฒน์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
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METAL CHLORIDE IMPREGNATED-
PILLARED CLAY FOR COUMARIN SYNTHESIS AND ANION INTERCALATED Ni/Zn
CATALYST FOR MICHAEL ADDITION REACTIONS

Miss Laddawan Chareonsiriwat

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ลัดดาวรรณ เจริญศิริวัฒน์ : โลหะคลอไรด์อิมเพรกเนตพิลลาร์เคลย์สำหรับการสังเคราะห์คูมารินและตัวเร่งปฏิกิริยาแอนไอออนอินเทอร์คาเลตเทต Ni/Zn สำหรับปฏิกิริยาการเติมแบบไมเคิล (METAL CHLORIDE IMPREGNATED-PILLARED CLAY FOR COUMARIN SYNTHESIS AND ANION INTERCALATED Ni/Zn CATALYST FOR MICHAEL ADDITION REACTIONS) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ดร.วรินทร ชวศิริ, 156 หน้า.

ได้สังเคราะห์โลหะออกไซด์พิลลาร์มอนต์มอริลโลไนต์โดยวิธีอินเทอร์คาเลชันและนำไปเผาที่อุณหภูมิสูง อิมเพรกเนตด้วยโลหะคลอไรด์ ($CrCl_3$ และ $NdCl_3$) และนำไปเผาที่อุณหภูมิสูง พิสูจน์เอกลักษณ์ตัวเร่งปฏิกิริยาชนิดเคลย์ที่สังเคราะห์ได้ด้วยเทคนิคการเลี้ยวเบนของรังสีเอ็กซ์ เทคนิคการดูดซับ-การคายแก๊สไนโตรเจน และเทคนิคการคายออกของแอมโมเนียแบบโปรแกรมอุณหภูมิ นำตัวเร่งปฏิกิริยาที่สังเคราะห์ได้ไปใช้ในปฏิกิริยาการสังเคราะห์คูมาริน ปฏิกิริยาไอโซเมอไรเซชันของอิพอกไซด์ และปฏิกิริยาการสังเคราะห์แอซีโทไนด์จากอิพอกไซด์ ตัวเร่งปฏิกิริยาชนิดเคลย์ที่สังเคราะห์ได้มีความสามารถในการเร่งปฏิกิริยามากกว่าเคลย์ต้นกำเนิด ได้ภาวะที่เหมาะสมสำหรับปฏิกิริยาเหล่านี้ที่ใช้กรดเร่งปฏิกิริยา โดยให้ปริมาณผลิตภัณฑ์ในระดับดีถึงดีมากและมีความเลือกจำเพาะภายใต้ภาวะที่ไม่รุนแรง นอกจากนี้ได้เตรียมตัวเร่งปฏิกิริยาแอลคิลคาร์บอกซีเลตแอนไอออนอินเทอร์คาเลตเทต NiZn โดยวิธีอินเทอร์คาเลชัน พิสูจน์เอกลักษณ์ตัวเร่งปฏิกิริยาที่สังเคราะห์ได้ด้วยเทคนิคการเลี้ยวเบนของรังสีเอ็กซ์และนำไปใช้ในปฏิกิริยาการเติมแบบไมเคิล ตัวเร่งปฏิกิริยา NiZn ที่สังเคราะห์ได้มีความสามารถในการเร่งปฏิกิริยาสูง

สาขาวิชา	ปิโตรเคมี	ลายมือชื่อนิสิต	....
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LADDAWAN CHAREONSIRIWAT: METAL CHLORIDE IMPREGNATED-PILLARED CLAY FOR COUMARIN SYNTHESIS AND ANION INTERCALATED Ni/Zn CATALYST FOR MICHAEL ADDITION REACTIONS. ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 156 pp.

Metal oxide-pillared montmorillonites were synthesized by intercalation method and calcination. The impregnation with metal chloride ($CrCl_3$ and $NdCl_3$) was carried out with calcination. The synthesized clays were characterized by powder X-ray diffraction, N_2 adsorption-desorption and temperature programmed desorption of ammonia techniques. These synthesized clays were utilized as catalysts for the synthesis of coumarins, isomerization of epoxides and synthesis of acetonides from epoxides. The synthesized clays provided considerably higher catalytic activities than the parent clay. The optimized conditions for these acid-catalyzed reactions were scrutinized. These reactions could be expediently proceeded using synthesized clay catalysts to provide good to excellent yield and selectivity of the corresponding products under mild reaction conditions. In addition, the alkylcarboxylate anion-intercalated NiZn catalysts were prepared by intercalation method, characterized by powder X-ray diffraction and utilized for Michael reaction. The synthesized NiZn catalysts furnished high catalytic activities.

Field of Study: Petrochemistry	Student's Signature ....
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LIST OF SCHEMES

LIST OF ABBREVIATIONS

%	percent
BET	Brunauer-Emmett-Teller
°C	degree of Celsius
Å	Angstrom unit
anh	anhydrous
β	beta
$CDCl_3$	deuterated chloroform
$CHCl_3$	chloroform
d	doublet (NMR)
dd	doublet of doublet (NMR)
ddd	doublet of doublet of doublet (NMR)
DMSO	dimethyl sulfoxide
Et_2O	diethyl ether
EtOAc	ethyl acetate
EtOH	ethanol
Fig	figure
GC	Gas chromatography
Hz	hertz
h	hour (s)
J	coupling constant (NMR)
MeOH	methanol

M	molar
m	multiplet (NMR)
m.p.	melting point
mg	milligram (s)
min	minute (s)
mL	milliliter
mm	millimeter
mmol	millimole
MW	molecular weight
MB	Mass balance
nm	nanometer
NMR	nuclear magnetic resonance
q	quartet (NMR)
quant	quantitative
quin	quintet (NMR)
RT	room temperature
s	singlet (NMR)
t	triplet (NMR)
TPD	Temperature Programmed Desorption
TLC	thin layer chromatography
vol	volume
wt	weight
XRD	X-ray diffraction

α	alpha
θ	theta
δ	chemical shift
λ	wavelength

CHAPTER I

INTRODUCTION

Solid catalysts were used for decades in most petrochemical processes. Heterogenization is one of new clean technologies which are being developed to reduce waste in liquid phase organic reactions. In order to exploit this greener technology in organic chemical manufacturing, the highly effective catalysts need to produce to suit a multitude of chemical process technologies.

The use of clay minerals has expanded in catalytic reactions including for organic synthesis, chemical evolution and environmental problems. Reactions of organic molecules on clay minerals have been investigated from different aspects. Their Brønsted and Lewis acidities have been exploited for catalytic applications. Clays and modified clays are utilized as efficient catalyst for numerous organic reactions such as hydrogenation, dehydrogenation, protection-deprotection reactions, Michael addition, alkylation, acylation, aldol formation, condensation, oxidation of alcohols, epoxidation, esterification, cyclization, rearrangement/isomerization, synthesis of heterocycles and many more [1, 2]. In addition, clays have been modified by intercalated with a variety of inorganic and organic ions, metal complexes, and organic compounds. These have brought about the performance of clays in terms of increasing the rates of reactions, yields and product selectivity [3, 4]. Moreover, these catalysts could be easily separated from the reaction mixture by filtration or centrifugation and reused.

For several decades, the modification of clays is most commonly carried out either by exchanging the cations present in the clay with any other appropriate cations or by increasing the interlamellar space by pillaring. Cation-exchanged clays were prepared by stirring a mixture of clay and metal salt in aqueous medium or aqueous acetone at RT or above. Pillared interlayered clays (PILCs) were prepared by exchanging the interlayered cations of layered clays with bulky inorganic polyoxocations, followed by calcination. The intercalated polycations increase the basal spacing of clays and, upon heating, they are transformed to metal oxide clusters by dehydration and dehydroxylation. These metal oxide clusters are inserted between clay layers, yielding oxide pillars that permanently keep the layers apart. The microporous structure of pillared with high surface area and high thermal stability is obtained. Both Brønsted and Lewis acid sites are present. A variety of pore dimensions and catalytic activities are obtained by different types of pillared clays [5, 6]. Pillared interlayered clays are very efficient catalysts in various applications such as reduction of pollutants, synthesis of fine chemicals and acid catalyzed reactions [1, 7] due to pillared interlayered clays have higher thermal stability, surface area and pore volume than raw clays. Organic reactions under acid catalysis can be occurred very efficiently using pillared interlayered clay catalysts.

In this research, the utilization of synthesized clays (Fe-pillared clay, metal chloride-impregnated Fe-pillared clay and Cr-pillared clay) for acid-catalyzed reactions (the synthesis of coumarins, isomerization of epoxides and synthesis of acetonides from epoxides) and the utilization of alkylcarboxylate anion-intercalated NiZn catalysts for Michael reaction, has been focused. To our best knowledge, there is no report on the use of Fe- and Cr-pillared clay as catalysts for these reactions.

CHAPTER II
CLAY CATALYSTS

2.1 Clays

Clay minerals are crystalline hydrated aluminosilicates with layered structures. They are wildly distributed over the surface of the earth. The distinctive properties of clays consist of high surface area, high sorption, high cation-exchange capacity and high acidity. Their Brønsted and Lewis acidities have also been exploited for catalytic applications. Numerous organic reactions use clays as efficient heterogeneous catalysts. Modified clays could be utilized as highly selective catalyst in organic transformations to furnish excellent yield with high regio- and stereo-selectivity. The advantages of easy removal of clay catalyst from the reaction mixture and reusable of the catalyst made a great interest in their application than homogeneous [8].

2.2 The structure of clay minerals

The basic building block in the clay mineral structure is an aluminosilicate layer consisting of a silica tetrahedral sheet and an alumina octahedral sheet, joined together by sharing apical oxygen atoms [9].

2.2.1 Basic units

Tetrahedral sheet consists of continuous sheet of silica tetrahedral linked via three corners to form a hexagonal network. The fourth corner of each tetrahedron is corner shared with octahedral in adjacent layers. Each tetrahedron formally contains Si^{4+} at the center coordinated to an O^{2-} at each apex (Fig 2.1). Nevertheless, replacement of Si^{4+} with Al^{3+} in tetrahedral sites is common.

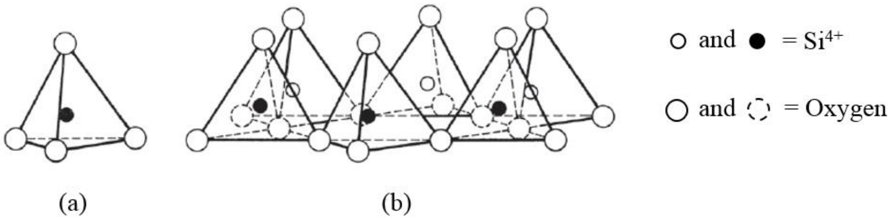


Figure 2.1 A single silica tetrahedral (a), and a sheet structure of silica tetrahedral arranged in a hexagonal network (b) [10]

Octahedral sheet consists of flat layers of edge-sharing octahedral as hexagonal network, each formally containing Al^{3+} or Mg^{2+} at its center and OH^- or O^{2-} at its apices (Fig 2.2). Which O^{2-} occupying apices corner shared with adjacent tetrahedra and OH^- occupying apices that are not shared.

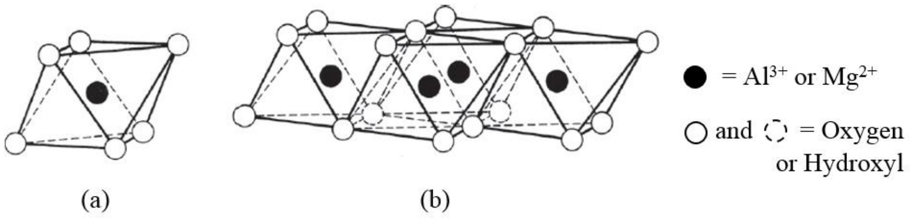


Figure 2.2 A single octahedral unit (a) and a sheet structure of octahedral unit arranged in a hexagonal network (b) [10]

2.2.2 The combination of basic sheets

The combinations of basic sheets of clays could be divided into two groups, 1:1- and 2:1-type, based on the number of tetrahedral and octahedral sheets in the layer structure.

2.2.2.1 The 1:1 layered type (T:O)

The 1:1 layer structure consists of a unit made up of one tetrahedral sheet (T) and one octahedral sheet (O). The apical O^{2-} ions of the tetrahedral sheets being shared with the octahedral sheet (Fig 2.3).

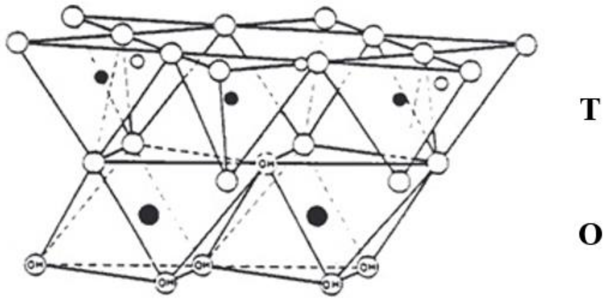


Figure 2.3 Structure of 1:1 layered type (T = tetrahedral sheet, O = octahedral sheet)

Kaolinite is the most common member of this group which the structure consists of 1:1 layers stacked one above the other. Kaolinite contains Al^{3+} in the octahedral sites and Si^{4+} in the tetrahedral sites and having the unit composition of $Al_2Si_2O_5(OH)_4$. The layers are held together by hydrogen bonding between the basal oxygens of the tetrahedral sheet and the hydroxyls of the exterior plane of the adjacent octahedral sheet, supplemented by dipole–dipole and van der Waals interactions [9, 11]. The layer thickness of ~0.7 nm also represents the basal or *d*(001) spacing.

2.2.2.2 The 2:1 layered type (T:O:T)

The 2:1 layer structure consists of two tetrahedral sheets with one bound to each side of an octahedral sheet. The combination makes a tetrahedral-octahedral-tetrahedral (T:O:T) sandwich layers. Montmorilonite is the common smectite clay mineral. The simplest members of this group are shown in Fig 2.4.

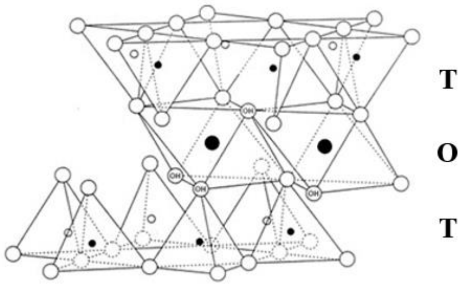


Figure 2.4 Structure of 2:1 layered type
(T = Tetrahedral sheet, O = Octahedral sheet)

2.3 Smectite clay minerals

The structure of smectite clay minerals consist of two silica tetrahedral sheets with one alumina octahedral sheet. The substitutions of Al^{3+} for Si^{4+} in tetrahedral sheets and Mg^{2+} for Al^{3+} in octahedral sheets cause the negative layered charge formation, which is balanced by hydrated interlayer cations, such as, Na^{+}, K^{+}, or Ca^{2+} [12]. The structure of smectite clay is displayed in Fig 2.5.

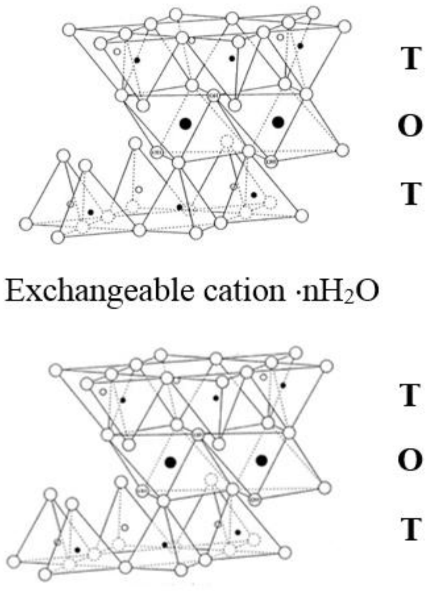


Figure 2.5 Structure of smectite clay

Smectite has the ability to adsorb large amount of water molecules between the layers, causing the volume of the clay minerals increase. Therefore, the smectites are expanding or swelling clays with the basal spacing of 10 to 20 Å. The most common smectite is montmorillinite.

Montmorillonite is the main component of the volcanic ash weathering product, bentonite (approximately 80-90 wt%). The impurities commonly present in bentonite clay are generally found as quartz, feldspar, crystobalite, and humic acids. Montmorillonite has an ideal formula of $(Si_8)(Al_{4-x}Mg_x)O_{20}(OH)_4A_x.nH_2O$ (where A is a monovalent cation), which the substitution of Mg/Al in the octahedral sheet produce the negative layered charge [13].

2.4 Properties of clay

2.4.1 Ion exchange

Clay minerals have the ability to adsorb and exchange cations from external solution. In general, the ideal neutral structure is disrupted by introduction of charged imbalance into the clay sheets. The two main causes of charged imbalance are (i) isomorphous substitution of cations by lower valent ions, such as the substitution of Al^{3+} for Si^{4+} in the tetrahedral layer, Mg^{2+} for Al^{3+} or Li^{+} for Mg^{2+} in the octahedral layer, and (ii) crystal defects, usually at the crystallite edges. Leading to, the clay layers have an overall negative charge which is balanced by adsorption of metal cations into the interlayers. These balance cations can be readily replaced by other cations in aqueous solution. In swellable clay minerals such as smectites clay, the interlayer cations can be exchanged with other cations from external aqueous solutions. It was observed that the smaller the size and the higher the charge of the exchange cations, the more powerful that cation is at replacing the interlayer exchangeable cations. Similarly the ease of replacement of interlayer cations follows the reverse trend [8]. The following series can be constructed:

$$M^+ \ll M^{2+} \ll H_2O^+ \approx K^+ \approx NH_4^+ < M^{3+} < M^{4+}$$

$$\xrightarrow{\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad}$$

Increasing exchange power
(Decreasing ease of exchange)

Scheme 2.1 The exchange properties of cations with clays

The cation exchange capacity (CEC) is often measured by uptake and release of ammonium ions from 1 M ammonium acetate solution, although other cations are sometimes used in place of NH_4^+. CEC is usually measured in milliequivalents per 100 gram of dried clay. Smectites clays have relatively high concentration of exchangeable interlayer cations therefore they have the high cation exchange capacities around 70-120 meq/100 g. Structural defects at layer edges give rise to an additional CEC and a small amount of anion exchange capacity [14]. The ion exchange is great important property of clay minerals. In the application of clay mineralogy, it is important because the nature of the exchangeable ion may influence substantially the physical properties of the material.

2.4.2 Swelling

Many clay minerals absorb molecule of water between their layers, which move the layers apart and cause the clay swells. For efficient swelling, the released energy must be sufficient to overcome the attractive forces between the adjacent layers, such as lattice energy and hydrogen bonding from layer solvation. In aqueous solution, hydroxyl groups on octahedral layers of clays forms strong hydrogen bonds with water [14]. The extent of clay swelling can be measured interlayer separations using power X-ray diffraction.

2.4.3 Acidity of clays

Acidity of clays is an important property that make them widely used as catalysts in organic reactions. Their acidic properties and catalytic activity depend on the exchanged cations. Clay minerals have both Brønsted and Lewis acidity. The interlayer cations contribute to the acidity of clay minerals. Some of these cations (*e.g.* Al^{3+}) dissociate their coordinated water molecule to produce acidic proton, which give Brønsted acidity. Being coordinated between an organic compound to cation, the cation is an electron pair acceptor and can act as Lewis acid catalyst [8].

2.5 Intercalation

Intercalation is the insertion of guest species (atoms, molecules, or ions) into the interlayer of clay with preservation of the layered structure. Intercalation compound is proven by the XRD pattern, which must unambiguously show an increase in the spacing between adjacent layers, *i.e.* an increase in the basal spacing [15].

2.6 Pillaring

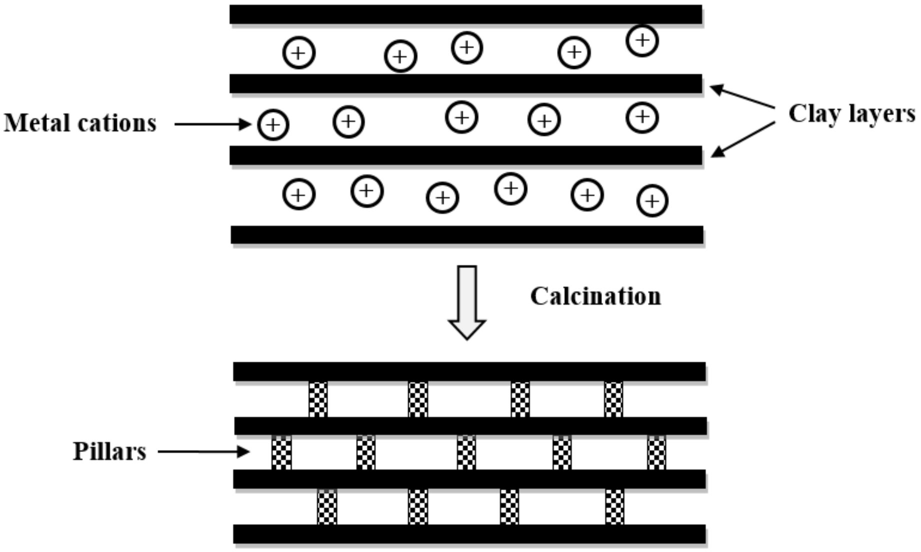
Pillaring is the process by which a layered compound is transformed into a thermally stable microporous and/or mesoporous material with preservation of a parent layer structure. The material obtained is a pillared compound or a pillared layered solid. A pillared derivative is distinguished from an ordinary intercalate by virtue of intracrystalline porosity made possible by the lateral separation of the intercalated guest [15].

2.6.1 Pillaring agent

The pillaring agents are any guest compounds, which could be intercalated between the clay interlayer which maintains the spacing between adjacent layers upon removal of the solvent, and which induces an experimentally observable pore structure between the layers [15].

2.6.2 Pillared clay

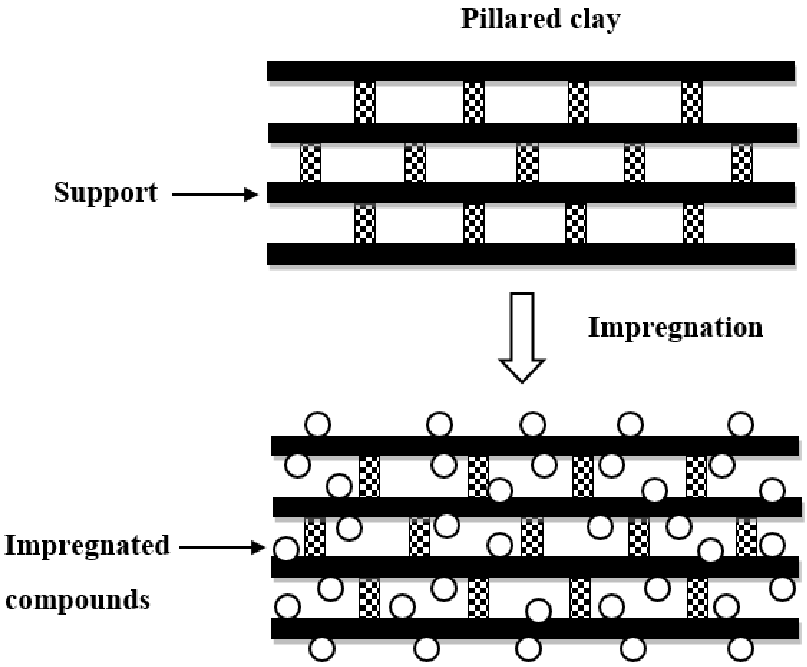
Pillared interlayered clays (PILCs) are microporous materials obtained by the intercalation of guest molecules, which prepared by exchanged cations and polyoxocations into the interlayer of swellable clay, leading to the intercalated clays. Then the intercalated clays are calcined, the polyoxocations are transformed into pillars, leading to the pillared solids. Inorganic oxide-pillared are formed with a permanent separation between the silicate layers. The microporous structure of pillared with high specific surface area and high thermal stability is obtained. Both Lewis and Brønsted acid sites are present. The clay nature (montmorillonite, taeniolite, saponite *etc*) and the intercalating species nature (polycations based on Al^{3+}, Si^{4+}, Zr^{4+}, Ti^{4+}, Fe^{3+}, Cr^{3+} or Ga^{3+}, *etc*) have possibility affected on the pillared solids interesting properties [16, 17]. Different types of pillared clays produce a variety of pore dimensions and catalytic activities. Pillared interlayered clays are very efficient catalysts in various applications. The example of pillared clay compounds is shown in Scheme 2.2.



Scheme 2.2 Diagram for the preparation of pillared clay compounds (cross section)

2.7 Impregnation

Impregnation is a catalyst preparation method by the adsorption of a precursor salt from solution onto a support or porous material. The impregnation method involves three steps: (i) contacting the support with the impregnating solution for a certain period of time, (ii) drying the support to remove the imbibed liquid and (iii) activating the catalyst by calcination, reduction or other appropriate treatment [18]. This method requires less equipment since the forming steps, filtering and washing are needless. The example of impregnated pillared clay is shown in Scheme 2.3.



Scheme 2.3 Diagram for the preparation of impregnated pillared clay (cross section)

2.8 Characterization of clays and clay catalysts

2.8.1 Powder X-ray diffraction (XRD)

X-ray diffraction (XRD) is an important and rapid analytical technique for characterization and identification of crystalline materials. A collimated beam of nearly monochromatic is a type of X-rays beam in this technique. X-rays beam is directed onto the flat surface of a thin layer of ground materials causing the diffracted X-ray to specific angles. The additional information from XRD data can be analyzed for the degree of crystallinity of the minerals present, determined the proportion of the different minerals present, the structural state of the minerals and the degree of hydration for minerals. Fig 2.6 shows a monochromatic beam of X-ray incident on the surface of crystal at an angle θ. The scattered intensity can be measured as a function of scattering angle 2θ [19]. An X-ray diffraction measurement the angle of incidence and detection was scanned. The X-ray diffraction pattern which is the characteristic for the sample material was obtained by plotting of the intensity of detected X-rays as a function of angle. The resulting XRD pattern efficiently determines the different phases present in the sample.

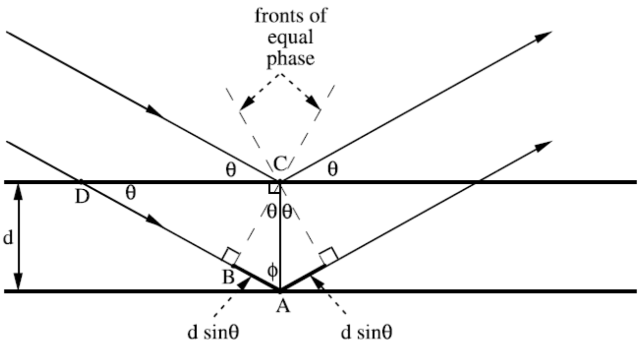


Figure 2.6 Diffraction of X-ray by regular planes of atoms [20]

The general relationship between the wavelength of the incident X-rays, angle of incidence and spacing between the crystal lattice planes of atoms is known as Bragg's Law, manifested as

$$n\lambda = 2\,d\,\sin\theta$$

Where n = an integer of order of the diffracted beam

λ = wavelength of the X-ray

d = a distance between adjacent planes of atoms (d-spacing)

θ = an angle between the incident beam and the scattering planes

Bragg's law is applied to determine the interplanar spacing (d-spacing) of the samples, from diffraction peak according to Bragg angle.

2.8.2 Nitrogen adsorption-desorption isotherm

The N_2 adsorption technique is widely used for the measurement the physical properties of porous materials such as the specific surface area, pore diameter, pore size distribution and pore volume of a variety of different solid materials. An adsorption isotherm can be expressed the adsorption of gas by porous materials. IUPAC classifying gas adsorption isotherms and pore sized have been suggested to indicate the relationship between adsorption and porosity. The adsorption isotherms are divided into six types as shown in Fig 2.7. The Type I isotherm is typical of microporous materials and chemisorption isotherms. Type II is shown by finely divided nonporous materials. Type III is typical of nonporous materials and materials which have the weak interaction between the adsorbate and adsorbent. Type IV and V feature a hysteresis loop generated by the capillary condensation of the adsorbate in the mesopores of the solid. Finally, the rare type VI step-like isotherm is shown by nitrogen adsorbed on homogeneous surface materials.

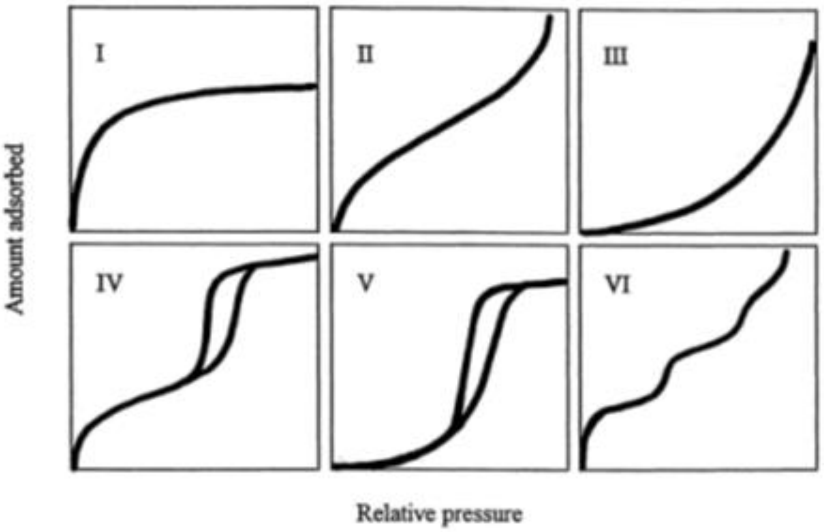


Figure 2.7 Types of adsorption isotherms [21]

Adsorption isotherms are described as shown in Table 2.1 based on the strength of the interaction between the sample surface and gas adsorbate and the existence or absence of pores [22].

Table 2.1 Features of adsorption isotherms

Type	Features	
	Interaction between sample surface and adsorbate	**Porosity**
I	Relatively strong	Micropore
II	Relatively strong	Nonporous
III	Weak	Nonporous
IV	Relatively strong	Mesopore
V	Weak	Micropore or Mesopore
VI	Relatively strong Sample surface has an even distribution of energy	Nonporous

The IUPAC classification of pore types is shown in Table 2.2. The use of nitrogen adsorption/desorption isotherm can be measured the pore size distribution. The classification of pore types are divided into the three types according to their sizes [22, 23].

Table 2.2 IUPAC classification of pores

Pore type	Pore diameter (nm)
Micropore	Up to 2
Mesopore	2 to 50
Macropore	50 or up

The multipoint Brunauer, Emmett and Teller (BET) method is commonly used to measure the total surface area. Thus, analogously to the Langmuir isotherm obtains the BET isotherm:

$$\frac{1}{W[(P_0/P)-1]} = \frac{1}{W_m C} + \frac{C-1}{W_m C}\left(\frac{P}{P_0}\right)$$

Where W = weight of nitrogen adsorbed at a given P/P_0

W_m = weight of gas to give monolayer coverage

C = a constants that is related to the heat of adsorption

P = the equilibrium pressure

P_0 = the saturation pressure

A linear relationship between $1/W[(P/P_0)-1]$ and P/P_0 is required to obtain the quantity of nitrogen adsorbed. The slope and intercept are used to determine the quantity of nitrogen adsorbed in the monolayer and calculate the surface area. For a single point method, the intercept is taken as zero or a small positive value. The surface area could be calculated from the slope of BET plot [22].

2.8.3 Temperature programmed desorption (TPD) of ammonia

Temperature programmed desorption of ammonia is the most widely used technique to feature the acidic properties of solid catalysts providing useful information on both the concentration and strength of acid sites. The acid-site concentration can be presented by the amount of ammonia desorbing above some characteristic temperature. The acidity of clay samples has been measured by adsorption-desorption of ammonia. Desorption temperature of the ammonia molecule can be related to the strength of the acidity of the materials tested. The ammonia adsorbed on the acid site require a different thermal energy level to break the bond and desorb, resulting in distinct peaks on the plot of the TCD output signal vs. temperature. Consequently, the maximum temperature in the ammonia desorption process is a qualitative indication of the strength of acid sites [24].

Principle of the measurement

TPD is the technique to measure the status of physical adsorption and chemisorptions. It can be obtained by measuring desorption of the decomposition of adsorption molecules from the surface while continually heated. TPD can determine the number of desorption peaks (type of adsorption active sites) from the spectrum of desorbed molecules, desorption temperature (activation energy of desorption), and volume of desorption (number of adsorption active sites).

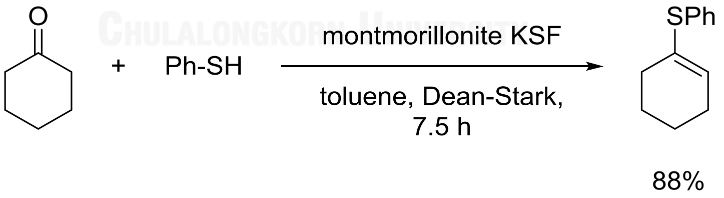
Although the condition of measurement varies the ambient pressure, desorption measurement can be basically done by heating under the carrier gas flow. Desorbed gas can be detected by Thermal Conductivity Detector (TCD) or mass analyzer (Q-mass) [24].

2.9 Literature reviews on clay catalysts

Numerous organic reactions use clays as efficient catalysts. Clay minerals and modified clays have been exploited for catalytic applications. Several methods have been used to modify the surface and structure of clay minerals to increase the catalytic activity. Clay catalysts offer many advantages over classical homogeneous catalysts, such as the strong acidity, non-corrosive properties, mild reaction conditions, high yields and selectivity, shorter reaction time, simple workup, recovery and reusability of the catalysts. A wide range of reactions were successfully carried out utilizing clay catalysts including protection-deprotection reactions, Michael addition, alkylation, acylation, aldol formation, condensation, oxidation of alcohols, epoxidation, esterification, cyclization, rearrangement/isomerization, synthesis of heterocycles.

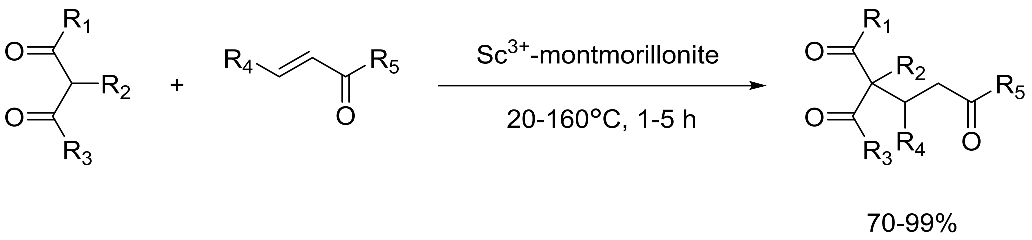
Protection-deprotection reactions

The conversion of the cyclic ketones to the enol thioethers could be catalyzed by montmorillonite KSF. This catalytic method was performed efficiently to avoid multiple steps, corrosive Lewis acids, or moisture-sensitive anhydrides as reagents. The phenyl vinyl sulfides were obtained from the cyclic ketones in high yields (86-88%) [25].



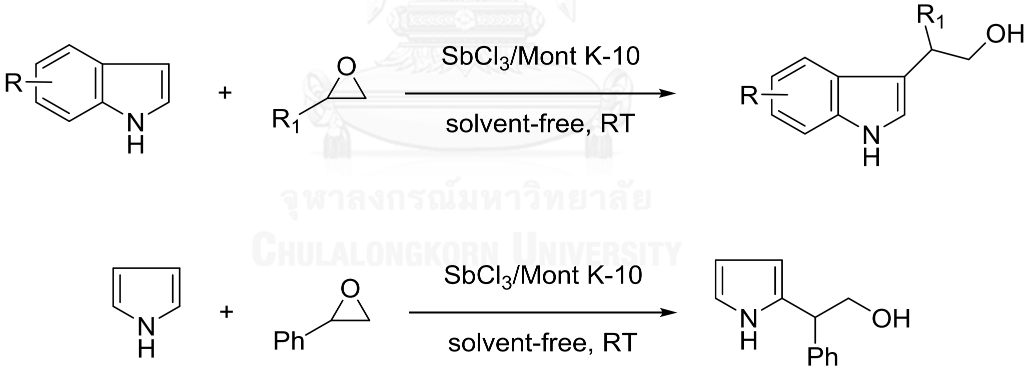
Michael addition

The Sc^{3+}-exchanged montmorillonite was showed to function as a highly active catalyst for the Michael reaction of 1,3-dicarbonyl compounds with enones under solvent-free conditions. Methyl vinyl ketone and other enones readily reacted with a variety of β-keto esters and 1,3-diketones to furnish the corresponding 1,5-dioxo compounds in high yields (70-99%) [26].



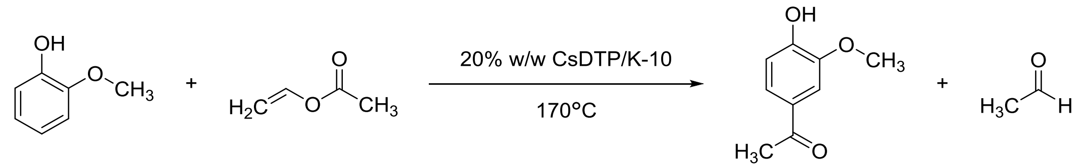
Alkylation

Friedel-Crafts alkylation of nitrogen heterocycles such as indoles and pyrroles with epoxides could be promoted by using $SbCl_3$/montmorillonite K-10 at room temperature under solvent-free conditions. The corresponding C-alkylated derivatives were obtained in good yields (30-90%) with a high regioselectivity. This procedure provided mild reaction conditions, short reaction times, wide applicability, and recyclability of catalyst [27].



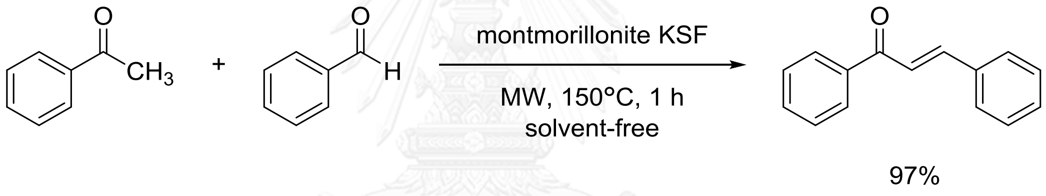
Acylation

The 20% w/w cesium modified dodecatungstophosphoric acid supported on K-10 clay (CsDTP/K-10) was found to be a very active and highly efficient catalyst for the Friedel–Crafts acylation of guaiacol with vinyl acetate. The acetovanillone product was furnished with 97% conversion. This catalyst could be reused at least three times [28].



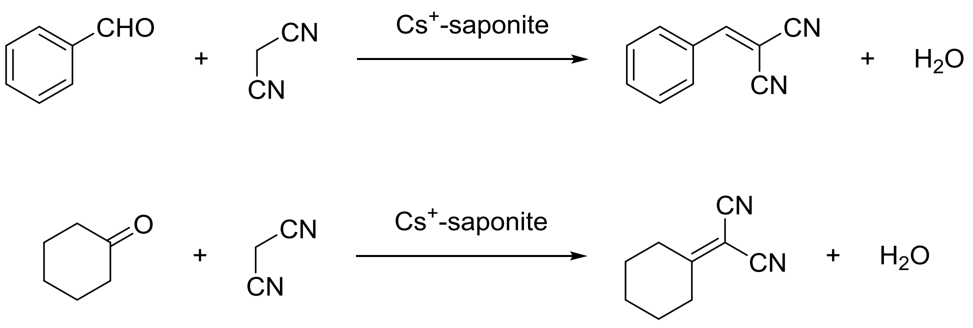
Aldol formation

The microwave-assisted method was developed for aldol condensation of acetophenone and benzaldehyde catalyzed by the acidic clay montmorillonite KSF. Chalcone was afford in excellent yield (97%) under the optimal conditions. A variety of aryl methyl ketones and aromatic aldehydes could proceeded smoothly in this method producing aryl and heteroaryl *trans*-chalcones. The good to excellent yields were obtained (43-97%) [29].



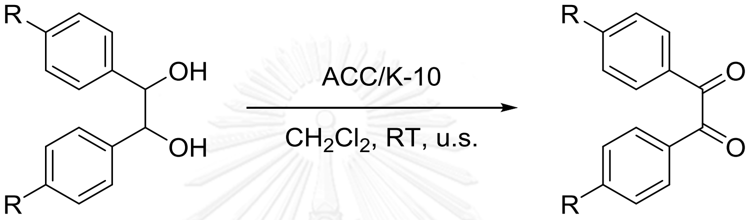
Condensation

Knoevenagel condensation of benzaldehyde or cyclohexanone with malononitrile were carried out employing Li$^+$- and Cs$^+$-exchanged saponites as catalysts. When the reaction is activated by ultrasound, the conversion values were increased as compared with the thermal activation. α,β-Unsaturated nitriles were produced in excellent yields (97%) when the Cs$^+$-saponite was used as catalyst [30].



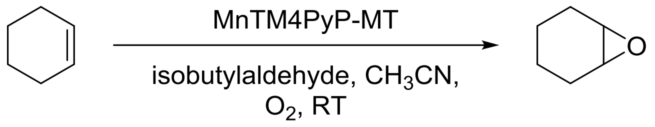
Oxidation

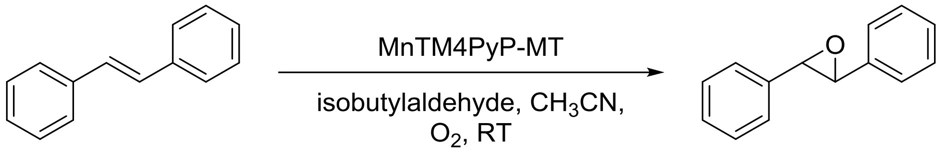
The oxidation of hydrobenzoins was performed by utilizing ammonium chlorochromate (ACC) supported on montmorillonite K10 in CH_2Cl_2 at room temperature under ultrasound irradiation. The corresponding benzils were obtained in excellent yield (88-96%). However, the oxidation of benzoin by ACC/K-10 was completed in 96% yield within 2 h under ultrasound irradiation [31].

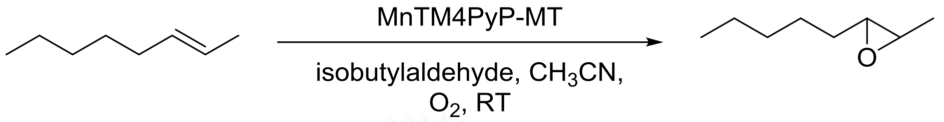


Epoxidation

The aerobic epoxidation of olefins could be catalyzed by cationic *meso*-tetrakis-(1-methyl-4-pyridyl) (TM4PyP) metalloporphyrins immobilized into montmorillonite (MT) interlayer. Manganese porphyrin (MnTM4PyP-MT) showed excellent activity and selectivity for the aerobic epoxidation of olefins under ambient conditions. The 80-98% yields of epoxides were obtained. The basal spacing of clay played significant role in the catalytic efficiency and selectivity for different olefins. The supported catalyst could be reused continuously five times without significant decrease in the catalytic activity [32].

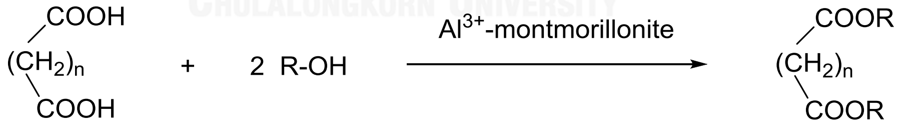






Esterification

Montmorillonite clay exchanged with Al^{3+} was found to be an active catalyst for the esterification of dicarboxylic acids with various alcohols and phenols. The esterification of dicarboxylic acids namely malonic, maleic, succinic, adipic and phthalic acid with simple alcohols, and phenols were carried out to produce the corresponding diesters. The good to excellent yields of esters were obtained under mild reaction conditions [33].



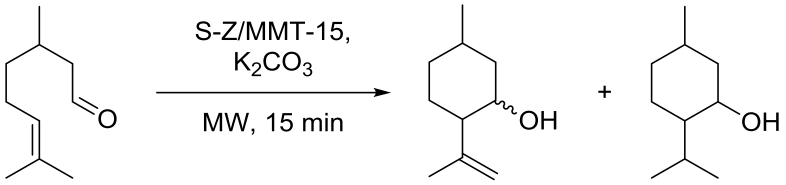
$$(CH_2)_n(COOH)_2 + 2\ R\text{-}OH \xrightarrow{Al^{3+}\text{-montmorillonite}} (CH_2)_n(COOR)_2$$

n = 1, 2 and 4

R = C_2H_5, n-C_3H_7, n-C_4H_9, i-C_4H_9, t-C_4H_9, C_6H_5 and p-$CH_3C_6H_4$

Cyclization

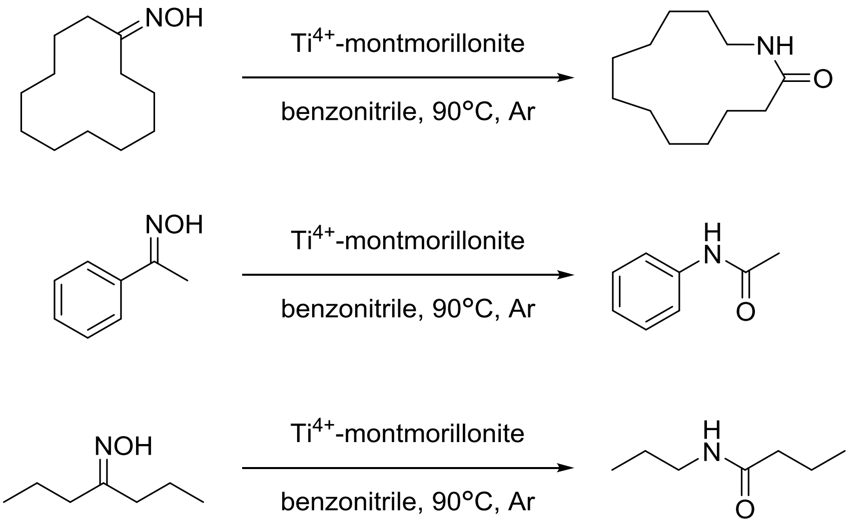
Sulfated zirconia-pillared montmorillonite (S-Zr/MMT-15) could promoted high catalytic activity for citronellal cyclization. The reactions were performed using microwave irradiation for 15 minutes.



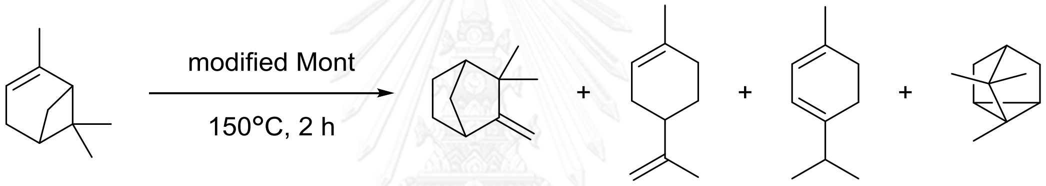
A total conversion of citronellal of 98.5% was obtained with 85% selectivity of isopulegol and 15% selectivity of menthol. The synergistic effect of sulfate acid sites and zirconium atoms and the larger specific surface area within the catalyst probably leads to the improvement of catalytic activity. While Zr/MMT-15 exhibits lower conversion compared to S-Zr/MMT-15, but the higher selectivity of isopulegol product was obtained as 100% [34].

Rearrangement/isomerization

Ti^{4+}-exchanged montmorillonite was used as a highly active catalyst for the Beckmann rearrangement under mild reaction conditions. Various ketoximes including alicyclic, aromatic, and aliphatic ketoximes were transformed into the corresponding lactams and amides in high yields (44-98%). The Ti^{4+}-montmorillonite was simply recovered and could be reused with retention of its efficiency [35].

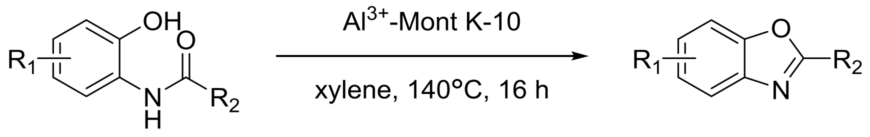


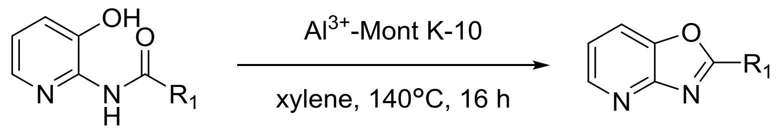
Some of the isomerised products are industrially valuable chemicals. For instance, camphene is used as an intermediate in camphor synthesis. Consequently, specific catalyst modifications were examined to improve selectivity to the desired isomer. The isomerisation of α-pinene with montmorillonite modified by sulphuric acid (1-9N) treatment shows α-pinene conversion of 85-100% with selectivity of 41-49% for camphene. Among monocyclic terpene products, low normality acid (1-4N) treated clays gave limonene as the main product, whereas high normality acid (5-9N) treated clays gave α-terpinene as a main product. Montmorillonite exchanged with Ce^{3+}, Fe^{3+}, La^{3+}, and Ag^{+} showed higher than 93% conversion for α-pinene with 47-49% selectivity for camphene. However, alkaline earth cations, Ca^{2+}, Mg^{2+} exchanged clay showed poor conversion (4-12%) and Li^{+} showed 47% conversion for α-pinene [36].



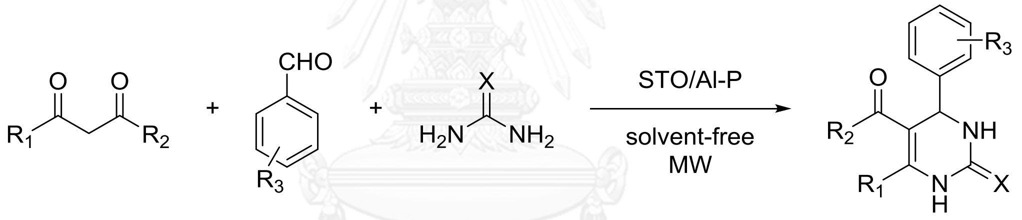
Synthesis of heterocycles

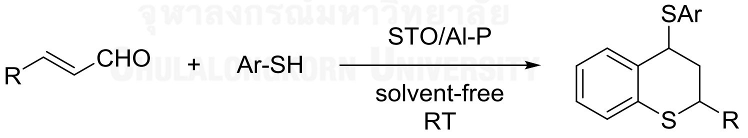
An efficient and green method for the synthesis of 2-substituted benzoxazole derivatives through N–C–O bond formation was developed using Al^{3+}-exchanged K10 clay (Al^{3+}-K10) as catalyst under mild reaction conditions. A wide range of benzoxazole derivatives were synthesized in high yields (61-98%) without affecting many functional groups. The catalyst could be reused for five times with only a slight decrease in yield. This catalytic system could be applied for the synthesis of 2-substituted oxazolopyridines from the corresponding amides. The high yields of 71-90% were observed [37].

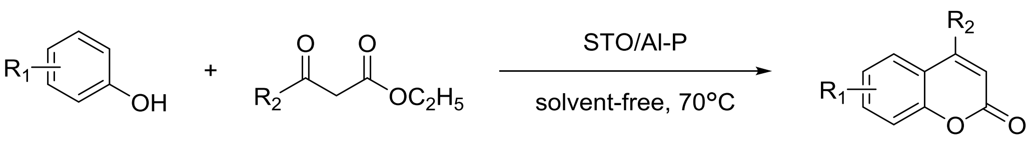




Nanosize sulfated tin oxide dispersed in the micropores of Al-pillared montmorillonite was demonstrated as an efficient catalyst for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones, thiochromans and coumarins. This method developed using the nanosize catalyst offer simple procedure, short reaction time, solvent-free conditions, catalyst reusability, high yield and purity of the products [38].







Clay or modified clay catalysts were accomplished in utilizing for a wide range of reactions. Montmorillonite or modified was the clay used in most of the applications as described above due to its commercial availability and possibility in designing. The development of new catalysts and/or the improvement in their properties for organic reactions and industrial production interest were the prospects for future.

2.10 The goal of this research

The goal of this research could be summarized as

1. To synthesize metal oxide-pillared clays and metal chloride-impregnated metal oxide-pillared clay catalysts for the acid-catalyzed reactions (the synthesis of coumarins, isomerization of epoxides and synthesis of acetonides from epoxides) and the alkylcarboxylate anion-intercalated NiZn catalyst for Michael reaction.
2. To study the optimum conditions for the acid-catalyzed reactions (the synthesis of coumarins, isomerization of epoxides and synthesis of acetonides from epoxides) by using synthesized metal oxide-pillared clays and the optimum conditions for Michael reaction by using the alkylcarboxylate anion-intercalated NiZn catalysts.
3. To apply the optimum conditions for the synthesis of coumarins, isomerization of epoxides, synthesis of acetonides from epoxides and Michael reaction.

2.11 Experimental

2.11.1 Instrument, equipments and analytical measurement

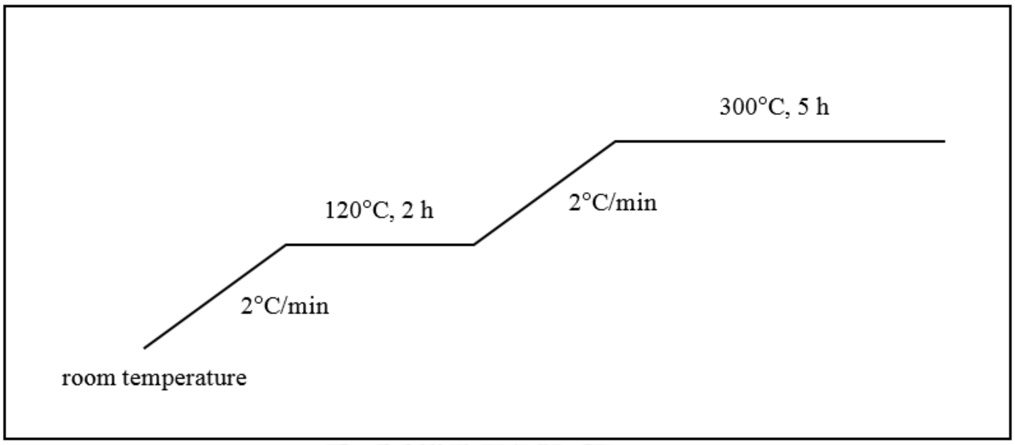
2.11.1.1 Centrifuge

The collection of the synthesized catalysts and the purification of clays were processed by Centurion Scientific C2 Series centrifuge. Clays was purified by removing quartz and other impurities from the centrifugation process.

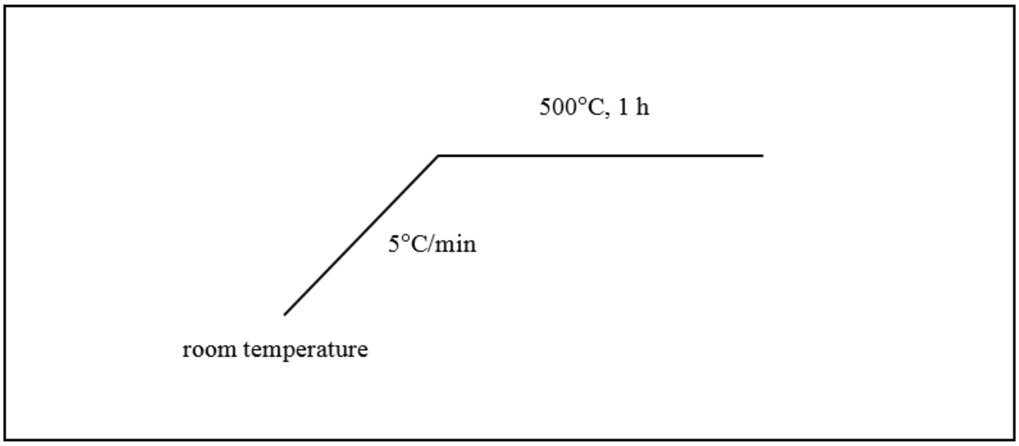
2.11.1.2 Oven and furnace

Raw clays and all synthesized catalysts were dried in a Memmert UM-500 oven at 100°C. The calcination was performed on a carbolite RHF 1600 muffle furnace in air.

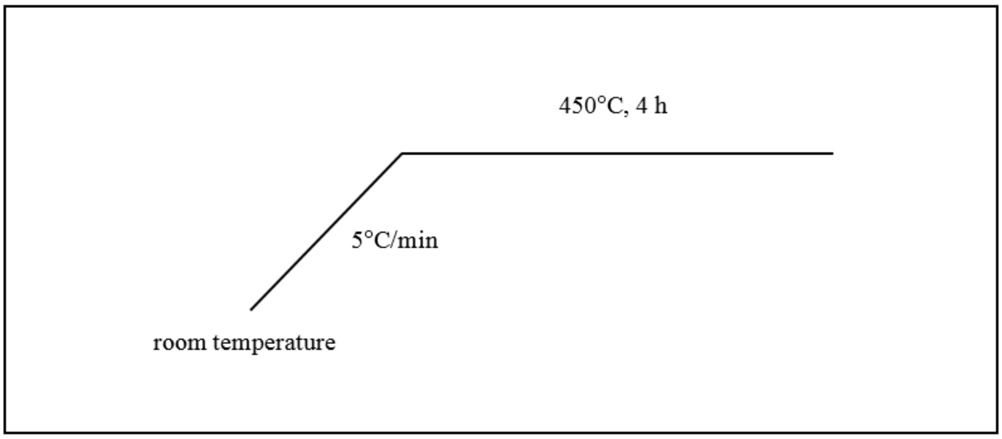
The calcination of the synthetic clay catalysts was performed to convert metal precursors in the interlayer of clays into metal oxides. The heating program used for the calcination of synthesized catalysts is shown in Scheme 2.4-2.6.



Scheme 2.4 The heating program used for the calcination of synthesized Fe- and Cr-pillared clay catalysts



Scheme 2.5 The heating program used for the calcination of synthesized Al-pillared clay catalysts



Scheme 2.6 The heating program used for the calcination of synthesized metal chloride impregnated Al-pillared clay catalysts

2.11.1.3 X-ray diffractometer (XRD)

The XRD patterns and consequence the basal spacings of catalysts (raw clays, synthetic clay catalysts) were determined using a Rigaku, Dmax 2200/utima+ X-ray powder diffractometer (XRD) with a monochromater and Cu Kα radiation (40 Kv, 30 mA). The 2-theta angle was ranged from 2 to 30 degree with scan speed of 3 degree/min and scan step of 0.02 degree. The scattering slit, divergent slit and receiving slit were fixed at 0.5 degree, 0.5 degree and 0.15 mm, respectively.

2.11.1.4 Nitrogen adsorption-desorption (Brunauer, Emmett and Teller method, BET)

The BET specific surface area of raw clays and all synthesized catalysts were measured by the Quantachrome Autosorb-1 nitrogen adsorptometer.

2.11.1.5 Temperature Programmed Desorption (TPD) of Ammonia

The NH_3-TPD of raw clays and all synthesized catalysts were measured by the BEL Japan, BELCAT.

2.11.2 Starting materials

Bentonite clay was kindly supported by Cernic International Co., Ltd. The chemical compositions of bentonite are displayed in Table 2.3.

Table 2.3 The chemical compositions of bentonite

Compositions	Bentonite[a]
SiO_2	63.60
Al_2O_3	17.60
MgO	-
K_2O	0.50
Fe_2O_3	3.10
CaO	3.00
Na_2O	3.40
FeO	-

[a] information from Cernic International Co., Ltd.

2.11.3 Homoionic clays

Homoionic clays were prepared by purification and then ion exchange following the previous work by Kanjanaboonmalert [39].

2.11.3.1 Purification of bentonite

Bentonite was purified by fractionated sedimentation. 30 g of raw bentonite were dispersed in 1,000 mL of deionized water under vigorous stirring at room temperature for 3 h. The colloid clay was centrifuged at 3,700 rpm for 10 min, after that quartz sediments could be separated. The colloid bentonite was collected and dried at 100°C. The purified bentonite as montmorillonite was characterized by XRD technique.

2.11.3.2 Na-ion exchange

Na-montmorillonite were prepared by cation exchange. Na-ions were intercalated between the clay layers. Montmorillonite was suspended in 5 M NaOH with the ratio of clay to NaOH-solution as 1 g: 50 mL at room temperature for 24 h. The Na-exchanged clay was collected by centrifugation, after that repeated the above exchanged process three times. Then Na-exchanged clay sediments were dialyzed with deionized water using cellulose tubing (Seamless Cellulose Tubing, small size 30, Wako chemical USA). Dialysis was continued, with water being renewed until hydroxide anions were eliminated. Finally, the Na-exchanged clay was dried at 100°C for a day. The Na-montmorillonite was characterized using XRD technique.

2.11.4 Synthesis of metal oxide-pillared clays

2.11.4.1 Synthesis of iron oxide-pillared clay

Iron oxide-pillared clay (Fe-pillared clay) was synthesized according to Kanjanaboonmalert [39] by intercalation of iron precursors, following by calcinations at high temperature. Na-clays were dispersed in deionized water (10% w/w) by vigorous stirring for 1 day at room temperature. Then 1 M $FeCl_3$ solution, by the ratio of Fe^{3+} to clay of 10 meq per gram, was slowly added in the suspended Na-clay under stirring at room temperature for 24 h. The products were collected by centrifugation and then washed with deionized water until chloride ions were eliminated. The synthesized Fe-intercalated montmorillonite was dried at 100°C for a few days and followed by calcined at 300°C for 5 h in a muffle furnace. The calcined products were designated as Fe-PLM. The obtained Fe-PLM was characterized using XRD technique.

2.11.4.2 Synthesis of aluminium oxide-pillared clay

2 g of Na-montmorillonite was dispersed in 100 mL of deionized water under stirring at room temperature for 48 h. The Al-pillaring agent was prepared by adding 0.2 M NaOH to 0.2 M $AlCl_3$ with the ratio of OH/Al was 1.9 and stirring at room temperature for 24 h. The Al-pillaring agent was then slowly added to the prepared clay suspension with the ratio of Al/clay of 3.8 mol/kg. The mixture was stirred at room temperature for 24 h. After that, the precipitates were collected by centrifugation at 3,700 rpm and washed with distilled water until free of chloride ion. The synthesized Al-intercalated montmorillonite was dried at 100°C for a few days, followed by calcined at 500°C for 1 h in a muffle furnace. The obtained Al-PLM were characterized using XRD technique.

2.11.4.3 Synthesis of chromium oxide-pillared clay

Cr-pillared montmorillonite was obtained according to the method reported by Yurdakoç and co-workers [40] with some modifications. $CrCl_3 \cdot 6\ H_2O$ (2.665 g) was dissolved in 100 mL of distilled water. Na_2CO_3 (0.011 g) was added to the solution of $CrCl_3$ at room temperature. This solution was then aged at 95°C under reflux for 40 h. At the same time, 2 g of montmorillonite was suspended with 100 mL of distilled water. Afterwards, the montmorillonite suspension and the hydrolyzed chromium solution were mixed while the former solution was still warm and then the mixture was stirred for 24 h. The Cr-pillared montmorillonite suspension was then collected by centrifugation, and washed with deionized water until chloride ions were eliminated. The synthesized Cr-intercalated montmorillonite was dried at 100°C and followed by calcinated at 300°C for 5 h. The calcined products were designated as Cr-PLM. The obtained Cr-PLM was characterized using XRD technique.

2.11.5 Synthesis of metal chloride-impregnated metal oxide-pillared clays

Metal trichlorides including $CrCl_3$ or $NdCl_3$ impregnated metal oxide-pillared clays were synthesized by the following method reported by Masaleh [41]. The metal oxide-pillared clay was impregnated using a solution of 2% metal trichloride in EtOH.

The slurry mixture was dried at 60°C. The impregnated Al-PLM was calcined with the rate of 5°C /min and holding at 450°C for 4 h. In the case of the impregnated Fe-PLM was calcined with the rate of 2°C /min and holding at 300°C for 5 h. The products were named as MCl_3/M-PLM. The obtained products were characterized using XRD technique.

2.12 Results and discussion

2.12.1 X-ray diffraction (XRD)

Clay mineral (bentonite) was characterized by X-ray diffraction (XRD). This technique was used to investigate the changes of clay structure, emphasizing on a basal spacing and the intensity of d_{001} reflection.

2.12.1.1 The characterization of raw bentonite

Bentonite is a phyllosilicate mineral species, impure clay consisting mostly of montmorillonite with impurities such as quartz, feldspars, crystobalite and humic acids. The major impurity of clay minerals is quartz that reduced surface area and acidic site of clays, which diminish the catalytic efficiency. The characteristic structures of raw clay was characterized by XRD technique. The X-ray diffraction patterns of raw bentonite was analyzed as displayed in Figure 2.8.

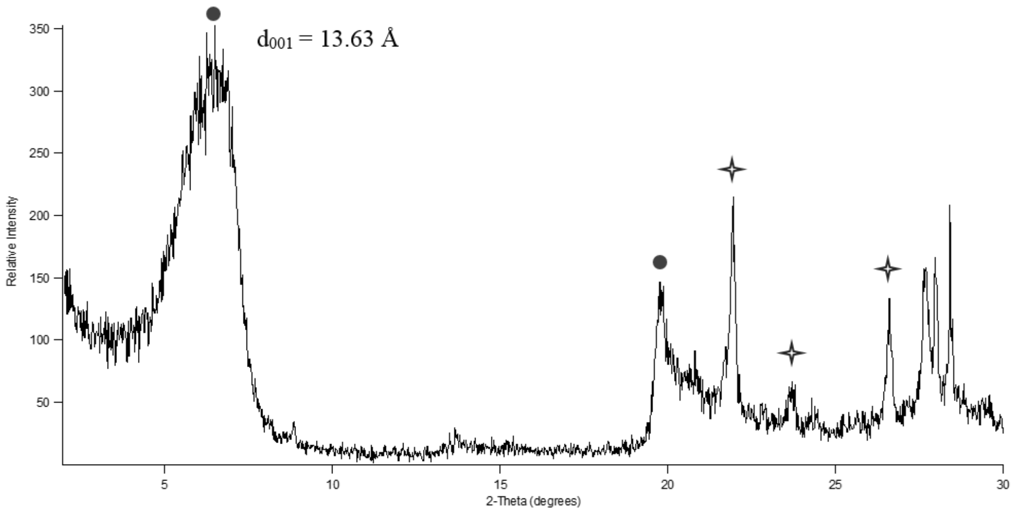


Figure 2.8 XRD patterns of raw bentonite

(● represents montmorillonite peaks and ✦ represents impurity quartz peak)

As displayed in Fig 2.8, the characteristic peak of montmorillonite was observed at 2θ of 6° and 19° corresponding to the 001 and 100 planes of montmorillonite, respectively [42]. The d_{001} basal spacing of raw bentonite is 13.63 Å. The peaks at 2θ of 22°, 24° and 27° were revealed the presence of quartz (SiO_2).

2.12.1.2 The characterization of purified bentonite

Montmorillonite contains as main constituent in bentonite with some other impurities. Dispersion and centrifugation processes could remove these impurities from raw bentonite. The X-ray diffraction patterns of raw bentonite and purified bentonite (montmorillonite) were shown in Figure 2.9. The quartz peak at 2θ of 22°, 24° and 27° were missing in the XRD patterns of purified bentonite. The quartz peak vanished after the centrifugation process. It could be demonstrated that quartz and other impurities were removed from raw bentonite, only montmorillonite was still remained. The structure of montmorillonite clay confirmed by the (001) peak was displayed at the 2θ of 6.9° corresponding to the d_{001} basal spacing of 12.80 Å.

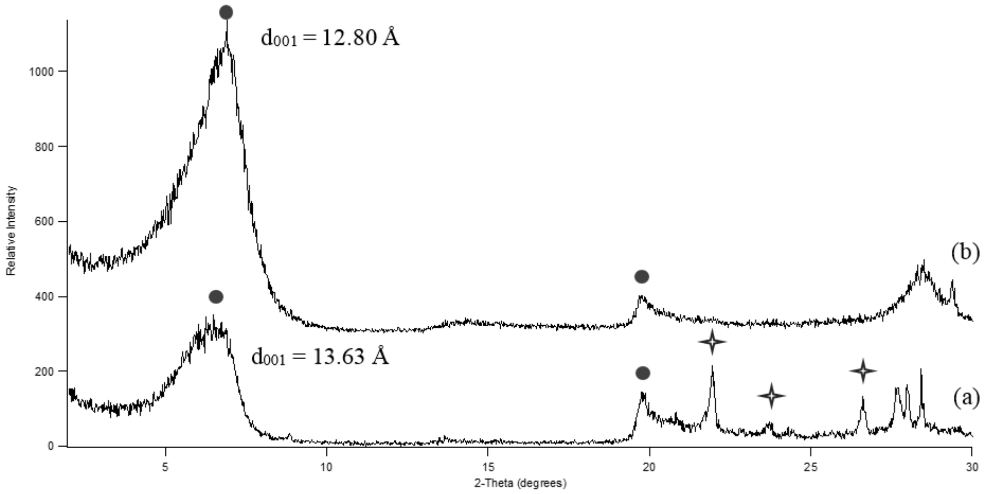


Figure 2.9 XRD patterns of (a) raw bentonite and (b) purified bentonite (montmorillonite)

(● represents montmorillonite peaks and ✦ represents impurity quartz peak)

2.12.1.3 The characterization of homoionic montmorillonite

Homoionic montmorillonite was prepared by ion-exchange process after purification to remove quartz and other impurities by centrifugation. The Na ions were intercalated between clay layers in order to provide homoionic montmorillonite as the starting material for synthesized clay catalysts. A net negative charges on clay layers was balanced by interlayer cations such as Na, K and Ca ions that occupied intercalated positions between the interlayers. The predominant exchangeable cation in the clay swelling is sodium ion owing to the large solvation energy (98 kcal/mol) [43] and its small electrostatic interaction between monovalent cation and negatively charged layer.

Na ions were intercalated between the clay layers by treating with 5 M NaOH for three times, and the obtained clay was designated as Na-montmorillonite. The XRD patterns of Na-montmorillonite and montmorillonite were displayed in Fig 2.10. Na-montmorillonite showed the d_{001} basal spacing of 14.77 Å which was increased from untreated montmorillonite, indicating that Na ions intercalate into the clay layers.

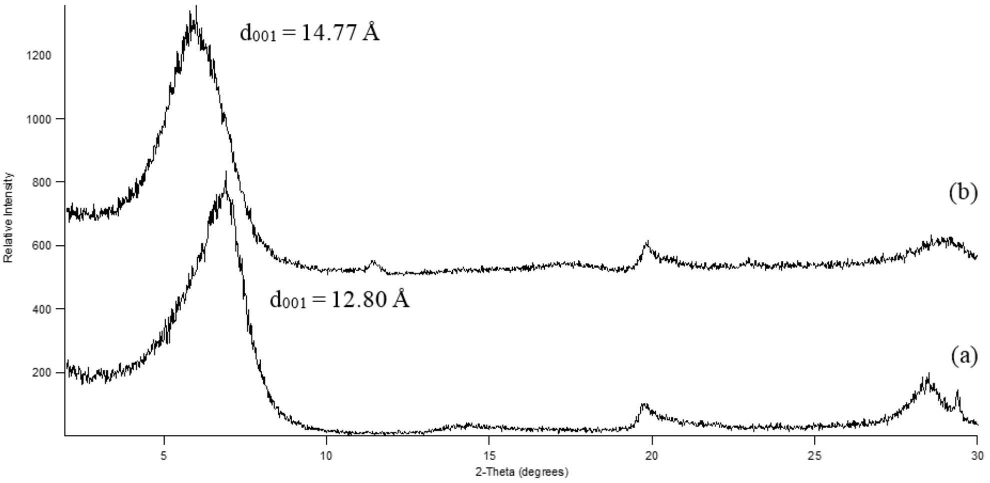


Figure 2.10 XRD patterns of (a) montmorillonite and (b) Na-montmorillonite

2.12.1.4 The characterization of metal oxide-pillared montmorillonite

Iron oxide-pillared montmorillonite, aluminium oxide-pillared montmorillonite and chromium oxide-pillared montmorillonite were synthesized by intercalation of iron, aluminium or chromium precursors between the clay layers, then follow by calcination at high temperature. Iron oxide-pillared montmorillonite (Fe-PLM), aluminium oxide-pillared montmorillonite (Al-PLM) and chromium oxide-pillared montmorillonite (Cr-PLM) were prepared. Fe-PLM was reddish brown solid, Al-PLM was light brown solid and Cr-PLM was dark yellowish green solid. The X-ray diffraction patterns of Fe-PLM, Al-PLM and Cr-PLM were shown in Fig 2.11.

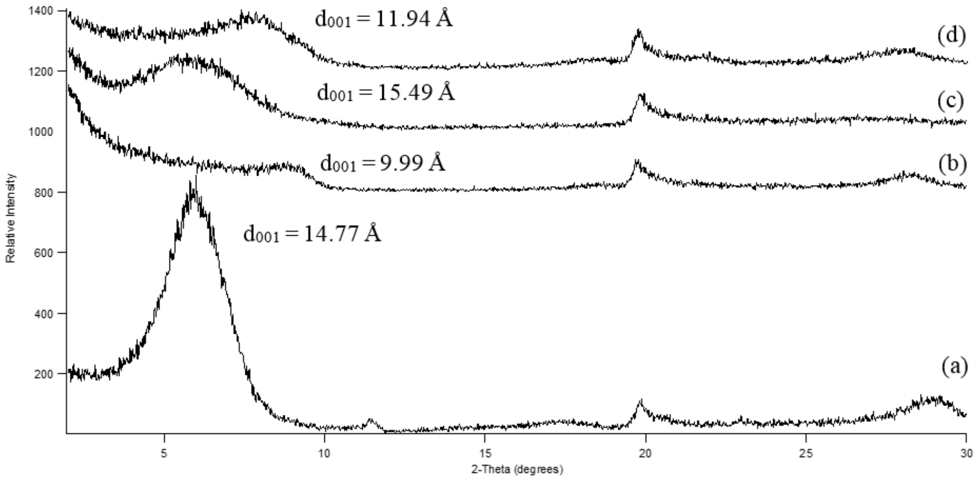


Figure 2.11 XRD patterns of (a) Na-montmorillonite (b) Fe-PLM (c) Al-PLM and (d) Cr-PLM

The XRD patterns of Fe-PLM showed the d_{001} basal spacing of 9.99 Å as a broad peak and smaller d-spacing compared with that of Na-montmorillonite. The intercalated iron precursors were transformed to iron oxide during the calcination at 300°C for 5 h. Since the adsorbed water molecule between clay layers was eliminated and dehydroxylation of the clay was occurred. The low d-spacing was detected because the intercalation of small iron precursor cluster [39]. In Al-PLM case, the d_{001} basal spacing of 15.49 Å was detected as a broad peak and higher intensity. The 2θ peak of Al-PLM shifted slightly to lower angle as compared with that of Na-montmorillonite which revealed that the aluminium polyoxocations $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}$ were exchanged with the sodium ions in the interlayer of montmorillonite [44]. The aluminium polyoxocations were converted to the rigid aluminium oxide-pillar during the calcination. The oxide-pillar solidly bound to the clay layer, increased the collapse within interlayer space of clay structure which led to the broader peak with lower intensity. The XRD patterns of Cr-PLM shown a broad d_{001} basal spacing peak of 11.94 Å with lower d-spacing compared to those of Na-montmorillonite. Due to the elimination of adsorbed water molecule between clay layers and dehydroxylation of chromium intercalated montmorillonite was taken place after calcination to form polymeric chromium oxide species. The intercalation of small Cr_2O_3 cluster led to the low d-spacing.

2.12.1.5 The characterization of metal chloride impregnated Al-pillared montmorillonite

$NdCl_3$ impregnated Al-pillared clays were synthesized by using a solution of 2% $NdCl_3$ in EtOH. The XRD patterns of neodymium(III) chloride impregnated Al-pillared montmorillonite ($NdCl_3$/Al-PLM) was compared with those of Al-pillared montmorillonite as displayed in Fig 2.12. The d_{001} basal spacing of $NdCl_3$/Al-PLM was 14.02 Å which was slightly lower than that of Al-PLM. Nevertheless, the d_{001} peak was broader with lower intensity, because of the metal chloride impregnation increased the disordering between the clay interlayer space and the recalcination process led to the structure of pillared collapse slightly.

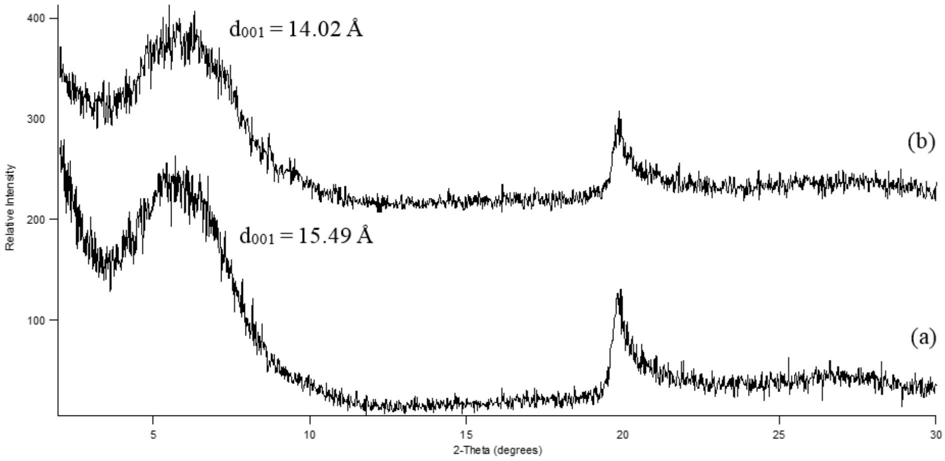


Figure 2.12 XRD patterns of (a) Al-PLM and (b) $NdCl_3$/Al-PLM

2.12.1.6 The characterization of metal chloride impregnated Fe-pillared montmorillonite

$CrCl_3$ and $NdCl_3$ impregnated Fe-pillared clays were synthesized by method as previously described for Al-PLM, but vary percent of metal chloride. The XRD patterns of metal(III) chloride impregnated Fe-pillared montmorillonite ($CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM) were compared with those of Fe-pillared montmorillonite as shown in Fig 2.13.

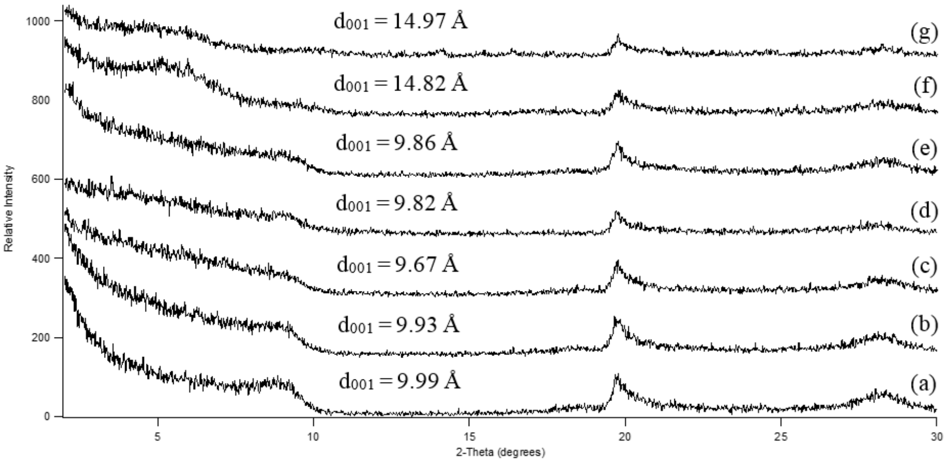


Figure 2.13 XRD patterns of (a) Fe-PLM (b) 2%$CrCl_3$/Fe-PLM (c) 5%$CrCl_3$/Fe-PLM (d) 10%$CrCl_3$/Fe-PLM (e) 2%$NdCl_3$/Fe-PLM (f) 5%$NdCl_3$/Fe-PLM and (g) 10%$NdCl_3$/Fe-PLM

In Fig 2.13, the d_{001} basal spacing of chromium chloride impregnated Fe-pillared montmorillonite series (2-10%$CrCl_3$/Fe-PLM) were approximately 9.67-9.93 Å which were slightly lower than that of Fe-PLM. The d_{001} peaks of 5% or 10% $CrCl_3$ impregnated Fe-PLM were found with lower intensity. It could indicate that the metal chloride impregnation increased the disordering between the clay interlayer space. The d_{001} basal spacing of 2% $NdCl_3$ impregnated Fe-pillared montmorillonite (2%$NdCl_3$/Fe-PLM) was 9.86 Å with low intensity. In the case of 5% and 10% $NdCl_3$ impregnated Fe-PLM, the d_{001} peak shifted to lower angle, increasing in the clay interlayer. Due to the high percentage of $NdCl_3$ impregnation caused the intercalation of polymeric neodymium species into the clay interlayer led to the higher interlayer space.

2.12.2 Temperature Programmed Desorption (TPD)

NH_3-TPD is one of the most widely used methods for measuring the surface acidity of porous materials. The total acidity values of synthesized clay catalysts were determined from the amount of ammonia desorbed. The two different peaks of temperature desorption ranges were observed around 200 and 600°C. Owing to the adsorption-desorption of ammonia on weak and strong acid sites. The total amount of acidity (mmol/g) of montmorillonite, Na-montmorillonite, Fe-PLM, Al-PLM, Cr-PLM and metal chloride impregnated pillared montmorillonite ($NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM) are displayed in Table 2.4.

Table 2.4 The total amount of acidity of synthesized clay catalysts

Entry	Samples	Acidity (mmol/g)		Total amount of acidity (mmol/g)
		Weak acid sites	Strong acid sites	
1	Montmorillonite	0.000	1.188	1.188
2	Na-montmorillonite	0.000	1.357	1.357
3	Fe-PLM	0.222	1.529	1.751
4	Al-PLM	0.392	1.223	1.615
5	2%$NdCl_3$/Al-PLM	0.374	1.377	1.751
6	Cr-PLM	0.126	1.913	2.039
7	2%$CrCl_3$/ Fe-PLM	0.089	1.221	1.310
8	2%$NdCl_3$/ Fe-PLM	0.139	1.219	1.358
9	5%$CrCl_3$/ Fe-PLM	0.251	1.344	1.595
10	5%$NdCl_3$/ Fe-PLM	0.306	1.046	1.352

From table 2.4, the acidity of all synthesized clay catalysts were higher than the untreated montmorillonite. The maximum acidity (2.039 mmol/g) for Cr-PLM and the second of 1.751 mmol/g for Fe-PLM and 2%$NdCl_3$/Al-PLM. The acidity of pillared clays derives from either Brønsted or Lewis acid site. Weak acid site supposed to be associated with the coordination of water molecule with metal in pillars, while strong acid site is ascribed to the metal oxide in pillars. The nature and strength of acid site were related to the types of clays and pillared species. The increase in total acidity of various synthesized metal oxide- and impregnated metal oxide-pillared clays compared to those of the untreated montmorillonite as a result of the pillaring process.

In the case of the impregnated clays, $NdCl_3$ impregnated Al-pillared clay showed slightly increasing in acidity of 1.751 mmol/g from 1.615 mmol/g (for Al-PLM). Nevertheless, $CrCl_3$ and $NdCl_3$ impregnated Fe-pillared montmorillonite clays showed significant diminish in acidities due to the surface acidic sites were blocked and major portion was covered by metal chloride species [45, 46].

2.12.3 Nitrogen adsorption-desorption (Brunauer, Emmett and Teller method, BET)

The BET specific surface area of montmorillonite, Na-montmorillonite, Fe-PLM, Al-PLM, Cr-PLM and metal chloride impregnated pillared montmorillonite ($NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM) are compared in Table 2.5.

Table 2.5 The BET specific surface area of synthesized clay catalysts

Entry	**Samples**	**BET specific surface area (m^2/g)**
1	Montmorillonite	58.37
2	Na-montmorillonite	104.03
3	Fe-PLM	145.34
4	Al-PLM	205.57
5	2%$NdCl_3$/Al-PLM	170.48
6	Cr-PLM	91.18
7	2%$CrCl_3$/Fe-PLM	148.90
8	2%$NdCl_3$/Fe-PLM	135.04
9	5%$CrCl_3$/Fe-PLM	135.27
10	5%$NdCl_3$/Fe-PLM	85.86
11	10%$CrCl_3$/Fe-PLM	85.53
12	10%$NdCl_3$/Fe-PLM	24.85

From table 2.5, the BET specific surface area of all the pillared clay showed higher surface area than the untreated montmorillonite except for 10%$NdCl_3$/Fe-PLM.

The nitrogen adsorption-desorption isotherms of all synthesized clays belong to type IV isotherm, corresponding to the mesoporous material as shown in Appendix. It could indicate that metal oxide in calcined samples transformed 2-dimensional clay-layered structure to 3-dimensional mesoporous structure.

The pore size distributions of Fe-PLM and 2%MCl_3 impregnated Fe-PLM in BJH analysis were in the range of 50 to 70 Å, presenting the mesopores of catalyst. The analysis result of more percentages metal chloride impregnated Fe-PLM (5-10%MCl_3/Fe-PLM) were in the lower range, demonstrated that metal chloride occupied on the pore wall of the pillared clay and also in mesoporous structure, led to the reducing in specific surface area.

Al-pillared montmorillonite showed higher specific surface area (m^2/g) than that of montmorillonite. The surface area enlargement related to the increasing of the d_{001} basal spacing from 12.80 to 15.49 Å. Al-oxide pillars expanded the clay gallery height and permitted more access of nitrogen probe molecules. In addition, the clay-layered structure was transformed to mesoporous structure by connecting the adjacent aluminosilicate layers with the Al-oxide pillars in the interlayered region. This result also confirmed the XRD results that aluminium oxide (Al_2O_3) distributed inside the interlayer of clay instead of agglomerated outside the clay structure. $NdCl_3$/Al-PLM showed the higher specific surface area than montmorillonite, but lower than that of Al-PLM. The pore size distribution of $NdCl_3$/Al-PLM in BJH analysis was in the range of 50 to 70 Å, presenting the mesopores of catalyst. This result also demonstrated that $NdCl_3$ occupied on the pore wall of the pillared clay and also in mesoporous structure.

In the case of Cr-pillared montmorillonite, showed lower specific surface area than that of other metal oxide pillared clays. The pore size distribution of Cr-PLM in BJH analysis were in the range of 30 to 50 Å, presenting the micro- and mesopores of the catalyst. It could indicate that chromium oxide distributed inside the interlayer and agglomerated outside the clay structure as a bulk Cr_2O_3. The surface area of Cr-PLM was quite low due to Cr_2O_3 possesses a dense structure.

2.13 Conclusion

Metal oxide-pillared clays (Fe-PLM, Al-PLM and Cr-PLM) were synthesized by intercalation method, followed by calcination at high temperature (300-500°C). Metal chloride-impregnated metal oxide-pillared montmorillonites ($NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM) were synthesized by the impregnation method of metal chloride ($NdCl_3$ and $CrCl_3$) on pillared montmorillonite, followed by calcination.

In the case of metal oxide-pillared clays, the d_{001} basal spacings of Fe-PLM, Al-PLM and Cr-PLM were 9.99, 15.49 and 11.94 Å, respectively. $NdCl_3$/Al-PLM showed the d_{001} basal spacing of 14.02 Å. Whereas the d_{001} spacings of metal chloride-impregnated iron oxide-pillared montmorillonites are about 9.67-9.93 Å, except for high loading of

5 and 10% $NdCl_3$ impregnated Fe-PLM clays. All synthesized clay catalysts still presented the parent clay layered characteristics. The nitrogen adsorption-desorption isotherms of all synthesized clay catalysts exhibited the type IV isotherm indicating their micro-mesoporous structure. The BET specific surface area of Fe-PLM, Al-PLM and Cr-PLM were greater than untreated montmorillonite. The BET specific surface area of $NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM showed lower than Al-PLM but higher than untreated montmorillonite, except for 2% $NdCl_3$ impregnated Fe-PLM. From the acidity determined by NH_3-TPD method, Cr-PLM showed the highest acidity among all synthesized clay catalysts.

CHAPTER III
SYNTHESIS OF COUMARINS CATALYZED BY CLAY CATALYST

3.1 Introduction

Coumarin is one of the most important aroma substances having unique characteristics because of its haylike bittersweet odor and its quality as a perfume fixative. Coumarin is widely distributed in the plant kingdom. But most of it has been produced synthetically. Previously, large quantities of coumarin were used in food industry mostly associated with vanillin for flavoring chocolates, baked goods, and in the confection of cream soda flavored beverages [47]. The synthesis of coumarins and their derivatives has attracted considerable attention from organic and medicinal chemists for many years as a large number of natural products containing this heterocyclic nucleus. They are widely used as additives in manufacture of food, perfumes, cosmetics, pharmaceuticals [48] and in the preparation of insecticides, optical brighteners [49] and dispersed fluorescent and laser dyes [50]. Also, coumarins have varied bioactivities, for example, inhibition of platelet aggregation [51, 52], anticancer [53] and inhibition of steroid 5α-reductase [54].

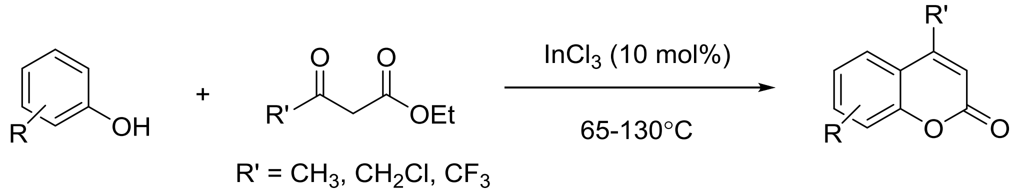
A large number of coumarin derivatives have been identified in plants and many of them have been synthesized and studied for their physiological activity. 3,4-Dihydrocoumarin is prepared by catalytic hydrogenation of coumarin. It is also used in the perfumery industry for its haylike odor. 3- and 6-Methylcoumarins have some use in the perfume industry. 6-Methyl derivative is permitted in flavor compositions. Derivatives of 4-hydroxycoumarin for instance dicoumarol, warfarin, cyclocoumarol, ethyl *bis*–coumaracetate, and *bis*-4-hydroxycoumarin are synthetic blood anticoagulants. 7-Hydroxycoumarin, known as umbelliferone and β-methyl umbelliferone (7-hydroxy-4-methylcoumarin) are used as fluorescent brighteners.

3.1.1 Literature review on the synthesis of coumarins

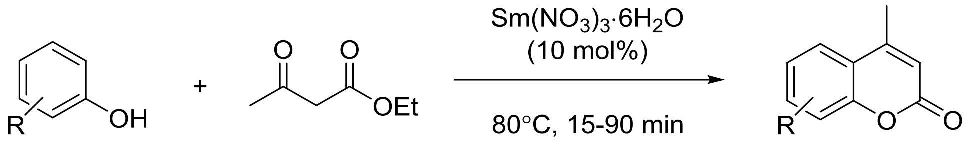
Pechmann condensation is one of the most simple and straightforward methods used to produce coumarins. Classically, the process consists of the condensation of phenols with β-ketoesters in the presence of a variety of reagents and gives good yields of 4-substituted coumarins. Several acid catalysts have been used in the Pechmann reaction including H_2SO_4, P_2O_5, $HClO_4$ and CF_3COOH. However, these catalysts have to be used in excess; for example, H_2SO_4 in 10-12 equivalents, CF_3COOH in 3-4 equivalents and P_2O_5 is required in a 5-fold excess. As a result, the disposal of excess acid waste leads to environmental pollution.

In recent years, Lewis acids such as $AlCl_3$ [55], $InCl_3$ [56], $Sm(NO_3)_3$ [57], $ZrCl_4$ [58] and $NbCl_5$ [59] as well as acidic ionic liquid [60-62] were employed to catalyze Pechmann reactions. However, some of these Lewis acids are moisture sensitive and require special care in handling and storage. Consequently, there is scope for further development of milder reaction conditions, increased variation of the substituents in both components and better yields.

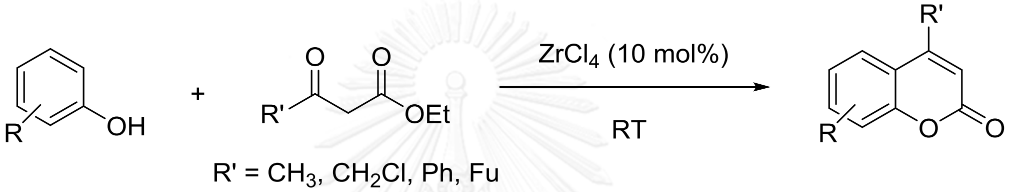
Bose and co-workers reported the utilization of indium trichloride ($InCl_3$) catalyzed coumarin derivatives synthesis. The Pechmann condensation was carried out in the presence of 10 mol% of $InCl_3$ under N_2 atmosphere at 65-130°C for 30-240 min. 4-Substituted coumarins were furnished in good to excellent yield [56].



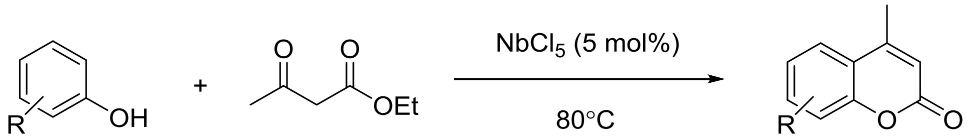
Bahekar and co-workers published the application of $Sm(NO_3)_3{\cdot}6H_2O$ in the Pechmann condensation leading to the formation of coumarins. The reaction was performed under solvent-free conditions under N_2 atmosphere at reflux temperature to give the moderate to excellent yield of corresponding coumarin products [57].



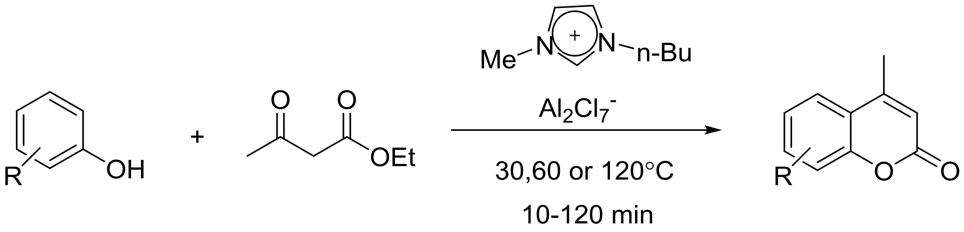
Sharma and co-workers reported the studies on zirconium tetrachloride ($ZrCl_4$) catalyzed one-pot protocol for the synthesis of 4-substituted coumarins. The reaction was carried out at ambient temperature and found to be adaptable to a variety of substrates. The corresponding of coumarin products were obtained in high yield [58].



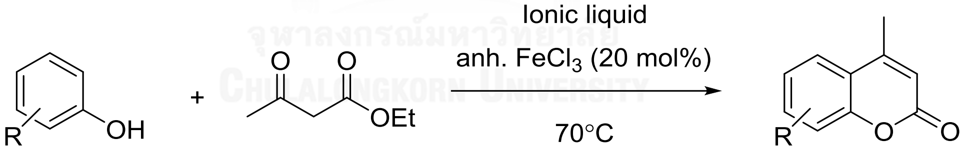
Niobium pentachloride ($NbCl_5$) was published as an efficient catalyst for the Pechmann condensation by Gao and co-workers. The reaction of phenols and ethyl acetoacetate were performed in the presence of 5 mol% of $NbCl_5$ at 80°C under solvent-free conditions. A wide range of structurally varied phenols could be reacted smoothly to give the coumarin derivatives in good to excellent yields [59].



Potdar and co-workers addressed the use of [bmim]Cl·2$AlCl_3$ ionic liquid. The chloroaluminate salt of 1-butyl-3-methylimidazolium has been found to be an alternative to conventional acid catalysts in Pechmann condensation of phenols with ethyl acetoacetate, leading to coumarin derivatives in 40-95% yield. The ionic liquid played the dual role of solvent and Lewis acid catalyst providing a quick route to syntheses of coumarins. As an additional advantage of the system, it was found that the reaction time is considerably reduced when this reaction is carried out in molten salts, even at RT. Nevertheless, this acid catalyst was sensitive to moisture and all additions were carried out in an inert atmosphere [60].



Kumar and co-workers reported the synthesis of coumarins *via* Pechmann reaction using anhydrous $FeCl_3$ as Lewis acid catalyst in ionic liquid medium. All reactions were carried out under similar conditions at 70°C using 20 mol% anhydrous $FeCl_3$ in 1 mL ionic liquid. The best results 89% yield were obtained with ionic liquids having *bis*(triflic)imide as a counteranion. The ionic liquid could be recovered and reused by extraction with CH_2Cl_2 and dried in a high vacuum oven for 6–10 h at 50°C [62].

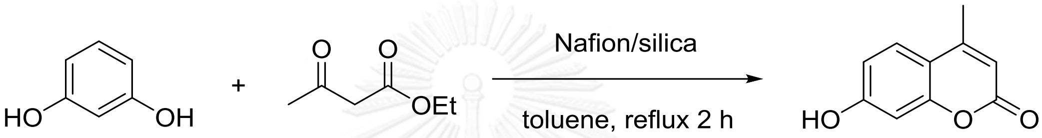


3.1.2 Literature review on heterogeneous catalysts used in the synthesis of coumarins

Solid catalysts were used for decades in most petrochemical processes. Heterogenization is one of the new clean technologies which are being developed to reduce waste in liquid phase organic reactions. In order to utilize this greener technology in organic chemical manufacturing, the highly effective catalysts need to produce to suit a numerous of chemical process technologies.

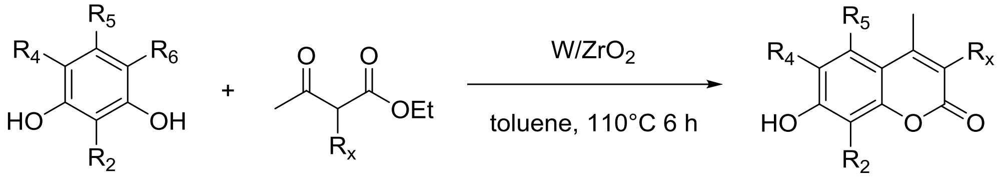
In recent years, solid acid and combination of solid acid and microwave irradiation [63, 64] have also been used to catalyze Pechmann condensation reactions.

Laufer and co-workers reported the Nafion resin/silica nanocomposite materials for the synthesis of 7-hydroxycoumarins. The reaction of resorcinol and ethyl acetoacetate in toluene was performed very satisfactorily and with short reaction time by using composites with 40 and 80% content of Nafion on silica. The 81–96% yield of 7-hydroxy-4-methylcoumarin were obtained. The composites were found to be directly recyclable, only a low catalyst deactivation occurred [65].



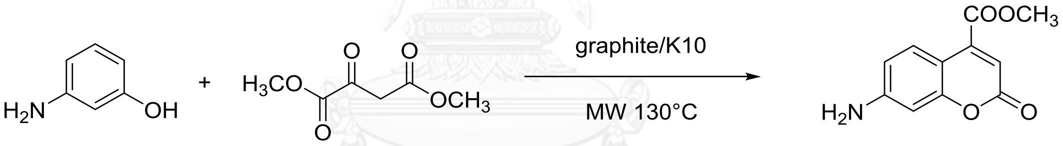
Amberlyst-type catalysts were applied for Pechmann reaction by Sabou and co-workers. The best-performing material was surface-sulfonated Amberlyst or Amberlyst-S, with 95% conversion and 98% selectivity in refluxing toluene after 2 h at 120°C. Furthermore, the new Amberlyst-type materials showed better activities and were more stable than Amberlyst-15. At the same time, Amberlyst catalysts are not as expensive as Nafion silica and BEA zeolite catalysts. However, upon regeneration in refluxing toluene, the catalyst activity decreased very slowly by 1–2% after each run [66].

Reddy and co-workers reported the utilization of tungsten doped ZrO_2 for the synthesis of substituted coumarins. The condensation of substituted resorcinols with ethyl acetoacetate and ethyl-α-methylacetoacetate were carried out over W/ZrO_2 under reflux temperature in toluene for 6 h. The coumarin derivatives in 50-80% yield were obtained [67].



(R_2 = OH, R_5 = CH_3, OH, R_x = H, CH_3)

Frère and co-workers performed the synthesis of rare aminocoumarins by exposition of the reactants to a microwave field on original support (2:1) graphite:montmorillonite K10 led to a reduction of the reaction time. The strong thermal effect due to graphite:microwave interaction is associated with the acidic catalyst role of the clay. This work also demonstrated that working under focused microwave irradiation needs special attention. In this case, simple fusion of the products or addition of an appropriate solvent may lead to more convenient mixtures or solutions for microwave applications [64].



Sinhamahapatra and co-workers addressed the application of mesoporous zirconium phosphate (m-ZrP) for Pechmann condensation. The catalytic activity of the condensation of phenols and ethyl acetoacetate in both conventional heating and microwave assisted method were high. Among the substituted phenols, *m*-amino phenol is more reactive and 100% yield is obtained in very short time at low temperature due to the presence of ring activating amine group in *meta* position [68].

3.2 Scope of this work

From the literature reviews, homogeneous catalysts and some heterogeneous catalysts could be employed as good catalysts for Pechmann condensation. However, the disadvantage of some catalysts is their toxicity and expensiveness, long reaction time and difficulty in separation from the reaction products. This research focused on the development of a new and efficient methodology for Pechmann condensation using metal oxide-pillared montmorillonite and metal chloride-impregnated metal oxide-pillared montmorillonite clay catalysts.

3.3 Experimental

3.3.1 Instruments and equipments

Spectrometers: The ^{1}H- and ^{13}C-NMR spectra were performed in $CDCl_3$ or DMSO-d_6 with tetramethylsilane (TMS) as an internal reference on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR 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: Gas chromatographic analysis was carried out on a Varian gas chromatography instrument equipped with a flame ionization detector (FID) with N_2 as a carrier gas and a 30-m long BP-1 column (0.25-mm outer diameter, 0.25 μm film thickness). Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's silica gel 60 G Art 7734 (70-230 mesh)).

Melting points (m.p.) were determined with a Fisher-Johns melting point apparatus and are uncorrected.

3.3.2 Chemicals

All solvents in this research were purified according to the procedures described in the standard methodology except for reagents and solvents that are reagent grade.

3.3.3 Syntheses

3.3.3.1 Preparation of coumarin derivatives

To phenol (5 mmol) and β-ketoester (5 mmol), $CrCl_3{\cdot}6H_2O$ catalyst (5 mol%) was added and the mixture was stirred in a pre-heated oil-bath at 80°C. After completion of the reaction, the reaction mixture was cooled to RT, poured into ice-cold water and stirred for 10-15 min. The crystalline products were collected by filtration under suction, washed with ice-cold water and then recrystallized from hot EtOH to afford the desired product. The coumarin derivatives are mostly well known in literature and were identified by comparison of their physical and spectral data.

7-hydroxy-4-methylcoumarin: white solid, m.p. 184-185°C, R_f 0.32 (hexane-EtOAc (1:1)); ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.57 (d, J = 8.7 Hz, 1H), 6.78 (dd, J = 2.3, 8.7 Hz, 1H), 6.68 (d, J = 2.3 Hz, 1H), 6.11 (s, 1H) and 2.34 (s, 3H).

5,7-dihydroxy-4-methylcoumarin: beige solid, m.p. 283–285°C, R_f 0.18 (hexane-EtOAc (1:1)); ^{1}H-NMR (DMSO-d_6) δ (ppm): 6.22 (s, 1H), 6.14 (s, 1H), 5.81 (s, 1H) and 2.48 (s, 3H).

7,8-dihydroxy-4-methylcoumarin: gray solid, m.p. 241–243°C, R_f 0.20 (hexane-EtOAc (1:1)); ^{1}H-NMR (DMSO-d_6) δ (ppm): 7.07 (d, J = 8.5 Hz, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.10 (s, 1H) and 2.33 (s, 3H).

3.3.3.2 General procedure for the synthesis of coumarin derivatives *via* Pechmann condensation

A round bottom flask was charged with phenol (1 mmol) and β-ketoester (1 mmol) and clay catalyst (30 wt%), connected with a condenser. The reaction mixture was continuous stirred in a pre-heated oil-bath at 130°C for desired time. After the reaction was finished, the clay catalyst was easily filtered out of the reaction mixture, and thoroughly washed with MeOH. The solvent was partly evaporated under reduced pressure. The obtained mixture was analyzed by GC with the addition of an exact amount of an appropriate internal standard (biphenyl).

3.3.3.3 General isolation procedure

After the reaction was finished, the products were separated as follows: the solvent was evaporated to dryness under reduced pressure. The crude products were purified by silica gel column using a mixture of hexane-EtOAc as a mobile phase. The equivalent fractions monitored by TLC were combined and the solvent was completely evaporated. The residue was characterized by ^{1}H NMR spectroscopy.

3.3.3.4 Optimum condition study on Pechmann condensation of resorcinol and ethyl acetoacetate

Effect of clay catalyst on Pechmann condensation

The Pechmann condensation was carried out according to the general procedure as previously described employing various clay catalysts: montmorillonite, Na-montmorillonite, Cr-pillared montmorillonite, Fe-pillared montmorillonite, Al-pillared montmorillonite, $NdCl_3$/Al-pillared montmorillonite as a catalyst.

Effect of reaction temperature and time on Pechmann condensation

The Pechmann condensation was carried out according to the general procedure as described above except for the reaction temperature was varied: 80, 130 and 160°C at different time.

Effect of solvent on Pechmann condensation

The Pechmann condensation was performed according to the general procedure as described above except for isooctane, *p*-xylene, toluene, THF, CH_3CN, EtOH and water were used as a reaction medium. 3 mL of each solvent was used.

Effect of substrate ratio on Pechmann condensation

The Pechmann condensation was carried out according to the general procedure as previously described employing various ratio of resorcinol to ethyl acetoacetate: 1:1, 1:1.2, 1:1.5 and 1:2 mmol.

Effect of catalyst amount on Pechmann condensation

The Pechmann condensation was performed according to the general procedure as described above, but the amount of catalyst was varied: 0, 10, 30, 50 and 75 wt% of catalyst to resorcinol.

Effect of percentage of metal chloride impregnated metal oxide-pillared clay catalyst on Pechmann condensations

The Pechmann condensation was carried out according to the general procedure as previously described using various percentage of metal chloride impregnated clay catalyst: 0, 2, 5 and 10%

3.3.3.5 Synthesis of various coumarin derivatives *via* Pechmann condensation

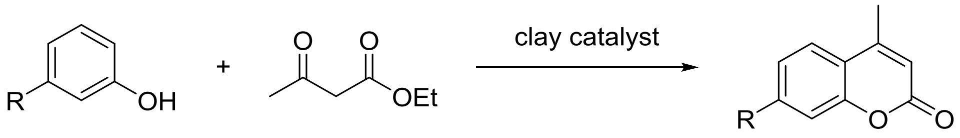
Various phenolic compounds

Selected phenolic compounds, namely pyrogallol and phloroglucinol were reacted according to the general procedure as previously described. Fe-PLM was utilized as catalyst. The crystalline products of coumarin derivatives were identified by comparison of their physical and spectral data with those reported in literature.

3.4 Results and discussion

3.4.1 Optimum conditions for Pechmann condensation of resorcinol and ethyl acetoacetate

Pechmann condensation of resorcinol and ethyl acetoacetate producing 7-hydroxy-4-methylcoumarin was selected for testing the catalytic activity of synthesized clay catalysts. Various factors were carefully investigated to optimize the conditions for the synthesis of coumarins. The type of clay catalyst, the type of solvent, the substrate ratio, the amount of catalyst, the percentage of metal chloride impregnated metal oxide-pillared clay catalyst and the type of additive were varied to search for the optimal conditions.



3.4.1.1 Effect of clay catalyst on Pechmann condensation

To screen for suitable catalysts that could furnish coumarin derivatives in high yield with good selectivity. The catalytic activity of three metal oxide-pillared clays namely Fe-PLM, Cr-PLM, Al-PLM, and $NdCl_3$ impregnated Al-PLM were compared with montmorillonite. The investigated conditions were 30 wt% catalyst to resorcinol at 130°C for 6 h. The results are shown in Table 3.1.

Table 3.1 The effect of clay catalysts on Pechmann condensation

Entry	Clay catalyst	BET Surface area (m^2/g)	Acidity (mmol/g)	d_{001} Basal spacing (Å)	%Yield[a]
1	-	-	-	-	0
2	montmorillonite	58.4	1.188	12.80	2
3	Na-M	104.0	1.357	14.77	1
4	Cr-PLM	91.2	2.039	11.94	19
5	Fe-PLM	145.3	1.751	9.99	42
6	Al-PLM	205.6	1.615	15.49	6
7	$NdCl_3$/Al-PLM	170.5	1.751	14.02	2

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), clay catalyst (30 wt%) at 130°C for 6 h

[a] The yield was determined by GC using biphenyl as an internal standard

All synthesized clays gave much higher yield of coumarin than montmorillonite except for Na-montmorillonite and $NdCl_3$/Al-PLM. No product was observed when the reaction was carried out in the absence of clay catalyst. The acidity of clay catalysts that determined from the temperature programmed desorption experiment and surface area of clay catalysts that determined from the nitrogen adsorption-desorption experiment corresponds to this result (entries 4-7). All Fe-PLM, Cr-PLM, Al-PLM and $NdCl_3$ impregnated Al-PLM had acidity and surface area higher than montmorillonite. Fe-PLM showed the highest activity in Pechmann condensation due to the appropriate acidity and specific surface area. The small interlayer space of Fe-PLM led to the reactant and product shape selectivity. The corresponding coumarin was obtained in 42% yield with 50% recovery. It should be noticed that Fe-PLM could be the best clay catalyst for the synthesis of coumarin.

3.4.1.2 Effect of reaction temperature and time on Pechmann condensation

The effects of reaction temperature and reaction time for the synthesis of 7-hydroxy-4-methylcoumarin were investigated to obtain the optimum conditions by carried out under various temperatures at different times. The results are displayed in Table 3.2.

Table 3.2 Effect of reaction temperature and time on Pechmann condensation

Entry	Catalyst	Temp (°C)	Time (h)	%Yield[a]
1	Fe-PLM	80	6	2
2		130	2	21
3		130	6	42
4		130	15	40
5		160	6	45

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), Fe-PLM (30 wt%)

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 3.2 showed that the condensation reaction of resorcinol and ethyl acetoacetate needed high temperature to proceed the catalytic reaction.

Performing the reaction at 130°C and prolonging the reaction time to 15 h, the yield of product was not improved (entry 4). Increasing the reaction temperature to 160°C, the yield of the product was raised insignificantly (entry 5). Thus, the reaction conditions at 130°C for 6 h were selected for additional experiments.

3.4.1.3 Effect of solvent on Pechmann condensation

To examine the effect of solvent for Pechmann condensation, various solvents including isooctane, *p*-xylene, toluene, THF, CH_3CN, EtOH and water were investigated. The effect of solvents on Pechmann condensation was performed with 3 mL of solvent using 1:1 mmol of resorcinol to ethyl acetoacetate and 30 wt% of Fe-PLM to resorcinol under refluxing conditions for 6 h or more. The results are demonstrated in Table 3.3.

Table 3.3 The effect of solvent on Pechmann condensation

Entry	Solvent	Amount of solvent (mL)	Time (h)	%Yield[a]
1	-	0	6	42
2	isooctane	1.5	6	16
3	isooctane	3	6	19
4	*p*-xylene	3	6	17
5	toluene	3	6	12
6	THF	3	6	1
7	CH_3CN	3	24	<1
8	EtOH	3	24	1
9	H_2O	3	6	<1

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), Fe-PLM (30 wt%), solvent (1.5-3 mL) at reflux temperature

[a] The yield was determined by GC using biphenyl as an internal standard

The Pechmann condensation of resorcinol and ethyl acetoacetate was carried out under solvent-free condition to produce 7-hydroxy-4-methylcoumarin in 42% yield. Isooctane, p-xylene and toluene as non-polar with high boiling point solvents gave the lower yield of coumarin product (entries 2, 4-5). In case of polar aprotic and polar protic solvents (entries 6-9), the solvent would block the access of hydroxyl group to attack the carbonyl to form intermediate. Reducing the amount of solvent by half to 1.5 mL could not improve the yield (entry 3).

3.4.1.4 Effect of substrate ratio on Pechmann condensation

The effect of substrate ratio of resorcinol to ethyl acetoacetate for Pechmann condensation was investigated. One mmol of resorcinol was tested with various amounts of ethyl acetoacetate to study the synthesis of coumarin. The results are presented in Table 3.4.

Table 3.4 The effect of substrate ratio on Pechmann condensation

Entry	β-ketoester (mmol)	Time (h)	%Yield[a]
1	1.0	6	42
2	1.2	6	44
3	1.5	6	46
4	2.0	6	45

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1-2 mmol), Fe-PLM (30 wt%) at 130°C for 6 h

[a] The yield was determined by GC using biphenyl as an internal standard

Increasing the amount of ethyl acetoacetate from 1:1 to 1:1.5, the yield of 7-hydroxy-4-methylcoumarin was insignificantly raised (entries 1-3). Even though the amount of resorcinol:ethyl acetoacetate was increased to 1:2, the desired product was obtained in almost the same yield (entry 4). Consequently, the substrate ratio of 1:1

was selected for additional experiments or the amount of ethyl acetoacetate in the range of 1.0-2.0 mmol could be used for some instances.

3.4.1.5 Effect of catalyst amount on Pechmann condensation

The efficiency of the reaction frequently influenced by the catalyst amount. The variation of the amount of Fe-PLM as 10, 30, 50 and 75 wt% was used to examine the suitable clay catalyst amount for the condensation of resorcinol and ethyl acetoacetate. The effect of the Fe-PLM amount for Pechmann condensation was investigated. The results are shown in Table 3.5.

Table 3.5 The effect of catalyst amount on Pechmann condensation

Entry	Catalyst	Amount of catalyst (wt%)	Time (h)	%Yield[a]
1	-	0	6	0
2	Fe-PLM	10	6	26
3	Fe-PLM	30	6	42
4	Fe-PLM	50	6	60
5	Fe-PLM	75	6	55

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), Fe-PLM (vary) at 130°C for 6 h

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 3.5 displayed that the Fe-PLM amount explicitly affected the product formation. When the Fe-PLM amount increased, the yield of desired coumarin product was significantly increased (entries 2-4). Although the addition of clay catalyst amount to 75 wt% could not enhance the yield (entry 5). Because 7-hydroxy-4-methylcoumarin remains adsorbed within the active sites of the catalyst and the diffusion of the reactants was restrained when excess catalyst was used. Hence, the result in decreased yield was observed. The Fe-PLM amount of 50 wt% was selected for additional experiments.

3.4.1.6 Effect of percentage of metal chloride impregnated metal oxide-pillared clay catalyst on Pechmann condensation

To enhance the catalytic activity of metal chloride-impregnated Fe-pillared montmorillonite ($CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM), increasing the percentage of impregnation was investigated. The results are shown in Table 3.6.

Table 3.6 The effect of percentage of metal chloride impregnated metal oxide-pillared clay catalyst on Pechmann condensation

Entry	Catalyst	%Yield[a]
1	Fe-PLM	42
2	2% $CrCl_3$/Fe-PLM	37
3	2% $NdCl_3$/Fe-PLM	41
4	5% $CrCl_3$/Fe-PLM	30
5	5% $NdCl_3$/Fe-PLM	33
6	10% $CrCl_3$/Fe-PLM	21
7	10% $NdCl_3$/Fe-PLM	41

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), clay catalyst (30 wt%) at 130°C for 6 h

[a] The yield was determined by GC using biphenyl as an internal standard

From Table 3.6, it demonstrated that increasing the percentage of $CrCl_3$ impregnation on Fe-PLM was retarded the catalytic activity of Pechmann condensation (entries 2, 4 and 6). In spite of the percentage of $CrCl_3$ impregnation was increased, the total acid site and the specific surface area was reduced due to $CrCl_3$ blocked some active pore make difficulty in accessibility. As for $NdCl_3$ impregnation percentage increasing was not retarded the reaction, nevertheless could not enhance the catalytic activity due to the lower acidities and increasing in the clay interlayer (entries 3, 5 and 7). It should be noted that Fe-PLM without impregnation of metal chloride afforded the highest yield of coumarin product.

3.4.1.7 Effect of additive on Pechmann condensation

Improvement of reaction efficiency by using inorganic additives was observed. In this research, Na_2SO_4, $MgSO_4$ and molecular sieve were examined as additive to study the effect on Pechmann condensation reaction. The results are presented in Table 3.7.

Table 3.7 The effect of additive on Pechmann condensation

Entry	Additive	Amount of additive (mg)	%Yield[a]
1	-	0	63
2	molecular sieve 4A	50	42
3	Na_2SO_4	50	34
4	$MgSO_4$	50	61

Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (2 mmol), Fe-PLM (50 wt%)
with additive at 130°C for 6 h

[a] The yield was determined by GC using biphenyl as an internal standard

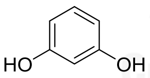
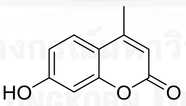
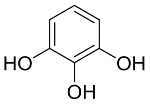
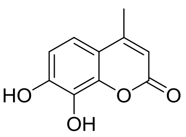
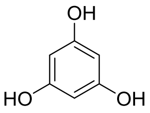
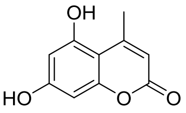
The ability of additive to remove water from the Pechmann condensation reaction was expected to promote more product formation. From Table 3.7, molecular sieve 4A and Na_2SO_4 were retarded the catalytic activity of Fe-PLM for Pechmann condensation. Because the starting phenolic compound was adsorbed by molecular sieve 4A and Na_2SO_4 led to the lower coumarin formation. The addition of $MgSO_4$ could not improve the coumarin product, the yield was still obtained in the same amount.

It could be summarized that the optimum conditions for the Pechmann condensation reaction of resorcinol and ethyl acetoacetate catalyzed by Fe-PLM are as follows: resorcinol 1 mmol, ethyl acetoacetate 1 mmol and Fe-PLM 50 wt% at 130°C for 6 h under solvent-free condition. 7-Hydroxy-4-methylcoumarin was obtained in good yield. Thus, these conditions were applied for additional experiments as standard conditions.

3.4.2 Synthesis of various coumarin derivatives *via* Pechmann condensation

Various phenolic compounds were selected as the next chemical models to be examined. The Pechmann condensation of phenolic compounds including pyrogallol and phloroglucinol with ethyl acetoacetate was carried out using the optimum conditions described above. The results are displayed in Table 3.8.

Table 3.8 Synthesis of coumarin derivatives *via* Pechmann condensation of phenols and ethyl acetoacetate

Entry	Phenol	Coumarins	Time (h)	%Yield[a]	Mp (°C)
1			6	60	184-185
2			6	34[b]	241-243
3			6	43[b]	283-285

Reaction conditions: phenol (1 mmol), ethyl acetoacetate (1 mmol), Fe-PB (50 wt%) at 130°C

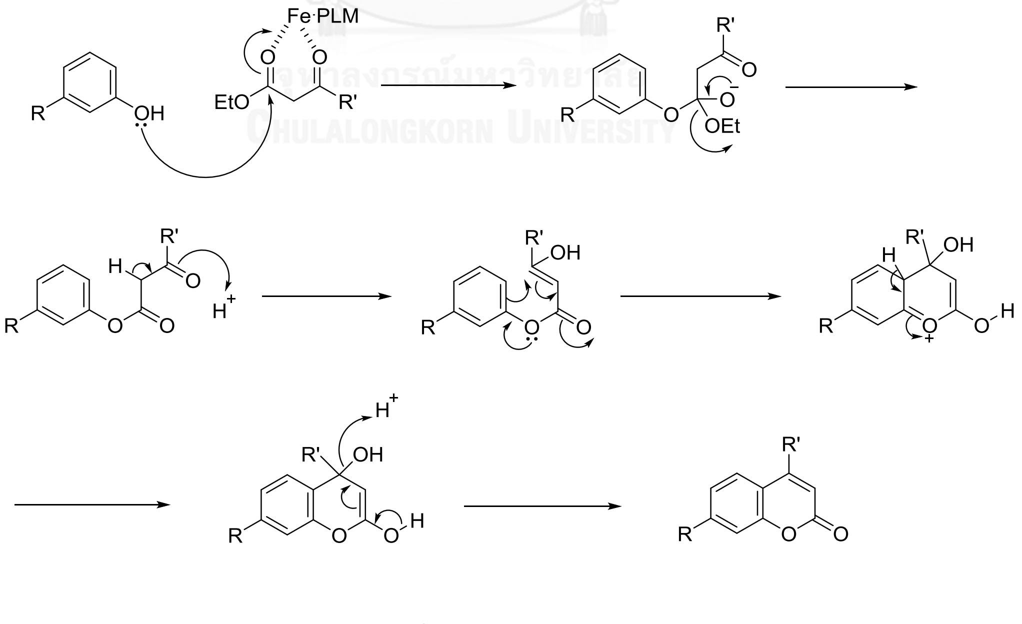
[a] The yield was determined by GC using biphenyl as an internal standard

[b] The yield referred to the pure isolated product

The effect of electron-donating groups at *para* position to the site of electrophilic substitution leading to the construction of the coumarin derivatives in high yield. From Table 3.8, the reactions of pyrogallol with ethyl acetoacetate (entry 2) gave the yield of corresponding coumarin lower than that of the reactions of resorcinol presumably due to steric hindrance of hydroxyl groups. The Pechmann condensation of phloroglucinol with ethyl acetoacetate gave the desired coumarin in higher yield (entry 3) as two hydroxyl groups of phloroglucinol at *ortho* and *para* positions.

3.5 The proposed mechanism for the synthesis of coumarin *via* Pechmann condensation

The mechanism of Pechmann condensation of phenols with β-ketoester employing Lewis acid catalyst was believed to proceed *via* the following pathway in the same fashion proposed in literature [69, 70]. The proposed mechanism is shown in Scheme 3.1.



Scheme 3.1 Proposed mechanism for Pechmann condensation catalyzed by Fe-PLM

The reaction is conducted with a strong Lewis acid. The acid catalyzes transesterification as well as keto-enol tautomerisation. The electrophilic attack on the benzene ring by protoned ketone carbonyl leads to the formation of the coumarin skeleton. This addition is followed by rearomatization. Afterward acid-induced elimination of water furnishes the product.

3.6 Conclusion

The catalytic activities of Fe-PLM were carried out for the Pechmann condensation of resorcinol and ethyl acetoacetate. The optimum conditions were using 50 wt% Fe-PLM to resorcinol at 130°C for 6 h under solvent-free condition. This catalytic system was carried out to provide the desired coumarin product in good yield. Fe-PLM showed higher catalytic efficiency than Cr-PLM, Al-PLM, $NdCl_3$/Al-PLM and montmorillonite under the same reaction conditions because of the appropriate acidity, specific surface area and interlayer space of Fe-PLM.

From various phenolic compounds, the yields of corresponding products highly depended on the position of electron donating groups. The optimum conditions could be applied and used for other phenols including pyrogallol and phloroglucinol to afford coumarin derivatives in moderate yield.

Clay catalysts were inexpensive, convenient, non-toxic, recoverable and reusable, which led to a highly attractive and efficient procedure for the synthesis of coumarins.

CHAPTER IV

THE ISOMERIZATION OF EPOXIDES CATALYZED BY CLAY CATALYST

4.1 Introduction

4.1.1 The importance of epoxides

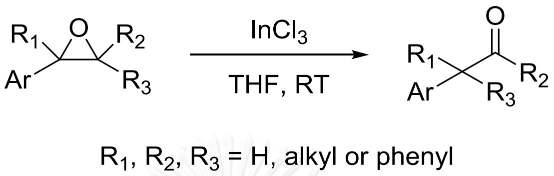
Epoxides are useful and versatile intermediates in organic synthesis because they can be readily transformed into a variety of functional groups [71]. Epoxides undergo numerous reactions for example: ring opening of epoxides with heteroatomic nucleophiles [72], ring opening of epoxides with carbon nucleophiles [73], deoxygenation of epoxides to olefins [74, 75], reduction of epoxides to alcohols [76-78], rearrangement of epoxides to allylic alcohols [79-81] and rearrangement of epoxides to carbonyl compounds [82-84]. Products from these synthetically useful reactions of epoxide are very important in pharmaceutical industries, perfumery and organic synthesis. Among these epoxides transformation, the isomerization of epoxides bearing the aryl group to carbonyl compounds by using Lewis acid reagents was widely examined.

4.1.2 Literature review on the isomerization of epoxides

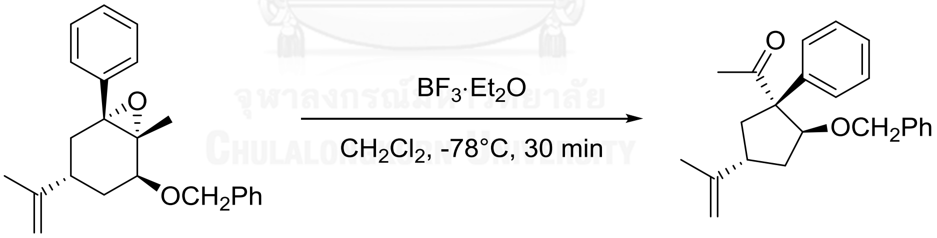
The isomerization of epoxides to carbonyl compounds is a useful synthetic transformation. A variety of catalytic conditions have been developed, with the most functional and widely used procedures using homogeneous and heterogeneous acid catalysts.

4.1.2.1 Homogeneous catalysis

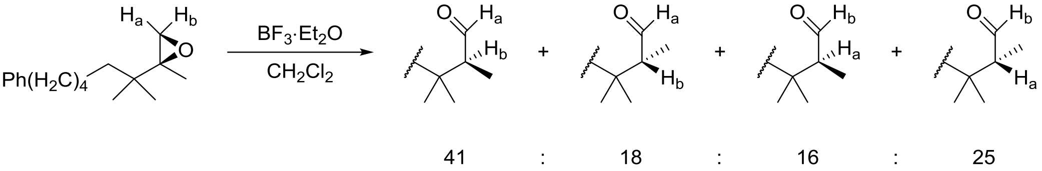
In 1998, Ranu and Jana reported the rearrangement of substituted epoxides catalyzed by $InCl_3$. Aryl-substituted epoxides isomerize *via* the benzylic C-O bond cleavage to form a single carbonyl compound with complete regioselectivity. 1-Aryl-, 1,1-diaryl-, and 1,1-alkyl, aryl-substituted epoxides underwent rearrangement by hydride shift to give the respective aryl-substituted acetaldehydes as the only isolable compounds. The rearrangement of tri- and tetrasubstituted aryl epoxides selectively produced the corresponding methyl ketones by hydrogen migration occurred. This procedure offered fast reaction, mild reaction condition, simplicity in operation and mild nature of $InCl_3$ in comparison to other Lewis acids and its compatibility with sensitive functionalities [82].



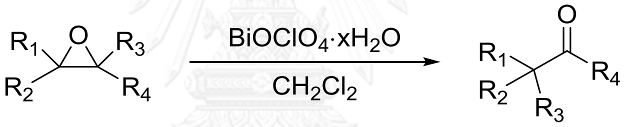
In 1999, Neef and co-workers reported the utilization of $BF_3 \cdot Et_2O$ for the rearrangement of carvone-derived 2,3-epoxy alcohol derivatives to aldol adduct. BF_3-etherate treatment of benzyl ether-protected epoxy alcohol proceeded the formation of a single ring-contracted ketone with pure and high yield [83].



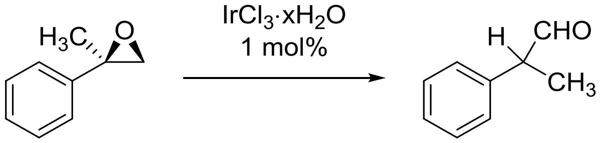
A number of examples have been reported on cyclic epoxides such as steroidal epoxides, whereas few studies have been done on the stereochemistry at the migration terminus in the rearrangement of acyclic epoxides. In 2000, Hara and co-workers reported the study on the rearrangement mechanism of optically active 1,1-disubstituted epoxides to aldehydic products catalyzed by $BF_3 \cdot Et_2O$. They verified that the two hydrogens migrate at the migration terminus with opposite stereochemical preferences. The hydrogen *anti* to the bulky substituent prefers to migrate with inversion of configuration at the migrating terminus, while the hydrogen *syn* to the bulky substituent prefers to migrate with retention of configuration [84].



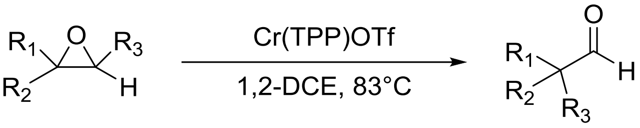
Anderson and co-workers reported a new method for high-yielding, selective rearrangement of aromatic epoxides to carbonyl compounds using $BiOClO_4{\cdot}xH_2O$. Aliphatic epoxides that contained a tertiary epoxide carbon also underwent rearrangement readily. Advantages of this method include low toxicity and low cost of the Lewis acid catalyst, fast reaction rates and insensitivity to air and moisture [85].



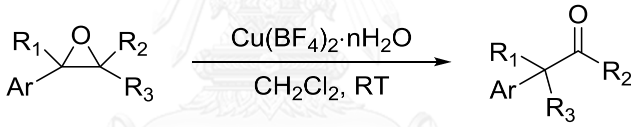
In 2003, Karamé and co-workers reported an effective and regioselective alternative for the Meinwald rearrangement of epoxides catalyzed by iridium(III) chloride. The hydrated iridium complex used was very stable and the reaction could be run under mild conditions, no inert atmosphere or high temperature are required [86].



In 2004, Suda and co-workers reported a highly regio- and stereoselective rearrangement of epoxides to aldehydes with a porpyrin-based Lewis acid catalyst, chromium(III) tetraphenylporphyrin triflate, Cr(TPP)OTf, in low catalyst loading (1-20 mol%) under very mild conditions. This Cr(TPP)OTf-catalyzed reaction is especially appropriate for the optically active β-siloxy aldehydes synthesis, useful intermediates in natural product synthesis, from 2,3-epoxy silyl ethers [87].



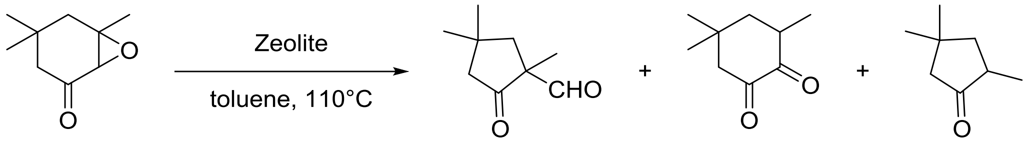
In 2006, Robinson and co-workers reported the utilization of copper tetrafluoroborate as a highly efficient and effective reagent for the Meinwald rearrangement of styrene oxide derivatives to carbonyl compounds under mild reaction conditions. The benign nature of the catalyst in addition to its low cost and ease of use offers an attractive alternative to established methodologies [88].



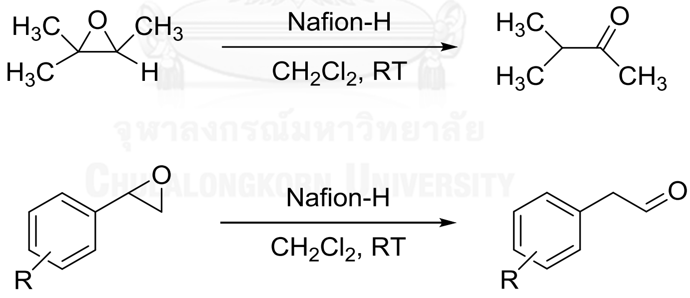
In 2010, they have demonstrated that $Cu(BF_4)_2{\cdot}nH_2O$ could be utilized as a highly efficient reagent to catalyzes the Meinwald rearrangement of a range of epoxides to produce carbonyl compounds in high yields under mild reaction conditions. The reagent shows excellent regioselectivity, as demonstrated by the rearrangement of stilbene oxide and α-pinene oxide, which gave high yields of diphenylacetaldehyde and campholenic aldehyde with excellent selectivity, respectively [89].

4.1.2.2 Heterogeneous catalysis

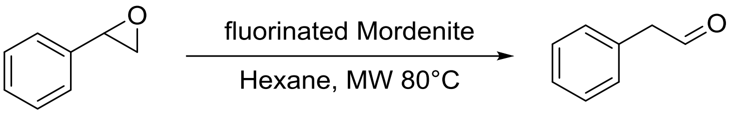
In 1998, Meyer and co-workers reported the isomerization of isophorone oxide by use of zeolites as catalysts. The high yield of the keto aldehyde, 2-formyl-2,4,4-trimethylcyclopentanone, was obtained. The reaction could be carried out in a discontinuous liquid-phase batch reactor as well as in a continuous vapor-phase fixedbed reactor. The formation of the ketone by the decarbonylation of the keto aldehyde could be reduced by increasing the catalyst loading or by carrying out the reaction under short contact time in gas phase conditions [90].



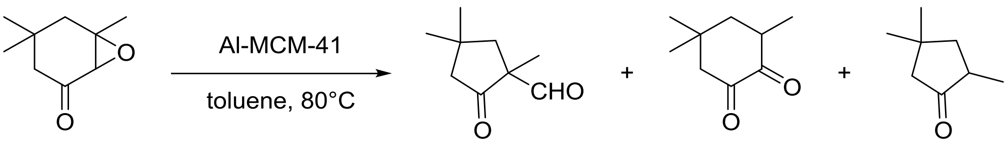
In 1999, Prakash and co-workers reported the utilization of Nafion-H, a perfluorinated resin sulphonic acid as an efficient catalyst for the isomerization of epoxides to carbonyl compounds. The obtained products was found to be ketones or aldehydes depending on the nature of the substituents on the epoxide carbons. This reaction was very straightforward giving the products in high yield. Styrene oxide and its derivatives gave phenylacetaldehyde and its derivatives, whereas β-isoamylene oxide gave only isopropyl methyl ketone [91].



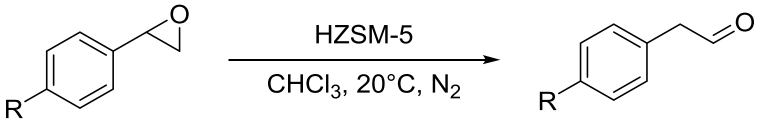
In 2005, Salla and co-workers studied the acidity of several mordenite samples, which were modified to have 1% (HM1F) and 10% (HM10F) in fluorine w/w, through their catalytic behaviour in the isomerisation of styrene oxide to phenylacetaldehyde. The catalytic experiments were performed by using microwaves as a new method and with a conventional heated batch reactor for comparison. Catalyst HM1F was the most active at batch reaction conditions, but underwent faster deactivation when using microwaves. Fluorination in low amounts gave to accessible stronger Brönsted acid sites due to the fluorine located in the external structure framework. This explains the higher activity in the batch reactor and the acceleration of condensation and coke products formation in microwaves experiments [92]. When methanol was used as a solvent, the ring opening of styrene oxide was catalyzed by Lewis and Brönsted acid sites. The existence of high amounts of Lewis acid sites for HM10F explains its highest activity.



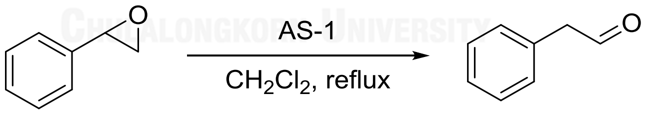
van Grieken and co-workers investigated different Si/Al molar ratios of Al-MCM-41-type mesostructured catalysts for the rearrangement of isophorone oxide. The main rearrangement products were the α-diketone and the keto aldehyde, whereas the minor amount of product coming from the decarbonylation of the keto aldehyde was detected. A catalyst with a molar Si/Al ratio around 40 showed the best catalytic performance in terms of epoxide conversion owing to the proper contribution of acid site concentration and pore size. However, irrespective of the aluminium content of the catalysts and the reaction temperature, the selectivity to the desired keto aldehyde was around 80%. Al-MCM-41 materials were superior catalysts compared with zeolites in terms of both activity and aldehyde selectivity [93].



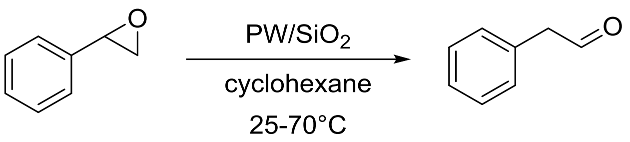
In 2006, Smith and co-workers reported the rearrangement of 4-substituted styrene oxides with acidic zeolite catalysts. The reactions were performed in the presence of catalyst in chloroform at room temperature under nitrogen gave the corresponding 4-substituted phenylacetaldehydes in high yields. The procedure has been applied successfully to the rearrangement of disubstituted epoxides. The zeolite could be easily recovered, regenerated by heating and reused for at least six times with only modest reduction in the yield [94].



In 2009, Robinson and co-workers reported the mesoporous aluminosilicate materials effectively catalyzed the Meinwald rearrangement of epoxides to the corresponding aldehydes. The rearrangement reaction proceeded efficiently in dichloromethane to give the high yield of aldehyde product which could be trapped *in situ* to provide the corresponding acetals in an efficient tandem process. They have also demonstrated that these aluminosilicate materials could be used as a highly effective catalysts for the formation of β-alkoxyalcohols from epoxides and a range of alcohols under mild conditions. The facile synthesis of these materials using the EISA approach, their benign nature, the ease of handling and the simplified reaction and isolation procedures made them a highly attractive alternative to current methodologies [95].



In 2010, Costa and co-workers reported the application of silica-supported $H_3PW_{12}O_{40}$ (PW), the strongest heteropoly acid in the Keggin series, as an efficient, environmentally friendly catalyst for the isomerization of styrene oxide to phenylacetaldehyde. The reaction occured in cyclohexane as a solvent under mild conditions at 25–70°C with low catalyst loadings and without PW leaching in solution. At 60°C, the yield of phenylacetaldehyde reaches 95% at 97% styrene oxide conversion, with a catalyst turnover number of 19600. The catalyst can be recovered and reused without any loss in its activity and selectivity in first run [96].



In 2014, Gou and co-workers demonstrated the isomerization of styrene oxide to phenylacetaldehyde under a gas-phase atmosphere free of solvents catalyzed by a series of phosphorus modified HZSM-5 (SiO_2/Al_2O_3= 25, P/Al = 0.5, 1.0, 1.5, 2.0). The strength and concentration of Brønsted acid sites of the modified catalysts decreased with increased phosphorus content, while all catalysts exhibited initial conversions of styrene oxide greater than 99%. External acid sites were gradually deactivated with phosphorus addition, improving the phenylacetaldehyde selectivity by suppressing its trimerization which occurred at external acid sites. When the P/Al ratio ≤ 1, catalyst lifetimes extended because of the decrease in strong acid strength. Hard coke, which preferentially formed on strong acid sites, was considerably inhibited in the presence of phosphorus [97].

4.2 Scope of this study

From previous literature reviews, some of homogeneous and heterogeneous catalysts were found to be used as an efficient catalyst for the isomerization of epoxides. Nonetheless, there are some disadvantages in using these catalysts, such as high cost, toxic, sensitive to air and moisture, high temperature and long reaction time required, and difficulty in separation and recovery. The development of catalytic processes for the aldehyde synthesis from epoxide is still of interest in the fine chemistry. This research focused on the methodology toward the isomerization of epoxides to aldehydes catalyzed by the synthesized metal oxide-pillared clay catalysts.

4.3 Experimental

4.3.1 Instruments and equipments

Spectrometers: The ^{1}H- and ^{13}C-NMR spectra were performed in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR 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: Gas chromatographic analysis was carried out on a Varian gas chromatography instrument equipped with a flame ionization detector (FID) with N_2 as a carrier gas and a 30-m long BP-1 column (0.25-mm outer diameter, 0.25 μm film thickness). Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's silica gel 60 G Art 7734 (70-230 mesh)).

4.3.2 Syntheses

4.3.2.1 Synthesis of starting materials

α-Methyl styrene oxide [95]

α-Methyl styrene (25 mmol) was added to a solution of *N*-bromosuccinimide (25 mmol) in distilled water (40 mL) at room temperature and the reaction mixture was stirred vigorously at room temperature for 2 hours. After that, the product bromohydrin was separated from the aqueous layer which was extracted with diethyl ether. The extracts were combined with the bromohydrin, dried over magnesium sulfate and the solvent removed under reduced pressure. The crude bromohydrin was then dissolved in sodium hydroxide (40 mL, 15% solution) and the mixture stirred for 1 hour at 60°C. After that, the epoxide product was separated from the aqueous layer which was extracted with diethyl ether. The ether extracts were combined with the crude epoxide, dried over magnesium sulfate and the solvent removed under reduced pressure.

α-Methylstyrene oxide: colorless liquid; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.17-7.31 (m, 5H), 2.89-2.90 (d, *J* = 5.4 Hz, 1H), 2.72-2.73 (d, *J* = 5.4 Hz, 1H), 1.64 (s, 3H).

***trans*-Anethole oxide [98]**

To a well-stirred biphasic mixture of 2.0 g of trans-anethole in 60 mL of methylene chloride and 60 mL of 10% sodium carbonate in water in an ice-water bath was added a solution of 5.6 g of m-chloroperoxybenzoic acid (85%, 0.028 mol) in 60 mL of methylene chloride over a period of 2.5 h by means of a syringe pump assembly. The methylene chloride layer was separated, washed with 10% sodium carbonate solution and saturated sodium chloride solution (25 mL), and dried over anhydrous sodium sulfate. Removal of the solvent on a rotary evaporator and distilled in a short path distillation apparatus.

trans-Anethole oxide: colourless to slightly yellow oil; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.18-7.22 (m, 2H), 6.87-6.91 (m, 2H), 3.81-3.83 (m, 3H), 3.55 (d, *J* = 2.0 Hz, 1H), 3.03-3.08 (qd, *J* = 5.1, 2.1 Hz, 1H), 1.45-1.46 (d, *J* = 5.1 Hz, 3H).

Isophorone oxide [99]

In a 100-mL three-necked flask, equipped with a dropping funnel and a thermometer, is placed a solution of 5.52 g (40 mmol) of isophorone and 11.5 mL (120 mmol) of 30% aqueous hydrogen peroxide avoid in 40 mL of methanol. After the contents of the flask have been cooled to 15°C by means of an ice bath, 3.3 mL (20 mol) of 6 N aqueous sodium hydroxide is added, dropwise and with stirring, over a period of 1 hour. During the addition the temperature of the reaction mixture is maintained at 15–20°C with a bath of cold water. After the addition is complete, the resulting mixture is stirred for 3 hours as the temperature of the reaction mixture is maintained at 20–25°C. The reaction mixture is then poured into 50 mL of water, and the resulting mixture is extracted with two 40-mL portions of ether. The combined extracts are washed with water and dried over anhydrous magnesium sulfate. After the bulk of the ether has been removed by distillation (or flash distillation) through a

Vigreux column at atmospheric pressure, the residual liquid is distilled through the Vigreux column under reduced pressure.

Isophorone oxide: colourless liquid; 1H NMR ($CDCl_3$) δ (ppm): 3.04 (s, 1H), 2.59-2.62 (d, J = 13.3 Hz, 1H), 2.05-2.08 (d, J = 14.9 Hz, 1H), 1.78-1.81 (d, J = 14.2 Hz, 1H), 1.64-1.70 (m, 1H), 1.41 (s, 3H), 1.01 (s, 3H), 0.90 (s, 3H).

4.3.2.2 General procedure for the isomerization of epoxides

A round bottom flask was charged with epoxide (1 mmol) in THF (5 mL) and clay catalyst (10 wt%), connected with a condenser. The reaction mixture was continuously stirred for desired time and temperature. After the appropriate time or the reaction was completed, the catalyst was easily filtered out, and thoroughly washed with Et_2O. The solvent was partly evaporated under reduced pressure. The obtained mixture was taken and analyzed by GC with the addition of an exact amount of an appropriate internal standard (biphenyl).

4.3.2.3 General isolation procedure

After the reaction was finished, the products were separated as follows: the solvent was evaporated to dryness under reduced pressure. The crude products were purified by silica gel column chromatography using a mixture of Hexane-EtOAc as a mobile phase. The equivalent fractions monitored by TLC were combined and the solvent was completely evaporated. The residue was characterized by ^{1}H-NMR spectroscopy.

Phenylacetaldehyde: colourless to slightly yellow oily liquid; ^{1}H NMR ($CDCl_3$) δ (ppm): 9.77 (t, J = 2.4 Hz, 1H), 7.28-7.36 (m, 5H), 3.71 (d, J = 2.3 Hz, 2H).

Diphenylacetaldehyde: light yellow liquid; ^{1}H NMR ($CDCl_3$) δ (ppm): 9.96 (d, J = 2.4 Hz, 1H), 7.39 (t, J = 7.3 Hz, 4H), 7.30-7.34 (m, 2H), 7.23 (d, J = 7.0 Hz, 4H), 4.90 (s, 1H).

4.3.2.4 Optimum conditions for the isomerization of styrene oxide

Effect of clay catalyst on the isomerization of styrene oxide

The isomerization of styrene oxide was carried out according to the general procedure as previously described employing various clay catalysts: montmorillonite, Na-montmorillonite, Cr-pillared montmorillonite and Al-pillared montmorillonite as a catalyst.

Effect of solvent on the isomerization of styrene oxide

The isomerization of styrene oxide was performed according to the general procedure as described above except for dichloromethane, 1,2-dichloroethane, 1,4-dioxane, ethylacetate, tetrahydrofuran, acetonitrile and toluene were used as a reaction medium. 5 mL of each solvent was used.

Effect of time and temperature on the isomerization of styrene oxide

The isomerization of styrene oxide was carried out according to the general procedure as previously described, but different reaction temperatures (30°C, reflux temperature) and reaction times (5 min, 15 min, 2 h, 4 h, 6 h) were varied.

Effect of catalyst amount on the isomerization of styrene oxide

The isomerization of styrene oxide was performed according to the general procedure as described above, but the amount of catalyst was varied: 0, 2.5, 5 and 10 wt% of catalyst to styrene oxide.

4.3.2.5 Study on the isomerization of various selected epoxides

According to the general procedure, the isomerization of various selected epoxides such as α-methylstyrene oxide, *trans*-stilbene oxide, *trans*-anethole oxide, phenyl glycidyl ether, *tert*-butyl glycidyl ether and isophorone oxide to the corresponding aldehydes were experimented using Cr-pillared montmorillonite as catalyst at reflux temperature for 15 min.

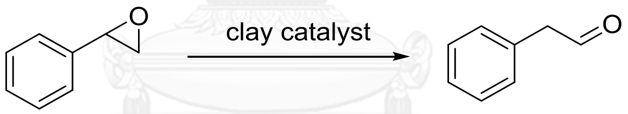
4.3.2.6 Reuse of catalysts

The used chromium oxide-pillared montmorillonite were easily regenerated by dried in an oven at 120°C for 2 h. Then, the regenerated clay catalyst was tested in the next run under the same reaction conditions for the isomerization of styrene oxide.

4.4 Results and discussion

4.4.1 Optimum conditions for the isomerization of styrene oxide

The isomerization of styrene oxide to produce phenylacetaldehyde was selected for testing the catalytic activity of synthesized clay catalysts. Various factors were carefully investigated to optimize the conditions for the synthesis of phenylacetaldehyde. The type of clay catalyst, the type of solvent, the reaction time and temperature and the amount of clay catalyst were varied to search for the optimal conditions.



4.4.1.1 Effect of clay catalyst on the isomerization of styrene oxide

The goal of this research was to screen for suitable catalysts that could furnish corresponding aldehyde in high yield with good selectivity. The catalytic activity of metal oxide-pillared clays such as Cr-PLM, Al-PLM, and $NdCl_3$ impregnated Al-PLM were compared with montmorillonite. The investigated conditions were 10 wt% catalysts to styrene oxide at reflux temperature for 4 h. The results are shown in Table 4.1.

Table 4.1 Effect of clay catalyst on the isomerization of styrene oxide

Entry	Clay catalyst	BET Surface area (m^2/g)	Acidity (mmol/g)	% Recovery	%Yield[a]
1	-	-	-	99	0
2	montmorillonite	58.4	1.188	97	0
3	Na-montmorillonite	104.0	1.357	98	0
4	Cr-PLM	91.2	2.039	0	quant.
5	Al-PLM	205.6	1.615	81	15
6	$NdCl_3$/Al-PLM	170.5	1.751	85	9

Reaction conditions: styrene oxide (1 mmol), clay catalyst (10 wt%), THF (5 mL) at reflux temperature for 4 h

[a] The yield was determined by GC using biphenyl as an internal standard

No product was obtained when the reactions were performed in the absence of clay catalyst or in the presence of montmorillonite or Na-montmorillonite. All synthesized clays gave much higher yield of phenylacetaldehyde than montmorillonite clay. The acidity of clay catalysts that determined from the temperature programmed desorption experiment corresponds to this result (entries 4-6). Cr-PLM, Al-PLM and $NdCl_3$ impregnated Al-PLM had acidity higher than montmorillonite. The reactions catalyzed by Al-PLM or $NdCl_3$ impregnated Al-PLM afforded low yields of the desired products (entries 5, 6). Cr-PLM showed the best catalytic activity in the isomerization of styrene oxide to produce quantitative yield of phenylacetaldehyde when performed the reaction in refluxing THF for 4 h (entry 4). Due to the highest acidity among all synthesized clay catalysts and the suitable interlayer spacing of Cr-PLM. Consequently, Cr-PLM was selected for additional experiments.

4.4.1.2 Effect of solvent on the isomerization of styrene oxide

To examine the effect of solvent for the isomerization of styrene oxide, various solvents including dichloromethane, 1,2-dichloroethane, 1,4-dioxane, ethylacetate, tetrahydrofuran, acetonitrile and toluene were investigated. The effect of solvents on the isomerization of styrene oxide was performed with 5 mL of solvent using 1 mmol of styrene oxide and 10 wt% of Cr-pillared montmorillonite to styrene oxide under room temperature for 15 min. The results are demonstrated in Table 4.2.

Table 4.2 Effect of solvent on the isomerization of styrene oxide

Entry	Solvent	%Recovery	%Yield[a]
1	CH_2Cl_2	88	6
2	1,2-DCE	81	12
3	1,4-dioxane	72	22
4	EtOAc	84	14
5	THF	70	35
6	CH_3CN	95	3
7	toluene	100	10

Reaction conditions: styrene oxide (1 mmol), Cr-PLM (10 wt%), solvent (5 mL) at room temperature (30°C) for 15 min

[a] The yield was determined by GC using biphenyl as an internal standard

The isomerization of styrene oxide to phenylacetaldehyde was performed in various solvents. The highest yield of product was obtained when using THF (entry 5). The use of 1,4-dioxane provided the desired product in 22% yield (entry 3), whereas using solvents which were inexpensive and commercially available such as dichloromethane, 1,2-dichloroethane, ethylacetate, acetronitrile or toluene, the products were obtained in low yields. Although previous studies have reported the use of dichloromethane, 1,2-dichloroethane and toluene as a reaction medium, when this catalytic system was performed in dichloromethane, 1,2-dichloroethane or toluene, the desired product was observed in low yield [85]. The yield of phenylacetaldehyde was found to depend on type of solvent. Hence, THF was selected as a solvent for additional experiments.

4.4.1.3 Effect of time and temperature on the isomerization of styrene oxide

The effect of time and temperature for the isomerization of styrene oxide were investigated by carried out under room temperature (30°C) and reflux temperature at different times to obtain the optimum conditions. The results are shown in Table 4.3.

Table 4.3 Effect of time and temperature on the isomerization of styrene oxide

Entry	Temperature	Time	%Recovery	%Yield[a]
1	RT (30°C)	15 min	70	35
2	RT (30°C)	2 h	24	76
3	RT (30°C)	4 h	0	93
4	RT (30°C)	6 h	0	quant.
5	reflux	5 min	14	89
6	reflux	15 min	0	quant.

Reaction conditions: styrene oxide (1 mmol), Cr-PLM (10 wt%), THF (5 mL)

[a] The yield was determined by GC using biphenyl as an internal standard

The reaction was perform under room temperature at first. The yield of the product was increased when the reaction time increased (entries 1-4). The isomerization of styrene oxide catalyzed by Cr-PLM could be completely performed under room temperature within approximately 6 h to obtain product in quantitative yield. Nevertheless, the shorten reaction time could be achieved by temperature increasing (entry 5). The appropriate reaction time and temperature for the isomerization of styrene oxide to phenylacetaldehyde were performed in refluxing THF for 15 min (entry 6).

4.4.1.4 Effect of catalyst amount on the isomerization of styrene oxide

The reaction efficiency mostly influenced by the amount of catalyst. The variation of the amount of Cr-PLM as 2.5, 5 and 10 wt% was used to examine the suitable clay catalyst amount for the isomerization of styrene oxide. The effect of the Cr-PLM amount for the isomerization was investigated. The results are shown in Table 4.4.

Table 4.4 Effect of catalyst amount on the isomerization of styrene oxide

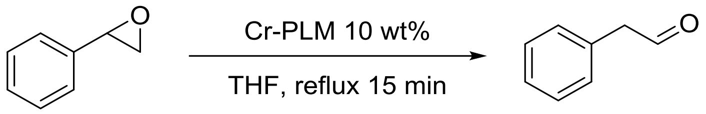
Entry	Catalyst amount	%Recovery	%Yield[a]
1	-	99	0
2	2.5 wt%	12	88
3	5 wt%	0	quant.
4	10 wt%	0	quant.

Reaction conditions: styrene oxide (1 mmol), Cr-PLM (vary), THF (5 mL) at reflux temperature for 15 min

[a] The yield was determined by GC using biphenyl as an internal standard

The result from table 4.4 demonstrates that the Cr-PLM amount obviously affected the yield. The yield of desired product was significantly increased when the amount of Cr-PLM increased (entries 1-3). The addition of clay catalyst amount to 5 or to 10 wt%, the yield of product could be obtained in quantitative. Thus, the Cr-PLM amount of 10 wt% was selected for additional experiments.

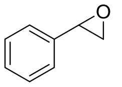
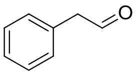
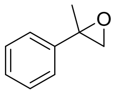
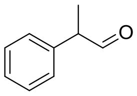
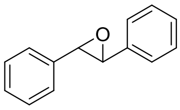
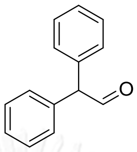
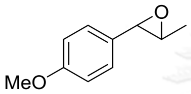
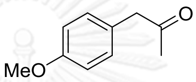
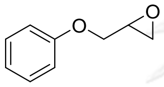
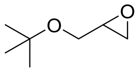
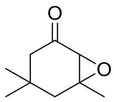
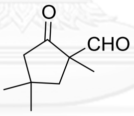
It could be summarized that the optimum conditions for the isomerization of styrene oxide catalyzed by Cr-PLM are as follows: styrene oxide 1 mmol, THF 5 mL, 10 wt% Cr-PLM to styrene oxide at reflux temperature for 15 min. The phenylacetaldehyde was obtained in quantitative yield. Therefore, these conditions were applied for additional experiments as standard conditions.



4.4.2 The isomerization of various epoxides catalyzed by Cr-PLM

A wide range of epoxides including α-methyl styrene oxide, *trans*-stilbene oxide, *trans*-anethole oxide, phenyl glycidyl ether, *tert*-butyl glycidyl ether and isophorone oxide were subjected to isomerization by standard conditions to provide the corresponding product. Some epoxides could not be obtained by commercial thus they were prepared from the corresponding alkenes with strong oxidizing agent according to the procedure as previously described [95, 98, 99]. α-Methyl styrene oxide, *trans*-anethole oxide and isophorone oxide were prepared and characterized by NMR Spectroscopy. The difference in the product formations was explained by the nature of epoxides and catalysts. The results are displayed in Table 4.5.

Table 4.5 The isomerization of various epoxides catalyzed by Cr-PLM

Entry	Substrate	Product	%Recovery	%Yield[a]
1			0	quant.
2			90	0
3			60	35
4			93	0
5			80	0
6			67	0
7			97	0

Reaction conditions: epoxide (1 mmol), Cr-PLM (10 wt%), THF (5 mL) at reflux temperature for 15 min

[a] The yield was determined by GC using biphenyl as an internal standard

Other epoxides such as α-methyl styrene oxide, *trans*-anethole oxide, phenyl glycidyl ether, *tert*-butyl glycidyl ether and isophorone oxide (entries 2, 4-7) could not isomerized to carbonyl compound under these standard conditions. While the isomerization of *trans*-stilbene oxide was carried out in low yields of the diphenylacetaldehyde (35%). Thus the appropriate conditions for enhance the yield of the isomerization reaction will be investigated as the following study.

4.4.2.1 The isomerization of trans-stilbene oxide catalyzed by Cr-PLM

The isomerization of trans-stilbene oxide has been used to demonstrate regioselectivity, since isomerization can take place with either phenyl migration to produce diphenylacetaldehyde or with hydrogen migration to furnish deoxybenzoin. The reaction time and the amount of Cr-PLM for the isomerization of trans-stilbene oxide were examined to optimize the reaction conditions. The results are shown in Table 4.6.

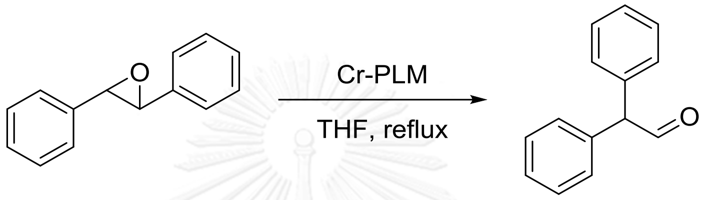


Table 4.6 The isomerization of trans-stilbene oxide catalyzed by Cr-PLM

Entry	Catalyst amount	Time	%Recovery	%Yield[a]
1	10 wt%	15 min	60	35
2	10 wt%	1 h	44	51
3	10 wt%	6 h	11	73 (12)*
4	30 wt%	1 h	5	91
5	30 wt%	4 h	6	92

Reaction conditions: *trans*-stilbene oxide (1 mmol), Cr-PLM (vary), THF (5 mL) at reflux temperature

[a] The yield was determined by GC using biphenyl as an internal standard

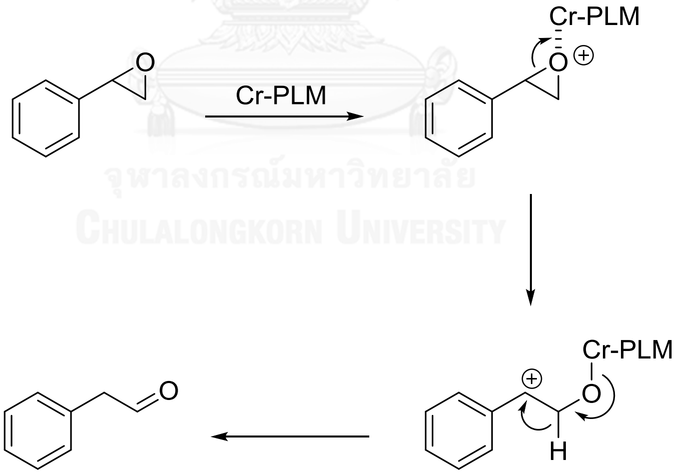
* The yield of the side products is shown in the parenthesis

From Table 4.6, the isomerization of *trans*-stilbene oxide to corresponding aldehyde could be carried out utilizing Cr-PLM at reflux temperature. The yield of product was increased when prolonged the reaction time (entries 1-3). However, a long reaction time as 6 h lead to the formation of undesired side products (entry 3).

Increasing amount of Cr-PLM from 10 to 30 wt%, only desired product was obtained in excellent yield (entries 2, 4). Prolonged the reaction time to 4 h could not enhanced the yield (entry 5). It could be concluded that reaction time and the amount of catalyst affected on the catalytic activity. Therefore, the appropriate conditions for the isomerization of *trans*-stilbene oxide to diphenylacetaldehyde are as follows: *trans*-stilbene oxide 1 mmol, THF 5 mL, 30 wt% Cr-PLM to *trans*-stilbene oxide at reflux temperature for 1 h. Under these conditions trans-stilbene oxide underwent regioselective isomerization to produce diphenylacetaldehyde in excellent yield as the major product.

4.4.3 The proposed mechanism for the isomerization of styrene oxide

The proposed mechanism of the isomerization of styrene oxide employing Lewis acid catalyst was believed to proceed *via* the following pathway as proposed in literature [82]. The proposed mechanism is presented in Scheme 4.1.



Scheme 4.1 Proposed mechanism for the isomerization of styrene oxide catalyzed by Cr-PLM

Formation of the aldehyde proceeds *via* coordination of metal cation of catalyst to the oxygen atom of the epoxide followed by C–O bond cleavage to form a more stable benzylic carbonium ion. Followed by 1,2-shift of a hydrogen atom and and regenerated the active catalyst to give phenylacetaldehyde.

4.4.4 Reuse of catalysts

4.4.4.1 Activity of regenerated Cr-PLM for the isomerization of styrene oxide

Chromium-pillared montmorillonite could be easily recovered by filtered out from the reaction mixture, washed with diethyl ether and then dried at 120°C in oven for 2-4 h. The recovered Cr-PLM was used in the next run under the same standard conditions. The results are displayed in Table 4.7.

Table 4.7 Activity of regenerated Cr-PLM for the isomerization of styrene oxide

Entry	Cr-PLM*	%Recovery	%Yield[a]
1	fresh	0	quant.
2	reused 1st	0	quant.
3	reused 2nd	0	quant.
4	reused 3rd	0	quant.
5	reused 4th	0	quant.
6	reused 5th	0	quant.

Reaction conditions: styrene oxide (1 mmol), Cr-PLM (10 wt%), THF (5 mL) at reflux temperature for 15 min

[a] The yield was determined by GC using biphenyl as an internal standard

The yield of the phenylacetaldehyde product from the isomerization of styrene oxide was remained in quantitative by the recovered catalyst for five times. The using of the sixth regenerated Cr-PLM, the lower yield was obtained corresponding to the result of the difference in d_{001} spacing and lower BET specific surface area (< 69.24 m^2/g). The X-ray diffraction patterns of fresh Cr-PLM and regenerated Cr-PLM from the isomerization of styrene oxide are displayed in Figure 4.1.

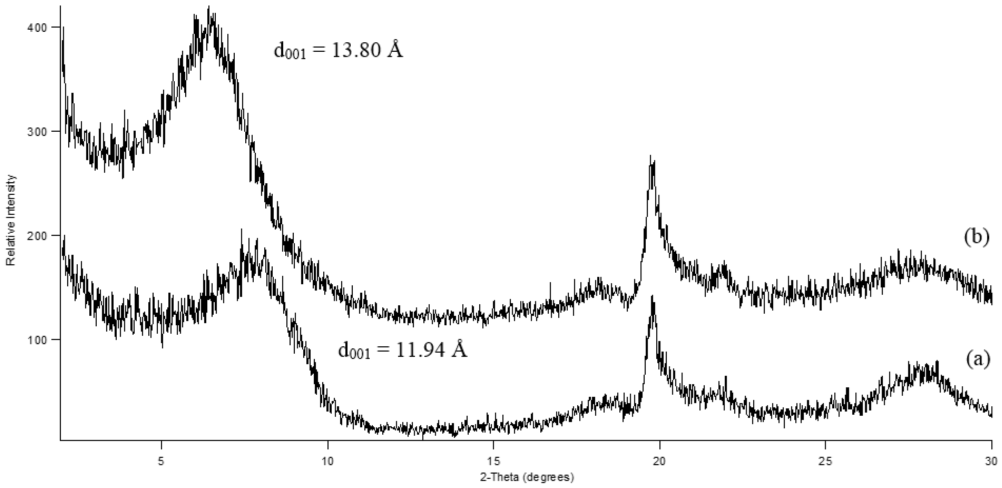


Figure 4.1 XRD patterns of (a) fresh Cr-PLM and (b) regenerated Cr-PLM

4.5 Conclusion

The Cr-PLM catalytic activities were performed for the isomerization of styrene oxide. The optimum conditions were 10 wt% Cr-PLM to styrene oxide at refluxing THF for 15 min. This catalytic system was performed in short period of time under mild conditions successfully providing the desired product in quantitative yield. Under the same reaction condition, Cr-PLM showed higher catalytic efficiency than Al-PLM, $NdCl_3$/Al-PLM and montmorillonite owing to the highest acidity of Cr-PLM.

From the variation of epoxides, the yields of products highly depended on the starting epoxide structure. The optimum conditions for *trans*-silbene oxide were 30 wt% Cr-PLM to *trans*-silbene oxide at refluxing THF for 1 h.

The Cr-PLM catalyst could be reused at least five times without loss of catalytic activity. Clay catalysts were inexpensive, convenient, non-toxic, recoverable and reusable, which led to a highly attractive and efficient procedure for the isomerization reaction.

CHAPTER V

THE SYNTHESIS OF ACETONIDES CATALYZED BY CLAY CATALYST

5.1 Introduction

5.1.1 The importance of acetonides

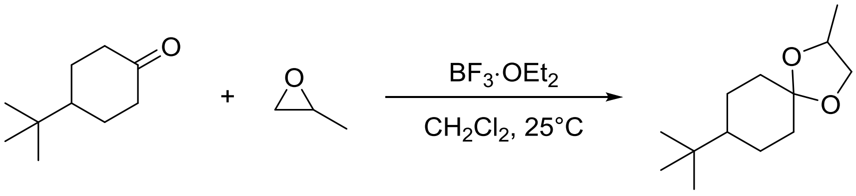
One of the most useful methods for protecting carbonyl functional groups is acetalization. 1,3-Dioxolanes are widely used in the synthetic carbohydrate and steroid chemistry [100-102]. In the pharmaceutical and fragrance industries, acetonides (1,3-dioxolanes) are used both as intermediates and as final products [103, 104]. Acetonides can be prepared from epoxides with carbonyl compounds, generally with ketones, in the presence of Brønsted or Lewis acid catalysts.

5.1.2 Literature review on the synthesis of acetonides

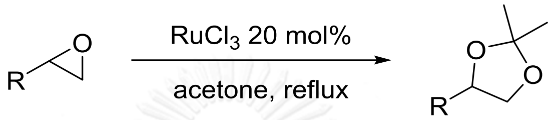
Epoxides can be transformed to acetonides straightforwardly by appropriate acid catalyst. Numerous procedures are reported in the literature for the synthesis of acetonides from epoxides using Brønsted or Lewis acid catalysts.

5.1.2.1 Homogeneous catalysis

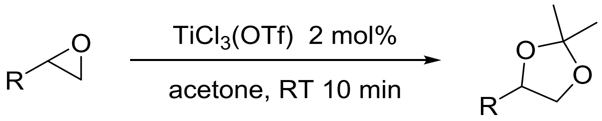
In 1993, Torok and co-workers reported the utilization of boron trifluoride diethyl etherate as Lewis acid for the reaction of epoxides with ketones leading to an acetal formation. $BF_3{\cdot}Et_2O$ was found to be an effective catalyst in reacting 4-*tert*-butylcyclohexanone with propylene oxide to produce the corresponding acetal in 80% isolated yield [105].



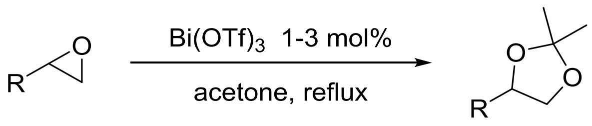
In 1998, Iranpoor and Kazemi reported that Ru(III) as anhydrous $RuCl_3$ could catalyze the reaction of epoxides with acetone to give the corresponding 1,3-dioxolane in 86-91% yield. Epoxides with both electron donating and withdrawing groups were reacted with acetone in the presence of anhydrous $RuCl_3$ under reflux for 1.5-4h. The high yield of products, simple work up and mild reaction conditions made this procedure a useful method for this transformation [106].



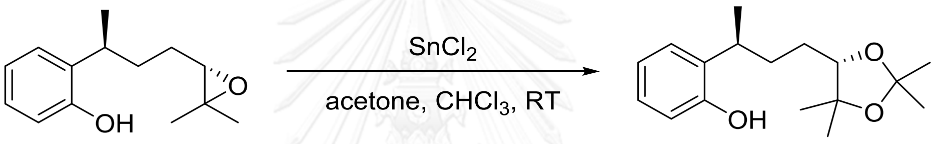
Iranpoor and Zeynizadeh reported the efficient reaction of epoxides with acetone catalyzed by $TiO(TFA)_2$ or $TiCl_3(OTf)$ to give the corresponding 1,3-dioxolanes in excellent yields. These solid titanium(IV) compounds are stable and can be prepared from $TiCl_4$. Epoxides with both electron-donating and withdrawing groups were treated with these catalysts in acetone. $TiCl_3(OTf)$ was observed to be more efficient than $TiO(TFA)_2$ which reactions could be occured at room temperature and only 2 mol% of the catalyst was used to convert epoxides to their corresponding product within 10 min in 92-98% yields [107].

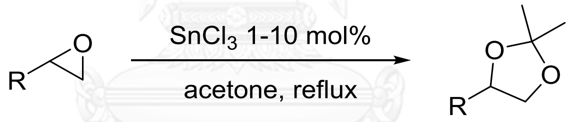


Bi(III) catalysts have attracted the attention since they could be an efficient catalyst for various epoxide transformations. In 2001, Mohammadpoor-Baltork and co-workers reported the conversion of epoxides with acetone catalyzed by $BiCl_3$, $Bi(TFA)_3$ and $Bi(OTf)_3$ affording their 1,3-dioxolanes in excellent yields. $Bi(OTf)_3$ displayed more efficient activity than $BiCl_3$ and $Bi(TFA)_3$ with lower catalyst loading and short reaction time [108].

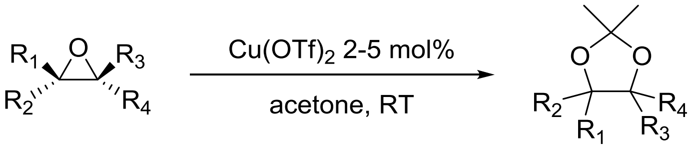


In 2003, Vyvyan and co-workers reported that anhydrous $SnCl_2$ is an efficient catalyst for the conversion of mono-, di-, and tri-substituted epoxides to their 1,3-dioxolane derivatives. The synthesis of benzoxocane-containing natural products by reacting 2-((S)-4-(2,3,3-trimethyloxiran-2-yl)butan-yl)phenol with acetone and anhydrous $SnCl_2$ in chloroform. The 2-((S)-4-(2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)butan-2-yl)phenol was obtained in moderate yield (46%) [109].

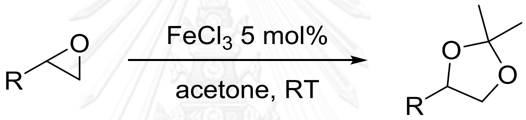




In 2005, Lee and co-workers reported the utilization of copper(II) triflate as catalyst for the formation of 1,3-dioxolanes from epoxides. In case of aryl-substituted epoxides, the rate of product formation was fast in the presence of 2 mol% of catalyst and the reaction was completed within 4 h at room temperature. With akyl-substituted epoxides the rate of product formation was slow under same reaction conditions. The Lewis acid-catalyzed reaction of an epoxide with a carbonyl compound proceeds *via* complexation of the acid with the oxygen atom of epoxide, followed by nucleophilic attack on the epoxide by the carbonyl oxygen to form the dioxolane ring formation [110].

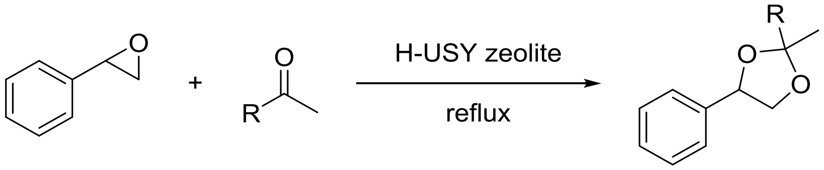


In 2008, Saha and co-workers demonstrated an efficient method for the preparation of acetonides from epoxides catalyzed by iron(III) chloride. The reaction carried out smoothly with 5 mol% of $FeCl_3$ and acetone under room temperature to yield the corresponding acetonides in high yields. Conversion of styrene epoxide derivatives to the 1,3-dioxolanes was quite faster than the conversion of aliphatic epoxides. This can be explained by the stability of the benzylic carbonium ion formed during epoxide cleavage [111].

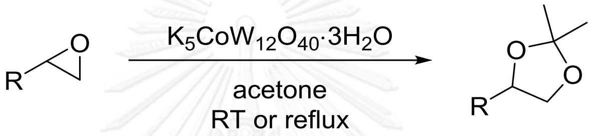


5.2.1.2 Heterogeneous catalysis

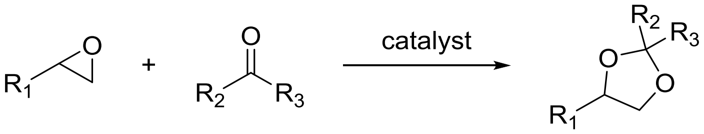
In recent years, catalysis research have great attempted on the development and application of effective heterogeneous catalysts. The synthesis of 1,3-dioxolanes catalyzed by several solid acids was found to be an another important goal for industry and organic synthesis. In 1991, Wieslaw Zatorski and Wierzchowski reported the reaction between styrene oxide and aliphatic ketone in the presence of H-form of zeolites affording almost complete conversion of the epoxide (except for HY zeolite). The application of H-USY for this reaction gave 15-56% dioxolane yield with 99% styrene oxide conversion. The dioxolane selectivity is strongly influenced by a structure of zeolite and ketone molecule and less by zeolite acidity [112].



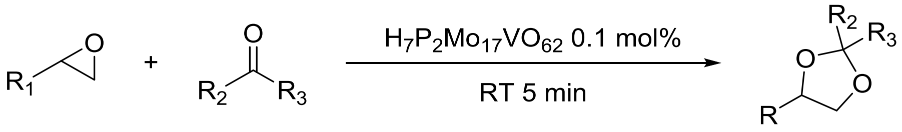
In 2001, Habibi and co-workers reported a mild and efficient the synthesis of 1,3-dioxolanes from epoxides using potassium dodecatungstocobaltate trihydrate ($K_5CoW_{12}O_{40}{\cdot}3H_2O$). 1,3-Dioxolanes were obtained high to excellent yields. Steric hindrance about the epoxide and electron withdrawing groups strongly inhibits acetal formation. $K_5CoW_{12}O_{40}{\cdot}3H_2O$ could be reused several times without loss of activity, only by filtering the catalyst, washing with acetone, drying and instantly reusing. The acetonide formation proceeded by the recovered catalyst for four times remained 95% yield and after seven times was around 85% yield [113].



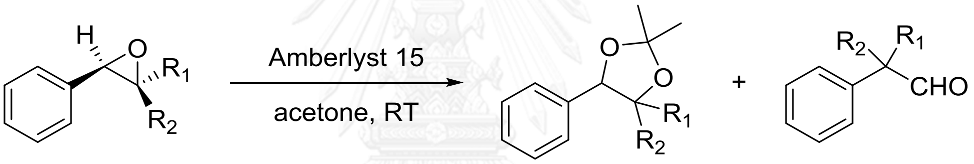
Bucsi and co-workers investigated various Brønsted acid catalysts for the synthesis of 1,3-dioxolanes from various epoxides and ketones. Nafion-H, heteropoly acids and K10 montmorillonite were tested under different conditions. K10 montmorillonite was the best catalyst to promote 1,3-dioxolanes. The yield of 1,3-dioxolane reduces with the increasing of the carbon number of ketones [114].



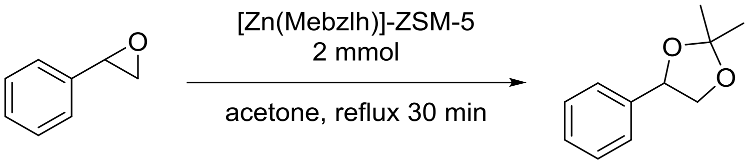
In 2005, Li and co-workers reported the utilization of Wells–Dawson type heteropoly acids ($H_{6+n}P_2Mo_{18-n}V_nO_{62}$) ($n = 0–2, 4$) as effective catalysts for the reactions between epoxides and aldehydes or ketones to produce 1,3-dioxolanes. A wide range of epoxides could be efficiently transformed to 1,3-dioxolanes over $H_7P_2Mo_{17}VO_{62}$ catalyst within 5 min at room temperature. Short reaction time, simple work up, mild reaction conditions and dependable reusability was obtained in this catalytic systems [115].



In 2006, Solladié-Cavallo and co-workers reported the enantiospecific conversion of mono- and diaryl-substituted epoxides directly to their 2,2-dimethyl-1,3-dioxolane derivatives by acetone in the presence of the acid resin Amberlyst 15. Under the standard conditions, the dioxolane (R_1 = R_2 = H) was obtained in 82% yield, together with an 18% yield of phenylacetaldehyde [116].



In 2010, Nethravathi and co-workers reported the reaction of styrene oxide with acetone catalyzed by zeolite encapsulated Zn(II) complexes with 2-methyl benzimidazole (Mebzlh). The 90% yield of 2,2-dimethyl-4-phenyl-[1,3]-dioxolane was observed with catalyst [Zn(Mebzlh)]-ZSM-5 under reflux condition. Furthermore, the catalyst could be reused twice and no leaching of metal complex was observed [117].



5.3 Scope of this study

From previous literature reviews, some of homogeneous and heterogeneous catalysts were found to be used as an efficient catalyst for the synthesis of acetonides. Nonetheless, there are some disadvantages in using these catalysts, such as high cost, toxic, sensitive to air and moisture, high temperature and long reaction time required, and difficulty in separation from the reaction mixture. The development of catalytic processes for the synthesis of acetonides from epoxide is still of interest in the fine chemistry. This research focused on the methodology toward the synthesis of acetonides catalyzed by the synthesized metal oxide-pillared clay catalysts.

5.4 Experimental

5.4.1 Instruments and equipments

Spectrometers: The ^{1}H- and ^{13}C-NMR spectra were performed in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR 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: Gas chromatographic analysis was carried out on a Varian gas chromatography instrument equipped with a flame ionization detector (FID) with N_2 as a carrier gas and a 30-m long BP-1 column (0.25-mm outer diameter, 0.25 μm film thickness). Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Merck’s, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck’s silica gel 60 G Art 7734 (70-230 mesh)).

5.4.2 Syntheses

5.4.2.1 General procedure for the synthesis of acetonides

A round bottom flask was charged with styrene oxide (1 mmol), acetone (3 mL) and clay catalyst (10 wt%), connected with a condenser. The reaction mixture was continuous stirred for desired time and temperature. After the specific time or the reaction was completed, the catalyst was easily filtered out, and thoroughly washed with acetone. The solvent was partly evaporated under reduced pressure. The obtained mixture was taken and analyzed by GC with the addition of an exact amount of an appropriate internal standard (biphenyl).

5.4.2.2 General isolation procedure

After the reaction was finished, the products were separated as follows: the solvent was evaporated to dryness under reduced pressure. The crude products were purified by silica gel column chromatography using a mixture of Hexane-EtOAc as a mobile phase. The equivalent fractions monitored by TLC were combined and the solvent was completely evaporated. The residue was characterized by ^{1}H-NMR spectroscopy.

2,2-dimethyl-4-phenyl-1,3-dioxolane; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.31 (m, 5H), 5.05 (dd, J = 8.6 Hz, 1H), 4.27 (dd, J = 8.6, 6.4 Hz, 1H), 3.67 (t, 1H), 1.52 (s, 3H), 1.48 (s, 3H).

5.4.2.3 Optimum conditions for the synthesis of acetonide from styrene oxide

Effect of clay catalyst on the synthesis of acetonide

The synthesis of acetonide was carried out according to the general procedure as previously described employing various clay catalysts: montmorillonite, Na-montmorillonite, Cr-pillared montmorillonite and Al-pillared montmorillonite as a catalyst.

Effect of reaction time on the synthesis of acetonide

The synthesis of acetonide was carried out according to the general procedure as previously described, but different reaction times (5 min, 10 min, 20 min, 1 h and 2 h) were varied.

Effect of the amount of catalyst on the synthesis of acetonide

The synthesis of acetonide was performed according to the general procedure as described above, but the amount of catalyst was varied: 2, 5, 10, 20 and 30 wt% of catalyst to styrene oxide.

Effect of the amount of substrate on the synthesis of acetonide

The synthesis of acetonide was carried out according to the general procedure as previously described employing various amount of acetone as 1, 2 and 3 mL.

5.4.2.4 The synthesis of acetonides from other epoxides with acetone

According to the general procedure, the conversion of various epoxides such as phenyl glycidyl ether, butyl glycidyl ether, *t*-butyl glycidyl ether and 1-dodecene oxide to the corresponding acetonides were tested using Cr-pillared montmorillonite as catalyst at room temperature for 20 min.

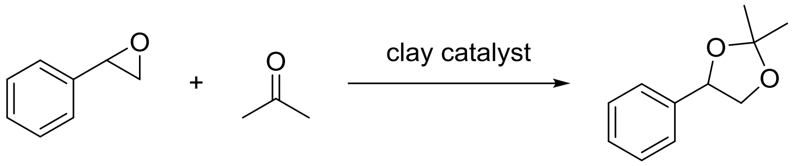
5.4.2.5 Reuse of catalysts

The used Cr-pillared montmorillonite were easily regenerated by dried in an oven at 120°C for 2 h. After that the regenerated clay catalyst was tested in the next run under the same reaction conditions for the synthesis of acetonide.

5.5 Results and discussion

5.5.1 Optimum conditions for the synthesis of acetonide from styrene oxide

The synthesis of 1,3-dioxolane from styrene oxide with acetone was selected for testing the catalytic activity of synthesized clay catalysts. Various factors were carefully investigated to optimize the conditions for the preparation of acetonide. The type of clay catalyst, the reaction time, the amount of catalyst and the amount of acetone were varied to search for the optimal conditions.



5.5.1.1 Effect of clay catalyst on the synthesis of acetonide

To screen for appropriate catalysts that could provide acetonide derivatives in high yield with good selectivity. The catalytic activity of metal oxide-pillared clays such as Al-PLM, $NdCl_3$ impregnated Al-PLM, and Cr-PLM were tested and compared with montmorillonite. The investigated conditions were 10 wt% clay catalysts to styrene oxide at room temperature (30°C) for 2 h. The results are displayed in Table 5.1.

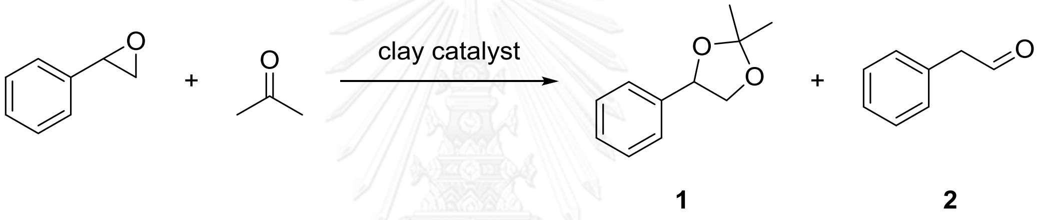


Table 5.1 Effect of clay catalyst on the synthesis of acetonide from styrene oxide

Entry	Catalyst	Acidity (mmol/g	%Recovery	%Yield[a]		MB
				1	2*	
1	-	-	96	0	2	98
2	Montmorillonite	1.188	88	0	3	91
3	Na-M	1.357	93	0	3	96
4	Al-PLM	1.615	85	0	3	88
5	$NdCl_3$/Al-PLM	1.751	90	0	3	93
6	Cr-PLM	2.039	0	96	8	104

Reaction conditions: styrene oxide (1 mmol), acetone (3 mL) and clay catalyst (10 wt%) under room temperature for 2 h, * %Yield of phenylacetaldehyde

[a] The yield was determined by GC using biphenyl as an internal standard

When the reactions were carried out in the absence of clay catalyst or in the presence of montmorillonite, Na-montmorillonite, Al-PLM and $NdCl_3$/Al-PLM, no desired product was obtained (entries 1-5). Although the result from the temperature programmed desorption experiment showed that Al-PLM and $NdCl_3$/Al-PLM had acidity higher than montmorillonite and Na-montmorillonite, these clay catalysts could not be used for catalyze the synthesis of acetonide. Cr-pillared clay gave 96% yield of acetonide much higher than all types of clay catalyst with 8% of the isomerized aldehyde according to the highest acidity and the suitable interlayer spacing of Cr-PLM (entry 6). Thus, it was revealed that Cr-PLM could be used as an appropriate catalyst for the synthesis of acetonide from styrene oxide.

5.5.1.2 Effect of reaction time on the synthesis of acetonide

The effect of reaction time for the synthesis of acetonide were investigated by performed under room temperature (30°C) at different times to obtain the optimum conditions. The results are shown in Table 5.2.

Table 5.2 Effect of reaction time on the synthesis of acetonide

Entry	Catalyst	Time (h)	%Recovery	%Yield[a]		MB
				1	2*	
1	Cr-PLM	2	0	96	8	104
2		1	0	102	9	111
3		20 min	0	93	11	104
4		10 min	1	92	10	103
5		5 min	2	93	11	106

Reaction conditions: styrene oxide (1 mmol), acetone (3 mL) and Cr-PLM (10 wt%) under room temperature, * %Yield of phenylacetaldehyde

[a] The yield was determined by GC using biphenyl as an internal standard

The effect of the reaction time of the Cr-PLM for the synthesis of acetonide was studied by charging with 10 wt% clay catalyst to styrene oxide. The recovery of substrate was reduced when the reaction time increased. It could be seen that the high yield of product was obtained while performing the reaction within 20 min (entry 3). The formation of phenylacetaldehyde as a side product proceeded *via* the pathway as proposed in Scheme 4.1.

5.5.1.3 Effect of the amount of catalyst on the synthesis of acetonide

The amount of catalyst frequently influenced the reaction efficiency. The amount of Cr-PLM as 2, 5, 10, 20 and 30 wt% was used to examine the appropriate clay catalyst amount for the synthesis of acetonide. The results are demonstrated in Table 5.3.

Table 5.3 Effect of the amount of catalyst on the synthesis of acetonide

Entry	Amount of catalyst	%Recovery	%Yield^a		MB
			1	2*	
1	2 wt%	6	81	10	97
2	5 wt%	4	96	11	111
3	10 wt%	0	93	11	104
4	20 wt%	0	95	10	105
5	30 wt%	0	96	11	107

Reaction conditions: styrene oxide (1 mmol), acetone (3 mL) and Cr-PLM (vary) under room temperature for 20 min, * %Yield of phenylacetaldehyde

[a] The yield was determined by GC using biphenyl as an internal standard

The result from table 5.3 showed that when the amount of catalyst was increased from 2-10 wt%, the recovery of substrate was reduced. The addition of clay catalyst amount to 20 or to 30 wt%, the high yield of product still be obtained with the same phenylacetaldehyde yield (entries 4, 5). Therefore, the Cr-PLM amount of 10 wt% was selected for additional experiments.

5.5.1.4 Effect of the amount of substrate on the synthesis of acetonide

The variation of the amount of substrate was investigated due to the interest in green chemistry, accomplished by waste minimization and process cost saving. Consequently, an immoderate amount employing should be avoided. The purpose of this effect study was to reduce the amount of substrate while maintaining the reaction efficiency. The effect of the variation of the amount of acetone on the synthesis of acetonide catalyzed by Cr-PLM was investigated and the results are displayed in Table 5.4.

Table 5.4 Effect of the amount of substrate on the synthesis of acetonide

Entry	Acetone	%Recovery	%Yield[a]		MB
			1	2*	
1	1 mL	0	92	10	102
2	2 mL	0	98	9	107
3	3 mL	0	93	11	104

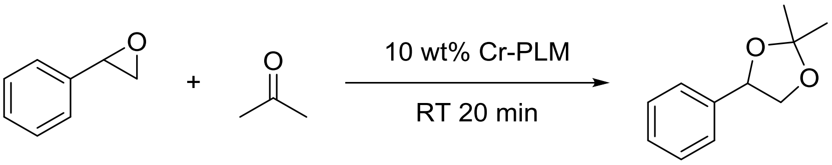
Reaction conditions: styrene oxide (1 mmol), acetone (vary) and Cr-PLM (10 wt%) under room temperature for 20 min, * %Yield of phenylacetaldehyde

[a] The yield was determined by GC using biphenyl as an internal standard

The high yield of acetonide product was obtained, when 2 mL of acetone was used. Furthermore, the yield was slightly diminished, when the amount of acetone was reduced to 1 mL. Since less amount of acetone made the difficulty in substrate diffusion. Thus, the amount of acetone 2 mL was selected for additional experiments.

It could be summarized that the optimum conditions for the synthesis of acetonide from styrene oxide catalyzed by Cr-PLM are as follows: styrene oxide 1 mmol, acetone 2 mL, 10 wt% Cr-PLM to styrene oxide at room temperature (30°C) for

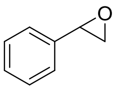
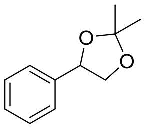
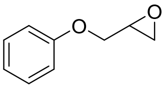
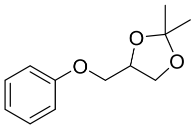
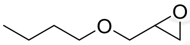
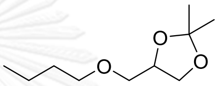
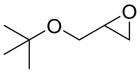
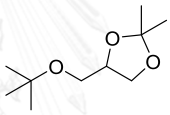
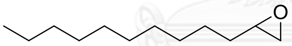
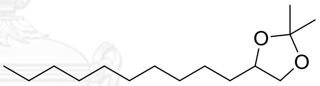
20 min. The 2,2-dimethyl-4-phenyl-1,3-dioxolane was obtained in excellent yield with a small amount of phenylacetaldehyde. Therefore, these conditions were applied for additional experiments as standard conditions.



5.5.2 The synthesis of acetonides from other epoxides with acetone

A variety of epoxides including phenyl glycidyl ether, butyl glycidyl ether, *tert*-butyl glycidyl ether and 1-dodecene oxide were subjected to synthesize by standard conditions providing the acetonide products. The synthesis of acetonides catalyzed by 10 wt% Cr-PLM were carried out under standard conditions (30°C for 20 min). The results are displayed in Table 5.5.

Table 5.5 The synthesis of acetonides from various epoxides under standard conditions

Entry	Epoxides	Acetonides	%Yield[a]
1			98
2			6
3			27
4			10
5			38

Reaction conditions: epoxide (1 mmol), acetone (2 mL) and Cr-PLM (10 wt%) under room temperature for 20 min

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 5.5 show that the styrene oxide could be transformed to acetonide in excellent yield under standard conditions. In the case of butyl glycidyl ether and 1-dodecene oxide, the corresponding acetonides were obtained in moderate yield (entries 3, 5). While the epoxides such as phenyl glycidyl ether and *tert*-butyl glycidyl ether were transformed to corresponding acetonides in low yield (entries 2, 4). The more bulky alkyl or aryl group contain, the less yield of acetonide were obtained. Thus, these standard conditions could be utilized to synthesize acetonides from various epoxides providing low to moderate yield. Consequently, the appropriate conditions for the reaction enhancement will be examined as the following studies.

5.5.2.1 The synthesis of acetonide from glycidyl ethers

Glycidyl ethers are epoxides with ether functional group containing. Some of glycidyl ethers such as phenyl glycidyl ether, butyl glycidyl ether and *tert*-butyl glycidyl ether were examined for acetonide synthesis.

The effect of the amount of Cr-pillared montmorillonite catalyst, reaction temperature and reaction time for the synthesis of acetonide from phenyl glycidyl ether were examined. The results are displayed in Table 5.6.

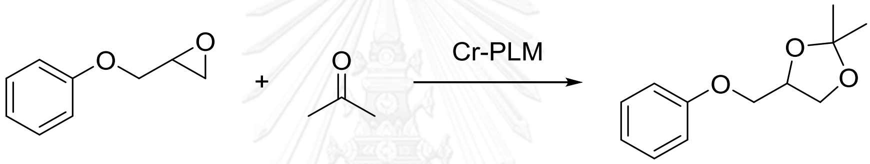


Table 5.6 The synthesis of acetonide from phenyl glycidyl ether

Entry	Cr-PLM	Temp	Time	%Recovery	%Yield[a]	MB
1	10 wt%	RT (30°C)	20 min	98	6	104
2	10 wt%	reflux	2 h	26	72	98
3	10 wt%	reflux	4 h	10	89	99
4	20 wt%	reflux	4 h	2	97	99

Reaction conditions: phenyl glycidyl ether (1 mmol), acetone (2 mL) and Cr-PLM catalyst

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 5.6 show that the synthesis of 2,2-dimethyl-4-(phenoxymethyl)-1,3-dioxolane from phenyl glycidyl ether could be carried out utilizing Cr-PLM catalyst. Carrying out the reaction under the standard conditions, the low yield of the desired product was obtained. As increase reaction temperature to reflux and prolong reaction time, higher yield were satisfactory furnished (entries 2, 3). The more product could be obtained with increasing the amount of Cr-PLM. The reaction gave almost excellent yield utilizing 20 wt% of Cr-PLM at reflux temperature for 4 h. It could be indicated that the reaction temperature, reaction time and the amount of catalyst affected on the catalytic activity.

The 2,2-dimethyl-4-(phenoxymethyl)-1,3-dioxolane product was isolated and identified by ^{1}H NMR spectroscopy.

2,2-dimethyl-4-(phenoxymethyl)-1,3-dioxolane; ^{1}H NMR ($CDCl_3$) δ (ppm): 7.18-7.37 (m, 2H), 6.83-7.03 (m, 3H), 4.42-4.54 (m, 1H), 4.13-4.21 (m, 1H), 4.04-4.08 (dd, *J* = 9.4, 5.5 Hz, 1H), 3.89-3.96 (ddd, *J* = 11.9, 8.9, 5.9 Hz, 2H), 1.47 (s, 3H), 1.41 (s, 3H).

The appropriate conditions for synthesis of acetonide from butyl glycidyl ether were examined by study the effect of the amount of catalyst, reaction time and temperature. The results are shown in Table 5.7.

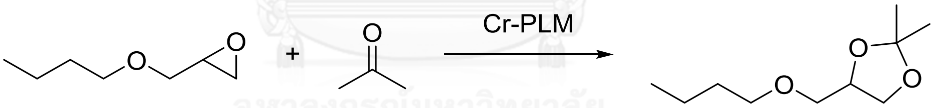


Table 5.7 The synthesis of acetonide from butyl glycidyl ether

Entry	Cr-PLM	Temp	Time	%Recovery	%Yield[a]	MB
1	10 wt%	RT (30°C)	20 min	72	27	99
2	10 wt%	RT (30°C)	2 h	51	52	103
3	10 wt%	reflux	2 h	0	102	102

Reaction conditions: butyl glycidyl ether (1 mmol), acetone (2 mL) and Cr-PLM catalyst

[a] The yield was determined by GC using biphenyl as an internal standard

From Table 5.7, the results indicate that the synthesis of 4-(butoxymethyl)-2,2-dimethyl-1,3-dioxolane from butyl glycidyl ether could be carried out utilizing Cr-PLM catalyst. The desired product was obtained in moderate yield, when the reaction was carried out under the standard conditions. Prolonging the reaction time at room temperature, the acetonide product was obtained more (52%) with starting material recovered (entry 2). Hence, the reaction temperature was increased to reflux utilizing the same amount of catalyst, the corresponding acetonide could be obtained in quantitative yield. The appropriate reaction conditions were utilizing 10 wt% of Cr-PLM at reflux temperature for 2 h.

The 4-(butoxymethyl)-2,2-dimethyl-1,3-dioxolane product was isolated and identified by ^{1}H NMR spectroscopy.

4-(butoxymethyl)-2,2-dimethyl-1,3-dioxolane; ^{1}H NMR ($CDCl_3$) δ (ppm): 4.23-4.29 (quin, 1H), 4.03-4.07 (dd, *J* = 8.2, 6.4 Hz, 1H), 3.70-3.74 (dd, *J* = 8.2, 6.4 Hz, 1H), 3.39-3.53 (m, 5H), 1.52-1.59 (m, 3H), 1.42 (s, 3H), 1.36 (s, 3H), 0.89-0.92 (t, *J* = 7.4 Hz, 3H).

The synthesis of acetonide from *tert*-butyl glycidyl ether were examined by study the effect of the amount of catalyst, reaction time and temperature to obtain the appropriate conditions. The results are displayed in Table 5.8.

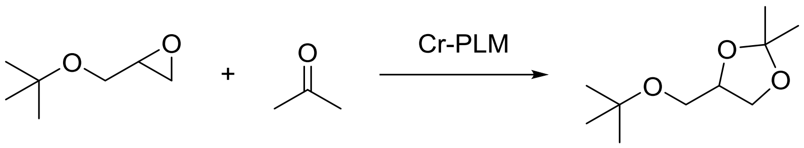


Table 5.8 The synthesis of acetonide from tert-butyl glycidyl ether

Entry	Cr-PLM	Temp	Time	%Recovery	%Yield[a]	MB
1	10 wt%	RT (30°C)	20 min	83	10	93
2	10 wt%	reflux	2 h	10	89	99
3	10 wt%	reflux	4 h	2	97	99

Reaction conditions: *t*-butyl glycidyl ether (1 mmol), acetone (2 mL) and Cr-PLM catalyst

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 5.8 exhibit that the synthesis of 4-(*tert*-butoxymethyl)-2,2-dimethyl-1,3-dioxolane from *tert*-butyl glycidyl ether could be carried out utilizing Cr-PLM catalyst. The low yield of the desired acetonide was obtained, when the reaction was carried out at room temperature under the standard conditions. Increasing the reaction temperature to reflux and prolonging the reaction time, the high yield were obtained (entry 2). The corresponding acetonide was furnished in excellent yield by prolonged the reaction time to 4 h. Thus, the appropriate conditions were using 10 wt% of Cr-PLM at reflux temperature for 4 h.

The 4-(*tert*-butoxymethyl)-2,2-dimethyl-1,3-dioxolane product was isolated and identified by ^{1}H NMR spectroscopy.

4-(tert-butoxymethyl)-2,2-dimethyl-1,3-dioxolane; ^{1}H NMR ($CDCl_3$) δ (ppm): 4.17-4.23 (quin, 1H), 4.06-4.10 (m, 1H), 3.74-3.78 (dd, *J* = 8.2, 6.0 Hz, 1H), 3.48-3.51 (dd, *J* = 9.0, 5.3 Hz, 1H), 3.30-3.34 (dd, *J* = 9.0, 6.7 Hz, 1H), 1.43 (s, 3H), 1.37 (s, 3H), 1.20 (s, 9H).

5.5.2.2 The synthesis of acetonide from aliphatic epoxide

A representative of terminal aliphatic epoxide, 1-dodecene oxide was selected. The effect of the reaction time and temperature were examined to obtain the appropriate conditions for the synthesis of acetonide from 1-dodecene oxide. The results are shown in Table 5.9.

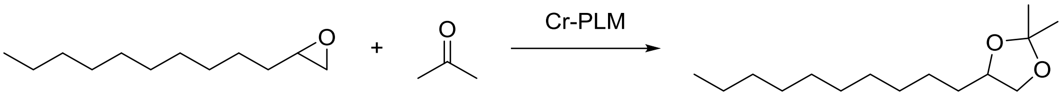


Table 5.9 The synthesis of acetonide from 1-dodecene oxide

Entry	Cr-PLM	Temp	Time	%Recovery	%Yield[a]	MB
1	10 wt%	RT (30°C)	20 min	64	38	102
2	10 wt%	RT (30°C)	2 h	12	86	98
3	10 wt%	reflux	2 h	0	99	99

Reaction conditions: 1-dodecene oxide (1 mmol), acetone (2 mL) and Cr-PLM catalyst

[a] The yield was determined by GC using biphenyl as an internal standard

From Table 5.9, the results indicate that the synthesis of 4-decyl-2,2-dimethyl-1,3-dioxolane could be performed utilizing Cr-PLM catalyst. When the reaction was performed at room temperature under the standard conditions, the moderate yield of the desired acetonide was obtained. Prolonging the reaction time to 2 h, the high yield of the corresponding acetonide was furnished (entry 2). The quantitative yield of acetonide was obtained, when increased the reaction temperature to reflux. The appropriate conditions for this reaction were utilizing 10 wt% of Cr-PLM at reflux temperature for 2 h.

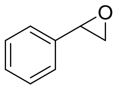
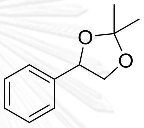
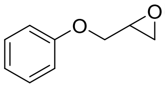
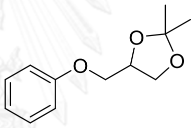
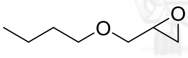
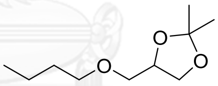
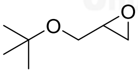
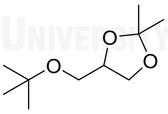
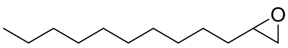
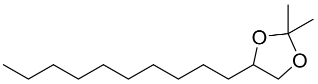
The 4-decyl-2,2-dimethyl-1,3-dioxolane product was isolated and identified by ^{1}H NMR spectroscopy.

4-decyl-2,2-dimethyl-1,3-dioxolane; ^{1}H NMR ($CDCl_3$) δ (ppm): 4.03-4.13 (m, 2H), 3.50-3.54 (t, J = 7.2 Hz, 1H), 1.63-1.68 (m, 2H), 1.43 (s, 3H), 1.38 (s, 3H), 1.28 (s, 16H), 0.88-0.92 (t, J = 6.8 Hz, 3H).

5.5.3 Summary of the synthesis of acetonides from other epoxides with acetone

A variety of epoxides including phenyl glycidyl ether, butyl glycidyl ether, *tert*-butyl glycidyl ether and 1-dodecene oxide were selected to carry out the synthesis of acetonides by utilizing 10-20 wt% of Cr-PLM at reflux temperature for 2-4 h. The results are summarized in Table 5.10.

Table 5.10 The synthesis of acetonides from various epoxides

Entry	Epoxides	Acetonides	%Yield[a]
1[b]			98
2[c]			97
3			102
4[d]			97
5			99

Reaction conditions: epoxide (1 mmol), acetone (2 mL) and Cr-PLM (10 wt%) at reflux temperature for 2 h

[a] The yield was determined by GC using biphenyl as an internal standard

[b] at RT (30°C) for 20 min (under standard conditions)

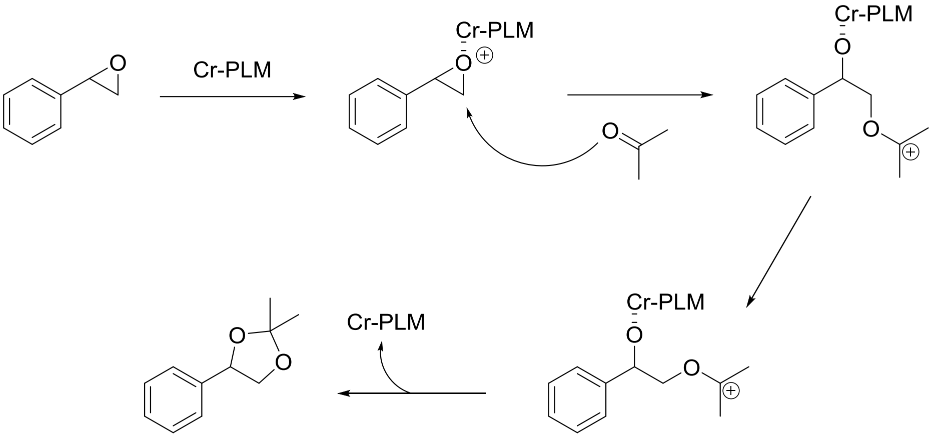
[c] Cr-PLM (20 wt%) at reflux temperature for 4 h, [d] at reflux temperature for 4 h

From Table 5.10, it could be summarized that excellent yields of the corresponding acetonides were obtained in all cases with different conditions. Various epoxides were reacted with acetone utilizing a catalytic amount of Cr-PLM. In a previous experiment, styrene oxide could be transformed to acetonide in excellent yield by performing in the presence of 10 wt% Cr-PLM and acetone at room temperature for 20 min.

In the case of the epoxides with ether functional group containing, the Cr-PLM could be utilized as the efficient catalyst to obtain their corresponding acetonides in high yields. But these epoxides with ethereal linkage need more strongly reaction condition according to the steric effect of bulky alkyl or aryl group (entries 2-4). In the case of terminal aliphatic epoxide such as 1-dodecene oxide, the lower conversions were obtained under the same conditions. The reactions were performed at refluxing acetone for 2 h with Cr-PLM catalyst to furnish quantitative yield (entry 5). The conversion of styrene oxide was much faster than the conversion of 1-dodecene oxide because of the stability of the benzylic carbonium ion formed during epoxide ring cleavage.

5.5.4 The proposed mechanism for the formation of 1,3-dioxolane

The proposed mechanism for the catalysis of the synthesis of acetonide from styrene oxide was believed to proceed *via* the following pathway as presented in Scheme 5.1.



Scheme 5.1 Proposed mechanism for the synthesis of acetonide catalyzed by Cr-PLM

The reaction of an epoxide with a carbonyl compound mediated by Lewis acid was reported to proceed *via* the coordination of a metal cation of the catalyst with the epoxide oxygen, followed by nucleophilic ring-opening of the epoxide by the carbonyl oxygen and finally dioxolane ring formation. Each step of the reaction is reversible, acetonides could be converted to the corresponding ketone in the presence of catalyst. Therefore, the acetal formation is sensitive to structural factors such as steric hindrance which retards the acetal formation.

5.5.5 Reuse of catalysts

5.5.5.1 Activity of regenerated Cr-PLM for the synthesis of acetonide from styrene oxide

Cr-pillared montmorillonite could be easily recovered by filtered out from the reaction mixture, washed with acetone and then dried at 120°C in oven for 2-4 h. The recovered Cr-PLM was used in the next run under the same conditions. The results are displayed in Table 5.11.

Table 5.11 The activity of regenerated Cr-pillared montmorillonite for the synthesis of acetonide from styrene oxide

Entry	Cr-PLM	%Recovery	%Yield[a]		MB
			1	2*	
1	fresh	0	98	9	107
2	reused 1st	0	93	12	105
3	reused 2nd	0	94	10	104
4	reused 3rd	0	92	10	102
5	reused 4th	2	92	8	102
6	reused 5th	0	92	9	101
7	reused 6th	8	78	8	94
8	reused 7th	38	55	8	101

Reaction conditions: styrene oxide (1 mmol), acetone (2 mL) and Cr-PLM (10 wt%) under room temperature for 20 min, * %Yield of phenylacetaldehyde

[a] The yield was determined by GC using biphenyl as an internal standard

The excellent yield of the acetonide product from the reaction of styrene oxide were still obtained by using the recovered catalyst for five times with a small amount of side product. The utilizing of the sixth regenerated Cr-PLM, the more styrene oxide recovered and lower yield was obtained corresponding to the result of the difference in d_{001} spacing of Cr-PLM. The X-ray diffraction patterns of fresh Cr-PLM and regenerated Cr-PLM from the synthesis of acetonide are displayed in Figure 5.1.

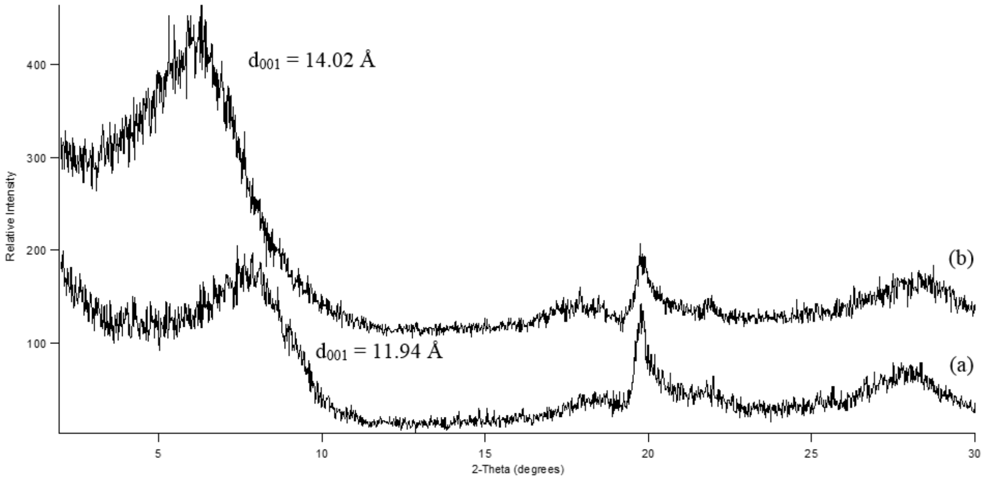


Figure 5.1 XRD patterns of (a) fresh Cr-PLM and (b) regenerated Cr-PLM

5.5.6 Conclusion

The Cr-PLM catalytic activities were carried out for the synthesis of acetonide from styrene oxide. The optimum conditions were using 10 wt% Cr-PLM to styrene oxide at room temperature for 20 min. This catalytic system was carried out in short period of time under mild conditions successfully providing the desired product in excellent yield. Cr-PLM showed higher catalytic efficiency than Al-PLM, $NdCl_3$/Al-PLM and montmorillonite under the same reaction condition because of the highest acidity of Cr-PLM.

From various epoxides, the yields of corresponding products highly depended on the epoxide structure. The optimum conditions could be applied and used for other epoxides including phenyl glycidyl ether, butyl glycidyl ether, *tert*-butyl glycidyl ether and 1-dodecene oxide to furnish acetonides in excellent yield.

The Cr-PLM catalyst could be reused at least five times without loss of catalytic activity. Clay catalysts were inexpensive, convenient, non-toxic, recoverable and reusable, which led to a highly attractive and efficient procedure for the synthesis of 1,3-dioxolanes.

CHAPTER VI

MICHAEL REACTION CATALYZED BY ANION INTERCALATED NiZn

6.1 Introduction

6.1.1 The importance of the Michael reaction

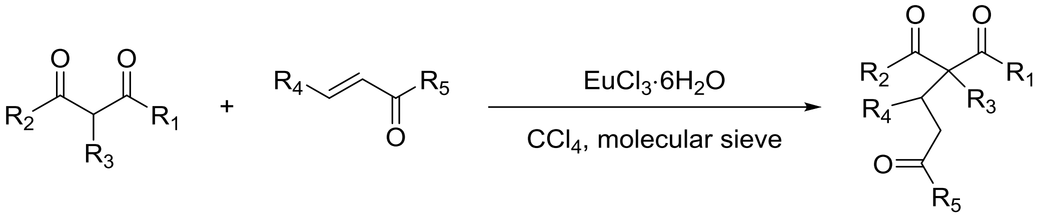
One of the most useful methods for the mild C–C bond formation is Michael reaction or Michael addition. The Michael reaction typically refers to the base catalyzed addition of a nucleophile such as an enolate anion (Michael donor) to an activated α,β-unsaturated carbonyl compound (Michael acceptor) [118]. Base-catalyzed reactions such as Michael addition are conventionally carried out using alkali metal hydroxides or alkoxides [119, 120]. In some cases, a number of side- and subsequent reactions, e.g. ester solvolysis, aldol-cyclizations, and retro-Claisen-type decompositions result in low selectivity of product. The drawbacks from Brønsted basic conditions should be avoided. To achieve this, high-performance catalytic systems employing neutral conditions are desired.

6.1.2 Literature reviews on the Michael reaction

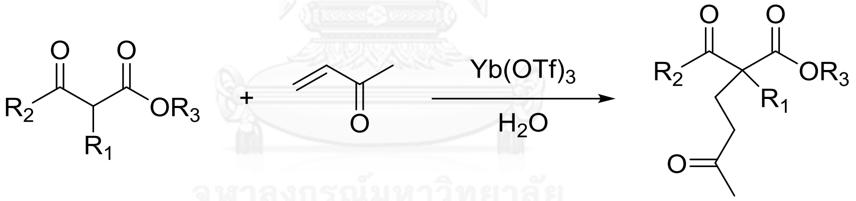
The Michael reaction of 1,3-dicarbonyl compounds with activated enones provides access to 1,5-dioxo synthons, which can be transformed into cyclohexanone derivatives for use as important intermediates in steroid and terpenoid synthesis [121, 122].

6.1.2.2 Homogeneous catalysis

In 1993, Bonadies and co-workers reported the Michael addition of 1,3-dicarbonyl compounds utilizing $EuCl_3$ as an efficient catalyst. The high yield of products (54-85%) could be furnished by performing in anhydrous CCl_4 with the catalytic amount of 10 mol% of $EuCl_3{\cdot}6H_2O$ and activated molecular sieves at RT or 60°C for 20-72 h [123].

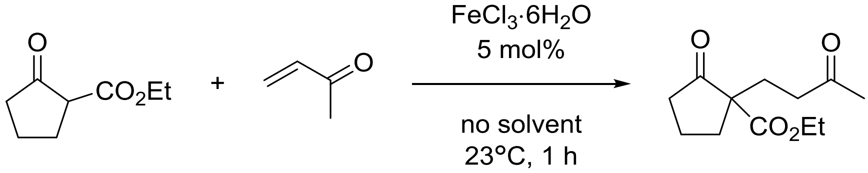


In 1996, Keller and Feringa reported the use of ytterbium triflate as a water-tolerant Lewis acid for Michael addition of various β-ketoesters towards α,β-unsaturated enones and enals under mild conditions. When water is used as the solvent in the presence of catalytic amount of ytterbium triflate, the yield and the purity of the product could be greatly improved compared to conventional systems using organic solvents. However, the reactions were carried out at RT for 3-5 days [124].

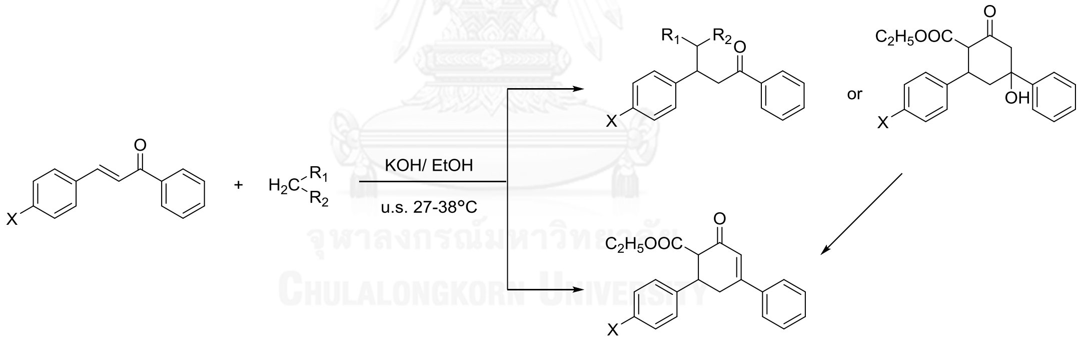


In 1997, Soriente and co-workers reported the MW-mediated Michael addition of 1,3-dicarbonyl compounds in the presence of catalytic amounts of $EuCl_3{\cdot}6H_2O$ (2-10 mol%). Michael adducts were obtained in satisfactory yields (54-95%) and very short reaction times (3-10 min) with no evidence of alkoxydecarbonylalion has been detected [125].

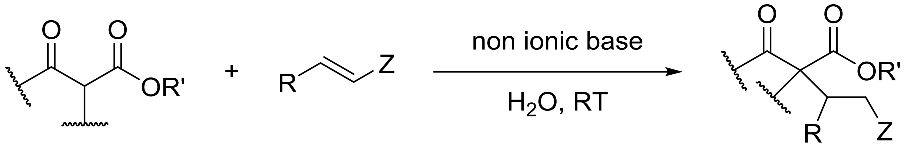
In 2001, Christoffers reported the utilization of $FeCl_3{\cdot}6H_2O$ as an efficient catalyst for the Michael reaction of 1,3-dicarbonyl compounds with enones. The reaction could be carried out with no need for anhydrous or inert conditions. The reaction workup and purification are very simple such direct distillation of the product from the reaction mixture or filtration through a short column of silica gel because of the high chemoselectivity and high conversion [126].



In 2003, Li and co-workers reported a facile sonochemical Michael addition catalyzed by potassium hydroxide. Michael addition of chalcone with active methylene compound such as diethyl malonate, nitromethane and ethyl acetoacetate catalyzed by KOH in anhydrous ethanol gave Michael adducts in 72–98% yield under ultrasound irradiation in 15–90 min. It was obvious that Michael addition could be completed in shorter reaction time [127].



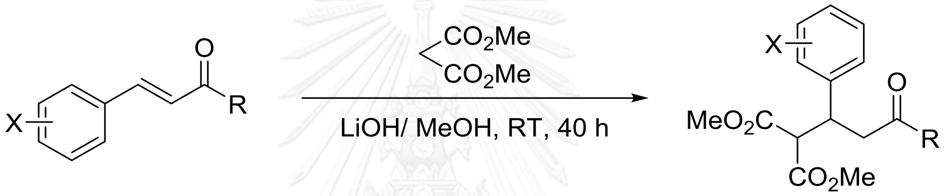
In 2004, Bensa and Rodriguez reported the study on the catalytic Michael addition in water using nonionic bases such as phosphazenes, guanidines, and more classical nitrogen containing derivatives or triphenyl phosphine. A new organocatalytic system for the Michael addition of β-ketoesters to α,β-unsaturated carbonyl compounds provided the selective and high yield of synthetically useful functionalized adducts [128].



Z = CHO, COOMe, CN

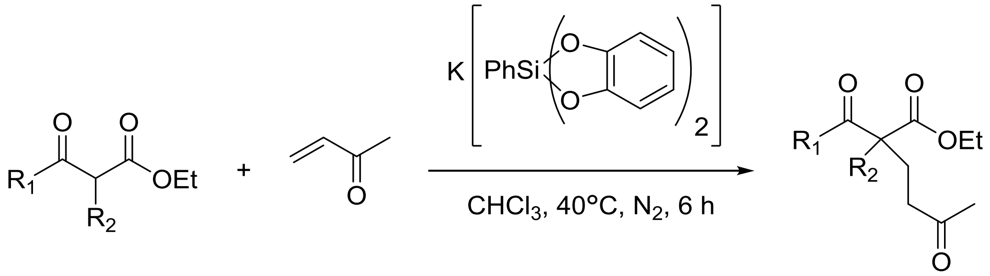
R = H, Me

In 2011, Sukanya and Deka reported the Michael addition of dimethyl malonate to α,β-unsaturated ketones catalyzed by lithium hydroxide. The reactions proceeded smoothly under the catalytic effect of LiOH in methanol at RT for 40 h providing moderate to high yields (64-88%) of the Michael adducts [129].

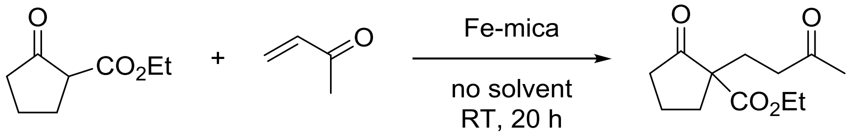


6.1.2.2 Heterogeneous catalysis

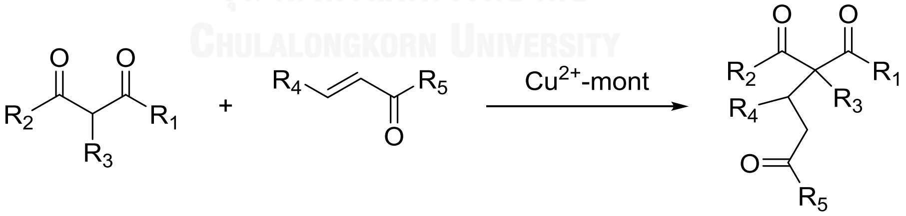
Many successful reports on the heterogeneous catalysts for Michael addition reaction. In 2001, Tateiwa and Hosomi published the utilization of pentacoordinate organosilicate for the Michael addition of β-ketoesters to methyl vinyl ketone. The corresponding 1,4-adducts could be furnished in moderate to good yields. Especially, potassium bis(1,2-benzenediolato)phenylsilicate proved to be the most effective catalyst. The silicate might work as Lewis acid and Brønsted base catalyst at the same time in this reaction [130].



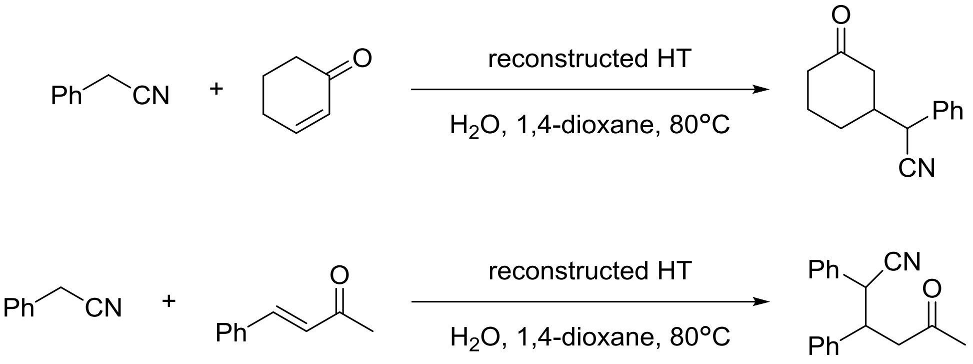
In 2005, Shimizu and co-workers reported the succeeded in developing Fe^{3+}-exchanged fluorotetrasilicic mica as a highly effective heterogeneous catalyst for the Michael reactions of β-ketoester with vinyl ketones. The reaction proceeded smoothly and selectively at room temperature under solvent-fee conditions providing Michael adducts in high yield. This catalyst was a stable, reusable, and non-toxic solid which offered easy handling and ready workup [131].



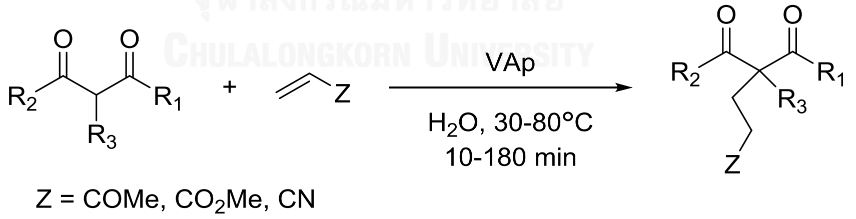
Montmorillonite-enwrapped copper and scandium aqua complexes have been developed by Kawabata and co-workers for use as versatile Lewis acid catalysts for Michael reactions of 1,3-dicarbonyl compounds with enones under solvent-free or aqueous conditions. The corresponding adducts were obtained in excellent yield. The activity of the montmorillonite catalysts was attributable to the negatively charged silicate layers that were capable of stabilizing metal cations. These catalysts were reusable without loss in activity and selectivity [132].



In 2006, Ebitani and co-workers reported the preparation of the facile structural change of HTs as hydrophilic heterogeneous base catalysts for selective carbon-carbon bond forming reactions in the presence of water. The reconstructed hydrotalcite possesses a highly effective acid-base bifunctional surface capable of mediating the Michael reactions of nitriles with carbonyl compounds gave the high yield of corresponding adducts. This highly functionalized metal hydroxide surface without any transition and rare earth metal catalyst offered the possibility of performing diverse and environmentally benign reactions [133].



Hara and co-workers reported the utilization of calcium vanadate apatite (VAp) as a high-performance heterogeneous base catalyst for Michael reactions of 1,3-dicarbonyl compounds with activated enones in aqueous media. The excellent to quantitative yield of products were obtain. This catalytic system possesses attractive features for organic synthesis such as high catalytic efficiency under mild reaction conditions, simple procedure which allows for large-scale operation, no requirement for organic solvents and easy separation and reusability of the catalyst [134].



In 2009, Banerjee and Santra demonstrated the catalytic activity of silica nanoparticles (NPs) in the unusual bis-Michael addition of active methylene compounds to conjugated alkenes at room temperature. The silica NPs efficiently catalyzed the bis-addition of methyl vinyl ketone, methyl acrylate and acrylonitrile within 2–6 h at room temperature providing high yields (78–95%). The catalyst could be reused up to seven times without loss of catalytic activity [135].

E_1, E_2 = COMe, COOEt, CN etc
X = COMe, COOMe, CN etc

To achieve green organic transformation, it is necessary to establish a catalyst design for high-performance recyclable solid base catalysts.

6.1.3 Anion-exchangeable layered compounds

Hydroxy double salts (HDSs) and layered double hydroxides (LDHs) have received considerable interest as anion exchangeable layered compounds due to their potential applications as catalyst supports. The NiZn mixed basic salt (NiZn), considered as a HDSs with a typical chemical composition of $Ni_{1-x}Zn_{2x}(CH_3COO)_{2x}(OH)_2 \cdot nH_2O$ (0.15 < x < 0.25) [136-139]. The structure of NiZn, where at most one quarter of the octahedral Ni sites in the $Ni(OH)_2$ layer are vacant and where the divalent tetrahedral Zn cations are coordinated and stabilized just below and above the empty Ni sites, facilitates the formation of an excess positive layer charge [140], as exhibited in Fig 6.1.

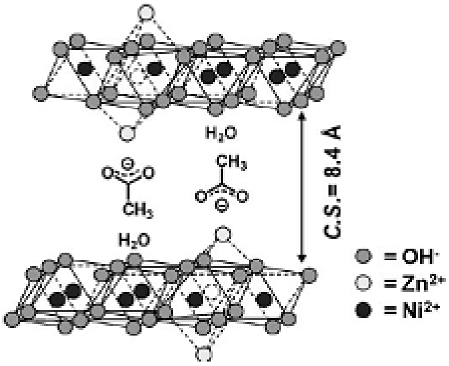
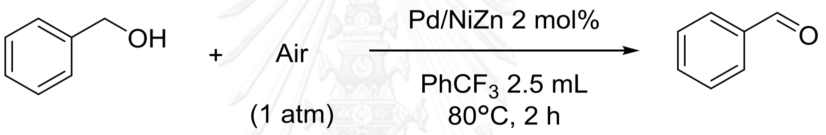


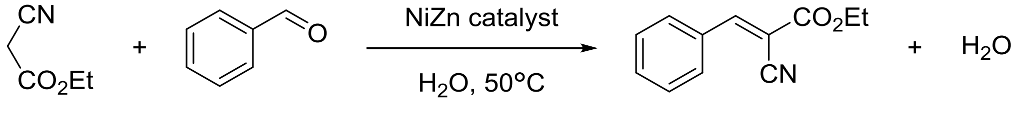
Figure 6.1 Schematic structure of NiZn mixed basic salt (NiZn) [140]

The novel features of the present NiZn-based catalyst system are facile preparation, controllable interlayer space, easy recovery, and simple recycling are particularly desirable.

Hara and co-workers reported the synthesis of a novel NiZn-Pd nanocomposite. The intercalated anionic Pd hydroxide complex was rigidly fixed by the strong electrostatic interaction of NiZn. Pd/NiZn could be used as an efficient heterogeneous catalyst for the oxidation of alcohols under an air atmosphere, with no need for any additives. The excellent yield of corresponding aldehydes could be obtained from the oxidation of benzylic alcohols with electron-donating substituents. This catalytic system was also applicable to oxidation of allylic alcohols, non-activated aliphatic alcohols and cyclic aliphatic alcohols [140].



They also reported the efficient Knoevenagel condensation catalyzed by alkylcarboxylate anion-intercalated Ni-Zn mixed basic salt (NiZn). The $C_3H_7COO^-$/NiZn showed the highest catalytic activity for the Knoevenagel condensation of ethyl cyanoacetate and benzaldehyde giving (2E)-2-cyano-3-phenyl-2-propenoic acid ethyl ester in quantitative yield after performed in water for 1 h. The catalyst was found to be reusable without any reduction in activity [141].



6.2 Scope of this work

From previous literature reviews, some of homogeneous and heterogeneous catalysts were found to be used as an efficient catalyst for the Michael reaction.

However, there are some disadvantages in using these catalysts, such as high cost, toxic, sensitive to air and moisture, long reaction time required, and difficulty in separation and recovery. The catalytic processes were developed and still of interest in the fine chemistry. This research focused on the methodology toward the Michael reaction of 1,3-dicarbonyl compounds with activated α,β-unsaturated ketones catalyzed by the synthesized NiZn catalysts.

6.3 Experimental

6.3.1 Instruments and equipments

Spectrometers: The ^{1}H- and ^{13}C-NMR spectra were performed in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR 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: Gas chromatographic analysis was carried out on a Varian gas chromatography instrument equipped with a flame ionization detector (FID) with N_2 as a carrier gas and a 30-m long BP-1 column (0.25-mm outer diameter, 0.25 μm film thickness). Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's silica gel 60 G Art 7734 (70-230 mesh)).

Powder X-ray diffraction (XRD) was conducted using a Bruker AXS MXP^{3}V with Cu Kα radiation.

6.3.2 Chemicals

$Ni(OCOCH_3)_2{\cdot}4H_2O$ and $Zn(OCOCH_3)_2{\cdot}2H_2O$ were obtained from Wako Pure Chemical Ind. Co. Ltd., supported by Professor Dr. Shogo Shimazu, Department of Applied Chemistry and Biotechnology, Faculty of Engineering, Chiba University, Japan.

All reagents and solvents in this research were purified according to the procedures described in the standard methodology except for solvents that are reagent grade.

6.3.2 Syntheses

6.3.2.1 Synthesis of NiZn catalyst

Preparation of Acetate-exchanged Ni–Zn Mixed Basic Salt (CH_3COO^-/NiZn)

$Ni(OAc)_2{\cdot}4H_2O$ (134 mmol) and $Zn(OAc)_2{\cdot}2H_2O$ (66 mmol) were dissolved in deionized water (200 mL). The solution was hydrolyzed by heating in a Teflon^{TM}-linked pressure bottle at 423K for 24 h. The precipitates were filtered, washed with deionized water, and dried under vacuum, yielding 5 g of CH_3COO^-/NiZn as a light green powder. The compositional formula of this compound was found to be $Ni_{0.78}Zn_{0.44}(OH)_2(OAc)_{0.44}{\cdot}0.86H_2O$.

Preparation of Alkylcarboxylate Anion-exchanged NiZn Catalyst (X/NiZn)

X/NiZn catalyst was prepared by a simple intercalation technique. Treatment of CH_3COO^-/NiZn (0.5 g) with 1 M of various sodium alkylcarboxylates solution (50 mL) at 60°C for 24-48 h yielded the anion-exchanged NiZn catalysts as a green powder.

6.3.2.2 General procedure for the Michael reaction

A two-neck round bottom flask was charged with 1,3-dicarbonyl compound (1 mmol), α,β-unsaturated ketone (1.2 mmol) in solvent (5 mL) and NiZn catalyst (0.1 g), connected with a condenser. The reaction mixture was continuous stirred for desired time and temperature. After the appropriate time or the reaction was completed, catalyst was separated from the reaction mixture by a simple centrifuge. The solvent was partly evaporated under reduced pressure. The obtained mixture was taken and analyzed by GC with the addition of an exact amount of an appropriate internal standard (biphenyl).

6.3.2.3 General isolation procedure

After the reaction was finished, the products were separated as follows: the solvent was evaporated to dryness under reduced pressure. The crude products were purified by silica gel column chromatography using a mixture of Hexane-EtOAc as a mobile phase. The equivalent fractions monitored by TLC were combined and the solvent was completely evaporated. The residue was characterized by ^{1}H-NMR spectroscopy.

ethyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate; ^{1}H NMR ($CDCl_3$) δ (ppm): 4.14 (qd, J = 7.1, 0.9 Hz, 2H), 2.68 (ddd, J = 17.9, 9.6, 5.7 Hz, 1H), 2.22-2.50 (m, 4H), 2.12 (s, 3H), 2.03-2.11 (m, 1H), 1.81-2.03 (m, 4H), 1.23 (t, J = 7.1 Hz, 3H).

ethyl 2-acetyl-5-oxohexanoate; ^{1}H NMR ($CDCl_3$) δ (ppm): 4.16 (qd, J = 7.1, 1.3 Hz, 2H), 3.42-3.50 (m, 1H), 2.47 (dd, J = 10.3, 4.2 Hz, 2H), 2.20-2.22 (m, 3H), 2.10 (s, 3H), 2.06 (ddd, J = 14.8, 7.2, 4.4 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H).

6.3.2.4 Optimum conditions for the Michael reaction

Effect of solvent on the Michael reaction

The Michael reaction was performed according to the general procedure as described above except for toluene, hexane, 1,2-dichloroethane, acetonitrile, dimethylformamide, ethanol and water were used as a reaction medium. 5 mL of each solvent was used.

Effect of various alkylcarboxylate anion-intercalated NiZn on the Michael reaction

The Michael reaction was carried out according to the general procedure as previously described employing various alkylcarboxylate anion-intercalated NiZn catalysts: $HCOO^-$/NiZn, CH_3COO^-/NiZn, $C_3H_7COO^-$/NiZn, $C_5H_{11}COO^-$/NiZn, $C_7H_{15}COO^-$/NiZn and $C_9H_{19}COO^-$/NiZn.

Effect of mole ratio of 1,3-dicarbonyl compound to α,β-unsaturated ketone

The Michael reaction was performed according to the general procedure as described above employing various ratio of both substrates: 0.5:1, 1:0.5, 1:1, 1:1.5 and 1.5:1.

6.3.2.5 Study on the Michael reaction of 1,3-dicarbonyl compounds with α,β-unsaturated ketones

Ethyl acetoacetate as 1,3-dicarbonyl compound and 2-cyclohexen-1-one as α,β-unsaturated ketone were selected for the further catalytic studies. The 1,3-dicarbonyl compound and enone were reacted according to the general procedure as previously described utilizing $C_3H_7COO^-$/NiZn as catalyst. The corresponding products were identified by comparison of their spectral data with those reported in literature.

6.4 Results and discussion

6.4.1 The characterization of NiZn catalyst

The acetate-intercalated NiZn mixed basic salt (CH_3COO^-/NiZn) was synthesized by previously described procedure. The characteristic structures of CH_3COO^-/NiZn was characterized by XRD technique. The X-ray diffraction patterns of CH_3COO^-/NiZn was analyzed as shown in Figure 6.2.

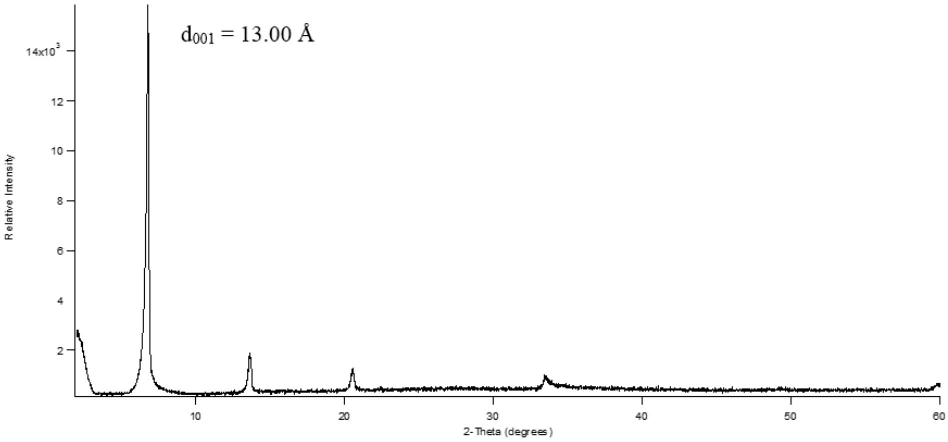


Figure 6.2 XRD patterns of CH_3COO^-/NiZn

From Fig 6.2, the characteristic peak of $Ni_{0.78}Zn_{0.44}(OH)_2(OAc)_{0.44}\cdot 0.86H_2O$ was observed at 2θ of 6°, 14°, 20° and 34° corresponding to the 001, 002, 003 and 020 planes of NiZn basic acetate, respectively. The d_{001} basal spacing of CH_3COO^-/NiZn is 13.0 Å.

The anion exchange in the NiZn interlayer was obtained by a simple anion-exchange process in water. The treatment of CH_3COO^-/NiZn with various sodium alkylcarboxylates provided the anion-exchanged NiZn catalysts (X/NiZn, X was exchanged alkylcarboxylate anion) as a green powder. The X-ray diffraction patterns of the synthesized NiZn catalysts were analyzed as displayed in Fig. 6.3. From the XRD results, the NiZn layered structure were maintained in all case.

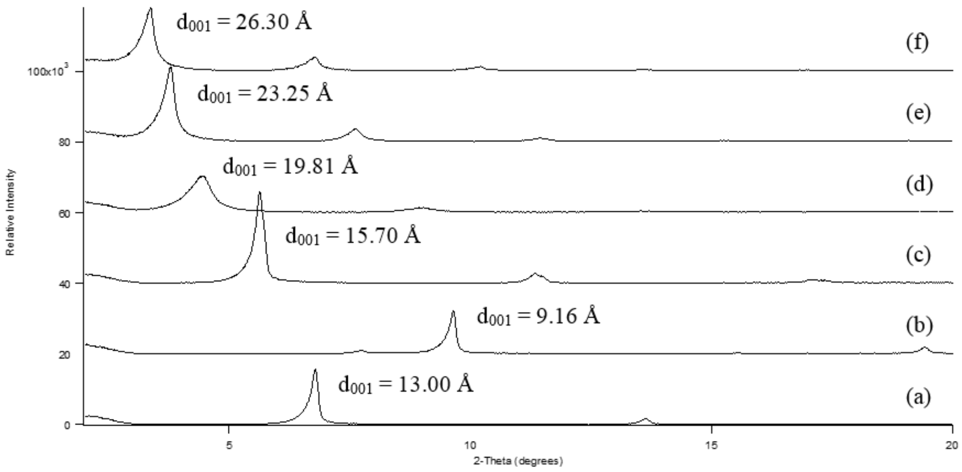


Figure 6.3 XRD patterns of (a) CH_3COO^-/NiZn (b) $HCOO^-$/NiZn (c) $C_3H_7COO^-$/NiZn (d) $C_5H_{11}COO^-$/NiZn (e) $C_7H_{15}COO^-$/NiZn and (f) $C_9H_{19}COO^-$/NiZn

In the case of $HCOO^-$/NiZn catalyst, the d_{001} peak shifted to higher angle from that of CH_3COO^-/NiZn catalyst, and the d_{001} basal spacing of $HCOO^-$/NiZn is 9.16 Å. Whereas the interlayer space of NiZn increased with increasing alkyl chain length as followed: $HCOO^-$/NiZn < CH_3COO^-/NiZn < $C_3H_7COO^-$/NiZn < $C_5H_{11}COO^-$/NiZn < $C_7H_{15}COO^-$/NiZn < $C_9H_{19}COO^-$/NiZn. The $C_3H_7COO^-$/NiZn, $C_5H_{11}COO^-$/NiZn, $C_7H_{15}COO^-$/NiZn and $C_9H_{19}COO^-$/NiZn showed the d_{001} basal spacing of 15.70, 19.81, 23.25 and 26.30 Å, respectively as the NiZn interlayer increased. It could be indicated that the NiZn interlayer as a catalytic reaction field could be controlled by simple intercalation with alkylcarboxylate anions.

6.4.2 Optimum conditions for the Michael reaction

The Michael reaction of ethyl 2-oxocyclopentanecarboxylate and methyl vinyl ketone was selected for the catalytic activity test of synthesized NiZn catalysts. Various factors were carefully examined to optimize the conditions for the Michael reaction. The type of solvent, the alkylcarboxylate anion-intercalated NiZn catalysts and the substrate concentration were varied to search for the optimal conditions.

6.4.2.1 Effect of solvent on the Michael reaction

To investigate the effect of solvent for the Michael reaction, various solvents including toluene, hexane, 1,2-dichloroethane, acetonitrile, dimethylformamide, ethanol and water were examined. The effect of solvents on Michael reaction were performed utilizing 1:1.2 mmol of ethyl 2-oxocyclopentanecarboxylate to methyl vinyl ketone with 5 mL of each solvent and 0.1 g of $C_3H_7COO^-$/NiZn at 50°C for 1 h or more. The results are presented in Table 6.1.

Table 6.1 The effect of solvent on Michael reaction

Entry	Solvent	Time (h)	%Yield[a]
1	-	1	quant.
2	toluene	1	92
3	hexane	1	96
4	1,2-DCE	1	40
5	EtOH	3	66
6	DMF	3	97
7	CH_3CN	3	82
8	H_2O	1	quant.

Reaction conditions: ethyl 2-oxocyclopentanecarboxylate (1 mmol), methyl vinyl ketone (1.2 mmol), $C_3H_7COO^-$/NiZn (0.1 g), solvent (5 mL) at 50°C

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 6.1 display that the Michael reaction was carried out under solvent-free condition gave almost quantitative yield. Nevertheless, the reaction mixture need some of suitable solvent to proceed the reaction smoothly. Utilizing water as solvent, the reaction also gave the quantitative yield. The more work up step such extraction causing water was an unsatisfactory choice. It was found that hexane was the most suitable reaction medium which gave 96% yield within 1 h (entry 3). The second was obtained as 92% yield from using toluene 1 h (entry 2). 1,2-Dichloroethane gave the moderate yield when performing for 1 h. While the use of dimethylformamide gave high yield as 97% after prolonged the reaction time for 3 h (entry 6). Followed by acetonitrile and ethanol gave 82 and 66% yield, respectively. Therefore, hexane was selected as a reaction medium for additional experiments.

6.4.2.2 Effect of various alkylcarboxylate anion-intercalated NiZn on the Michael reaction

The goal of this research was to screen for suitable catalysts that could provide corresponding product in high yield. The alkylcarboxylate anion-intercalated NiZn catalysts were prepared by a simple intercalation process. The catalytic activity of various alkylcarboxylate anion-intercalated NiZn such as $HCOO^-$/NiZn, CH_3COO^-/NiZn, $C_3H_7COO^-$/NiZn, $C_5H_{11}COO^-$/NiZn, $C_7H_{15}COO^-$/NiZn and $C_9H_{19}COO^-$/NiZn were examined for the Michael reaction. The investigated conditions were 1:1.2 mmol of ethyl 2-oxocyclopentanecarboxylate to methyl vinyl ketone and 0.05 g of catalysts at 50°C for 1 h. The results are displayed in Table 6.2.

Table 6.2 The effect of various alkylcarboxylate anion-intercalated NiZn on the Michael reaction

Entry	**Catalyst**	**d_{001} Basal spacing (Å)**	**%Yield[a]**
1	$HCOO^-$/NiZn	9.16	55
2	CH_3COO^-/NiZn	13.00	49
3	$C_3H_7COO^-$/NiZn	15.70	82
4	$C_5H_{11}COO^-$/NiZn	19.81	72
5	$C_7H_{15}COO^-$/NiZn	23.25	62
6	$C_9H_{19}COO^-$/NiZn	26.30	69

Reaction conditions: ethyl 2-oxocyclopentanecarboxylate (1 mmol), methyl vinyl ketone (1.2 mmol), NiZn catalyst (0.05 g), hexane (5 mL) at 50°C for 1 h

[a] The yield was determined by GC using biphenyl as an internal standard

From Table 6.2, it could be seen that the parent CH_3COO^-/NiZn and $HCOO^-$/NiZn could be used for catalyze this Michael reaction, 2-(3-oxobutyl) cyclopentanone-2-carboxylic acid ethyl ester was obtained in moderate yield after performing for 1 h (entries 1, 2). This slow reaction rate possibly due to the restriction of the mass transfer in the narrow interlayer space of NiZn catalysts. $C_3H_7COO^-$/NiZn showed the highest activity in Michael reaction to furnish the desired product in 82% yield (entry 3). $C_5H_{11}COO^-$/NiZn, $C_7H_{15}COO^-$/NiZn and $C_9H_{19}COO^-$/NiZn as extended interlayer space catalysts could not promote this reaction effectively (entries 4-6). Since the substrate could not diffuse smoothly into the interlayer space of these catalysts because of alkyl chains of the intercalated anion filled up the interlayer space. It should be noticed that $C_3H_7COO^-$/NiZn was the best catalyst for the Michael reaction.

6.4.2.3 Effect of mole ratio of 1,3-dicarbonyl compound to α,β-unsaturated ketone

The influence of the mole ratio of substrates was investigated for the Michael reaction. The various mole ratio of 1,3-dicarbonyl compound to α,β-unsaturated ketone were examined utilizing 0.05 g of $C_3H_7COO^-$/NiZn in hexane at 50°C for 0.5 h. The results are presented in Table 6.3.

Table 6.3 The effect of mole ratio of 1,3-dicarbonyl compound to α,β-unsaturated ketone

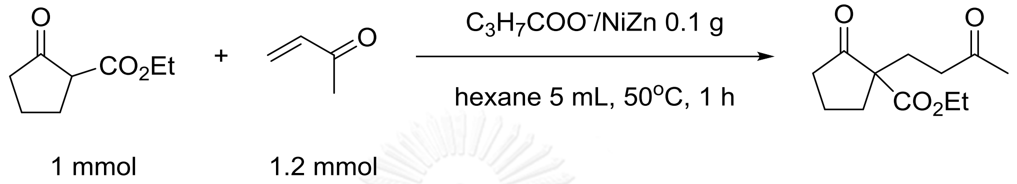
Entry	1,3-dicarbonyl compound (mmol)	Methyl vinyl ketone (mmol)	%Yield[a]
1	1	1	62
2	1	1.5	86
3	1.5	1	45
4	0.5	1	quant.
5	1	0.5	50

Reaction conditions: ethyl 2-oxocyclopentanecarboxylate (vary), methyl vinyl ketone (vary), $C_3H_7COO^-$/NiZn (0.05 g), hexane (5 mL) at 50°C for 0.5 h

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 6.3 exhibit that the mole ratio of substrates affect the Michael reaction. The increase in mole ratio of 1,3-dicarbonyl compound: methyl vinyl ketone from 1:1 to 1:1.5, the percentage yield of desired product increased from 62% to 86% (entries 1, 2). The quantitative yield was obtained when increase in mole ratio to 0.5:1 (entry 4). However, an immoderate amount of substrate employing should be avoided to obtain greener methodology. Reducing the mole ratio of methyl vinyl ketone, the percentage yield decreased (entries 3, 5). Thus, the appropriate mole ratio of substrates for Michael reaction that modified from this effect studied was 1:1.2.

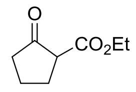
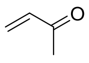
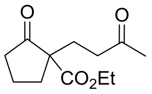
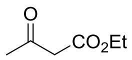
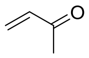
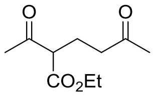
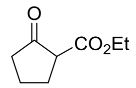
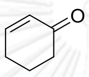
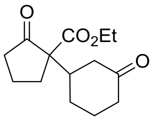
It could be summarized that the optimum conditions for the Michael reaction of ethyl 2-oxocyclopentanecarboxylate and methyl vinyl ketone catalyzed by $C_3H_7COO^-$/NiZn are as follows: ethyl 2-oxocyclopentanecarboxylate 1 mmol, methyl vinyl ketone 1.2 mmol, hexane 5 mL, $C_3H_7COO^-$/NiZn 0.1 g at 50°C for 1 h.



6.4.3 The Michael reaction of 1,3-dicarbonyl compounds with α,β-unsaturated ketones

The $C_3H_7COO^-$/NiZn-catalyzed Michael reaction was found to be expandable to include ethyl acetoacetate as 1,3-dicarbonyl compound and 2-cyclohexen-1-one as α,β-unsaturated ketone. The Michael addition reactions were carried out in hexane at 50°C as standard conditions. The results are displayed in Table 6.4.

Table 6.4 The Michael reaction of 1,3-dicarbonyl compounds with α,β-unsaturated ketones

Entry	1,3-dicarbonyl compound	a,b-unsaturated ketone	Time (h)	Product	%Yield[a]
1			1		96
2			3		66 (95)
3[b]			3		65 (77)
4			6		6

Reaction conditions: 1,3-dicarbonyl compound (1 mmol), α,β-unsaturated ketone (1.2 mmol), $C_3H_7COO^-/NiZn$ (0.1 g), hexane (5 mL), 50°C

[a] The yield was determined by GC using biphenyl as an internal standard

[b] 1,3-dicarbonyl compound (1 mmol), α,β-unsaturated ketone (1 mmol)

* %conversion is shown in the parenthesis

From Table 6.4, the Michael addition of ethyl acetoacetate and methyl vinyl ketone proceeded in the presence of $C_3H_7COO^-/NiZn$ in hexane at 50°C for 3 h producing the corresponding 1,4-adduct, ethyl 2-acetyl-5-oxohexanoate, in 66% yield with 95% conversion (entry 2). The bis-adduct, ethyl 2-acetyl-5-oxo-2-(3-oxobutyl)hexanoate, was found as a side product. The use of one equivalent of α,β-unsaturated ketone in this reaction could not produce only monoaddition product, while the bis-adduct was observed in lower yield (entry 3). The $C_3H_7COO^-/NiZn$ showed low catalytic activity for the reaction of ethyl 2-oxocyclopentanecarboxylate and 2-cyclohexen-1-one although prolonged the reaction time (entry 4). Hence, the appropriate conditions for the reaction enhancement will be investigated as the following study.

6.4.3.1 The Michael reaction of ethyl 2-oxocyclopentanecarboxylate with 2-cyclohexen-1-one

The effect of the solvent, reaction temperature and reaction time for the Michael addition of ethyl 2-oxocyclopentanecarboxylate and 2-cyclohexen-1-one were examined. The results are displayed in Table 6.5.

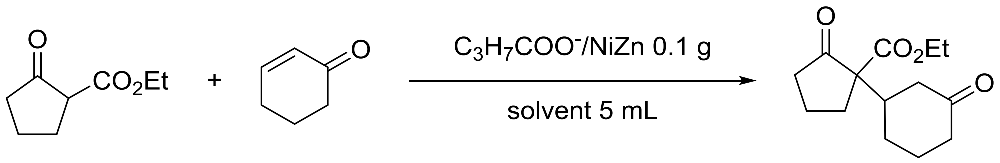


Table 6.5 The Michael reaction of ethyl 2-oxocyclopentanecarboxylate with 2-cyclohexen-1-one

Entry	Solvent	Temp (°C)	Time (h)	%Yield[a]
1	hexane	50	6	6
2		reflux	6	63
3		reflux	15	76
4	toluene	80	6	18
5	1,2-DCE	80	6	15
6	EtOH	80	6	4
7	DMF	80	6	13
8	CH_3CN	80	6	12
9	H_2O	80	6	38
10	-	80	6	22

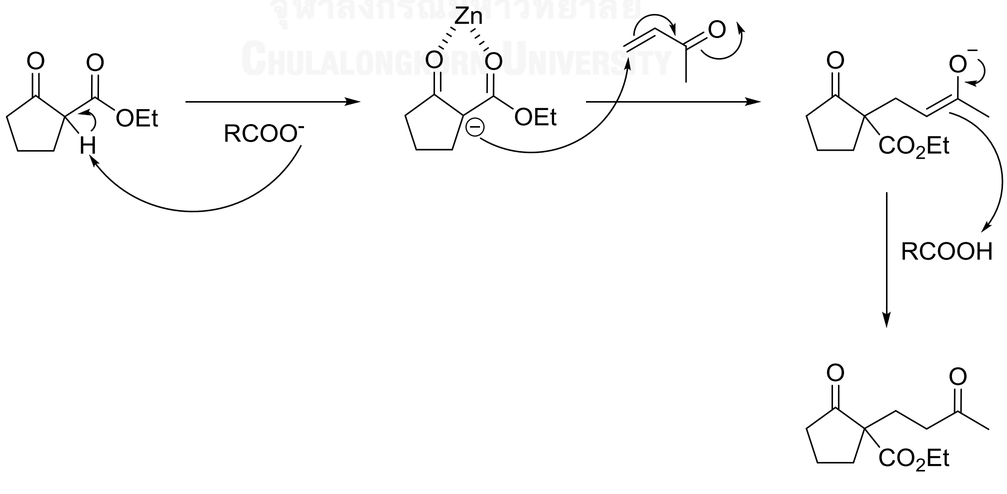
Reaction conditions: ethyl 2-oxocyclopentanecarboxylate (1 mmol), 2-cyclohexen-1-one (1.2 mmol), $C_3H_7COO^-$/NiZn (0.1 g), hexane (5 mL)

[a] The yield was determined by GC using biphenyl as an internal standard

The results from Table 6.5 show that increased reaction temperature to reflux temperature and prolonged reaction time, higher yield of ethyl 2-oxo-1-(3-oxocyclohexyl)cyclopentane-1-carboxylate were satisfactory furnished in 63 and 76% (entries 2, 3). The reactions could not proceed well when other polar or nonpolar solvent was used (entries 4-8). Under aqueous conditions, the desired product was formed in only 38% yield (entry 9). Performing the reaction under solvent-free conditions, the low yield of the Michael adduct was obtained (entry 10). Thus, the appropriate conditions for the Michael addition of ethyl 2-oxocyclopentanecarboxylate with 2-cyclohexen-1-one are as follows: ethyl 2-oxocyclopentanecarboxylate (1 mmol), 2-cyclohexen-1-one (1.2 mmol), $C_3H_7COO^-$/NiZn (0.1 g), hexane (5 mL) at reflux temperature for 15 h.

6.4.4 The proposed mechanism for the Michael reaction catalyzed by alkylcarboxylate anion-intercalated NiZn

The proposed mechanism for the Michael addition reaction of ethyl 2-oxocyclopentanecarboxylate and methyl vinyl ketone was believed to proceed *via* the following pathway as presented in Scheme 6.1.



Scheme 6.1 Proposed mechanism for the Michael reaction catalyzed by alkylcarboxylate anion-intercalated NiZn

An alkylcarboxylate anion abstracts the α-hydrogen to form carbanion and was stabilized by a coordination of the dicarbonyl to the Zn. Then, the nucleophile reacts with the electrophilic alkene to form enolate ion in a conjugate addition reaction. Proton abstraction from protonated base by the enolate lead to 1,4-Michael adduct.

6.5 Conclusion

The interlayer space controlled NiZn catalysts were prepared by anion exchange with alkylcarboxylate anions. Enlargement of NiZn interlayer was proportional to the alkyl chain length of the intercalated molecule.

The catalytic activities of alkylcarboxylate anion-intercalated NiZn were performed for the Michael addition reaction. The $C_3H_7COO^-$/NiZn showed higher catalytic efficiency than other alkylcarboxylate anion-intercalated NiZn. The optimum conditions for the Michael reaction of ethyl 2-oxocyclopentanecarboxylate and methyl vinyl ketone were using 0.1 g of $C_3H_7COO^-$/NiZn in hexane 5 mL at 50°C for 1 h. This catalytic system was successfully performed under mild reaction conditions providing the desired product in excellent yield. The reaction of ethyl acetoacetate with methyl vinyl ketone were carried out in the presence of $C_3H_7COO^-$/NiZn in hexane at 50°C for 3 h to obtain 66% yield with 95% conversion. The Michael addition of ethyl 2-oxocyclopentanecarboxylate with 2-cyclohexen-1-one proceeded in the presence of $C_3H_7COO^-$/NiZn in hexane at reflux temperature for 15 h providing 76% yield of desired adduct.

CHAPTER VII

CONCLUSION

7.1 Synthesis and characterization of clay catalysts

Metal oxide-pillared clays (Fe-PLM, Al-PLM and Cr-PLM) were synthesized by intercalation method, followed by calcination at high temperature (300-500°C). Metal chloride-impregnated metal oxide-pillared montmorillonites ($NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM) were synthesized by the impregnation method of metal chloride ($NdCl_3$ and $CrCl_3$) on pillared montmorillonite, followed by calcination.

In the case of metal oxide-pillared clays, the d_{001} basal spacings of Fe-PLM, Al-PLM and Cr-PLM were 9.99, 15.49 and 11.94 Å, respectively. $NdCl_3$/Al-PLM showed the d_{001} basal spacing of 14.02 Å. Whereas the d_{001} spacings of metal chloride-impregnated iron oxide-pillared montmorillonites are about 9.67-9.93 Å, except for high loading of 5 and 10% $NdCl_3$ impregnated Fe-PLM clays. All synthesized clay catalysts still presented the parent clay layered characteristics. The nitrogen adsorption-desorption isotherms of all synthesized clay catalysts exhibited the type IV isotherm indicating their micro-mesoporous structure. The BET specific surface area of Fe-PLM, Al-PLM and Cr-PLM were greater than untreated montmorillonite. The BET specific surface area of $NdCl_3$/Al-PLM, $CrCl_3$/Fe-PLM and $NdCl_3$/Fe-PLM showed lower than Al-PLM but higher than untreated montmorillonite, except for 2% $NdCl_3$ impregnated Fe-PLM. From the acidity determined by NH_3-TPD method, Cr-PLM showed the highest acidity among all synthesized clay catalysts.

The synthesized clays were utilized for acid-catalyzed reactions (1) the synthesis of coumarins, (2) isomerization of epoxides and (3) synthesis of acetonides from epoxides. The synthesized clays provided significantly higher catalytic activities than parent clays. These catalytic systems could be proceeded smoothly in the presence of synthesized clays as efficient catalysts to produce the corresponding products in good to excellent yield.

7.2 Synthesis of coumarins catalyzed by clay catalyst

The goal of this part is to search for the optimum conditions for the synthesis of coumarins catalyzed by clay catalysts. The catalytic activities of Fe-PLM were carried out for the Pechmann condensation of resorcinol and ethyl acetoacetate. The optimum conditions were using 50 wt% Fe-PLM to resorcinol at 130°C for 6 h under solvent-free condition. This catalytic system was carried out to provide the desired coumarin product in good yield. Fe-PLM showed higher catalytic efficiency than Cr-PLM, Al-PLM, $NdCl_3$/Al-PLM and montmorillonite under the same reaction conditions because of the appropriate acidity, specific surface area and interlayer space of Fe-PLM. From various phenolic compounds, the yields of corresponding products highly depended on the position of electron donating groups. The optimum conditions could be applied and used for other phenols including pyrogallol and phloroglucinol to afford coumarin derivatives in moderate yield.

7.3 Isomerization of epoxides catalyzed by clay catalyst

The goal of this part is to search for the optimum conditions for the isomerization of epoxides catalyzed by clay catalysts. The Cr-PLM catalytic activities were performed for the isomerization of styrene oxide. The optimum conditions were 10 wt% Cr-PLM to styrene oxide at refluxing THF for 15 min. This catalytic system was performed in short period of time under mild conditions successfully providing the desired product in quantitative yield. Under the same reaction condition, Cr-PLM showed higher catalytic efficiency than Al-PLM, $NdCl_3$/Al-PLM and montmorillonite owing to the highest acidity of Cr-PLM. From the variation of epoxides, the yields of products highly depended on the starting epoxide structure. The optimum conditions for *trans*-silbene oxide were 30 wt% Cr-PLM to *trans*-silbene oxide at refluxing THF for 1 h. The Cr-PLM catalyst could be regenerated and reused at least five times without loss of catalytic activity.

7.4 Synthesis of acetonides from epoxides catalyzed by clay catalyst

The goal of this part is to search for the optimum conditions for the synthesis of acetonides from epoxides catalyzed by clay catalysts. The Cr-PLM catalytic activities were carried out for the synthesis of acetonide from styrene oxide. The optimum conditions were using 10 wt% Cr-PLM to styrene oxide at room temperature for 20 min. This catalytic system was carried out in short period of time under mild conditions successfully providing the desired product in excellent yield. Cr-PLM showed higher catalytic efficiency than Al-PLM, $NdCl_3$/Al-PLM and montmorillonite under the same reaction condition because of the highest acidity of Cr-PLM. The optimum conditions could be applied and used for other epoxides including phenyl glycidyl ether, butyl glycidyl ether, *tert*-butyl glycidyl ether and 1-dodecene oxide to furnish acetonides in excellent yield. The Cr-PLM catalyst could be reused at least five times without loss of catalytic activity.

7.5 Michael reaction catalyzed by anion intercalated NiZn

The goal of this part is to prepare the anion intercalated NiZn as solid catalyst and search for the optimum conditions for the Michael addition reaction catalyzed by anion intercalated NiZn. The interlayer space controlled NiZn catalysts were prepared by anion exchange with alkylcarboxylate anions. Enlargement of NiZn interlayer was proportional to the alkyl chain length of the intercalated molecule. The $C_3H_7COO^-$/NiZn showed the highest catalytic efficiency. The optimum conditions for the reaction of ethyl 2-oxocyclopentanecarboxylate and methyl vinyl ketone were using 0.1 g of $C_3H_7COO^-$/NiZn in hexane 5 mL at 50°C for 1 h. This catalytic system was successfully performed under mild reaction conditions providing the desired product in excellent yield. The optimum conditions could be applied and used for the Michael reaction of ethyl acetoacetate and the reaction of ethyl 2-oxocyclopentanecarboxylate with 2-cyclohexen-1-one.

7.6 Propose for the future work

This research concerns with the methodology development for the clay-catalyzed reactions. Other preparation procedures and other types of metal oxide pillared clays should be used to investigate in order to improve product yield and selectivity of the acid catalyzed reactions such as the synthesis of coumarins, isomerization of epoxides and synthesis of acetonides. The obtained catalytic system should be applied for other substrates to expand the scope of these reactions.

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APPENDIX

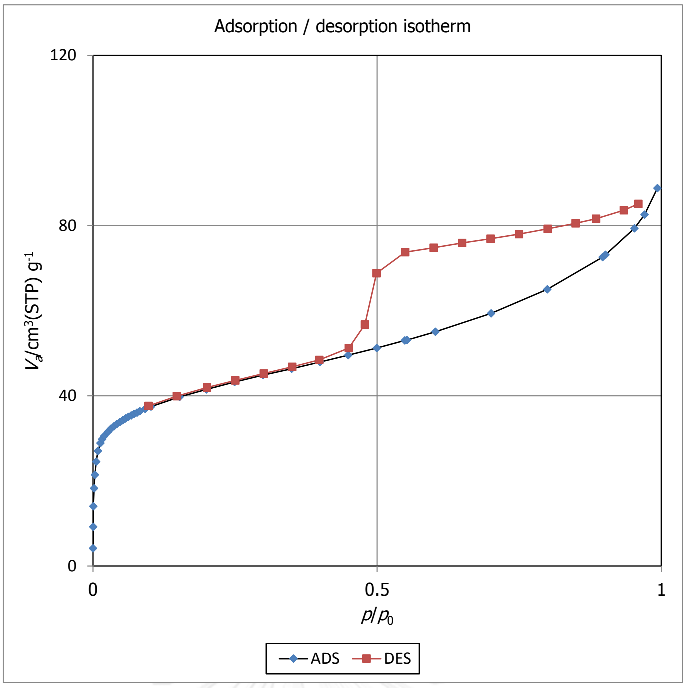

Figure A-1 N_2 adsorption-desorption isotherm of Fe-PLM

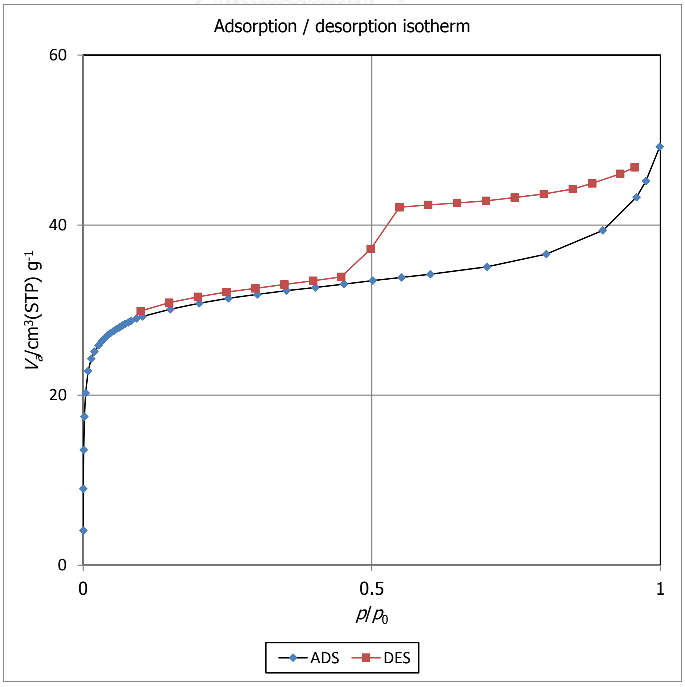

Figure A-2 N_2 adsorption-desorption isotherm of Cr-PLM

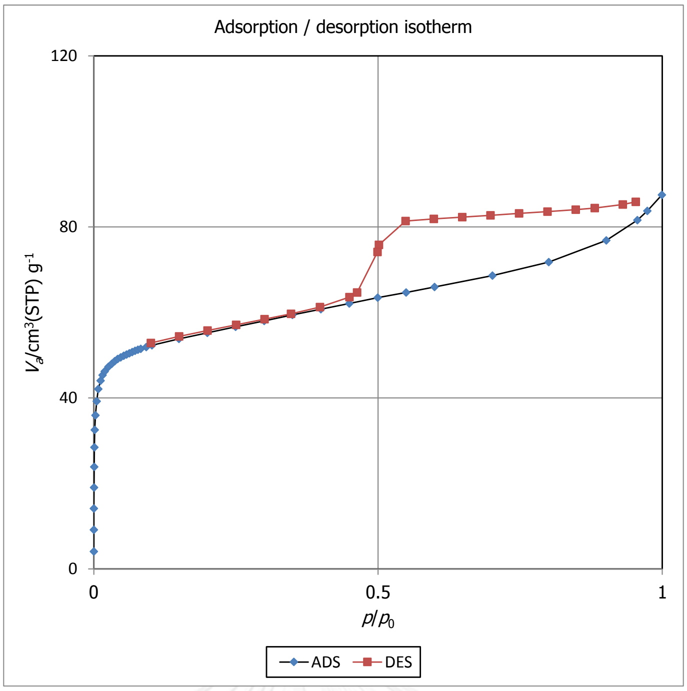

Figure A-3 N_2 adsorption-desorption isotherm of Al-PLM

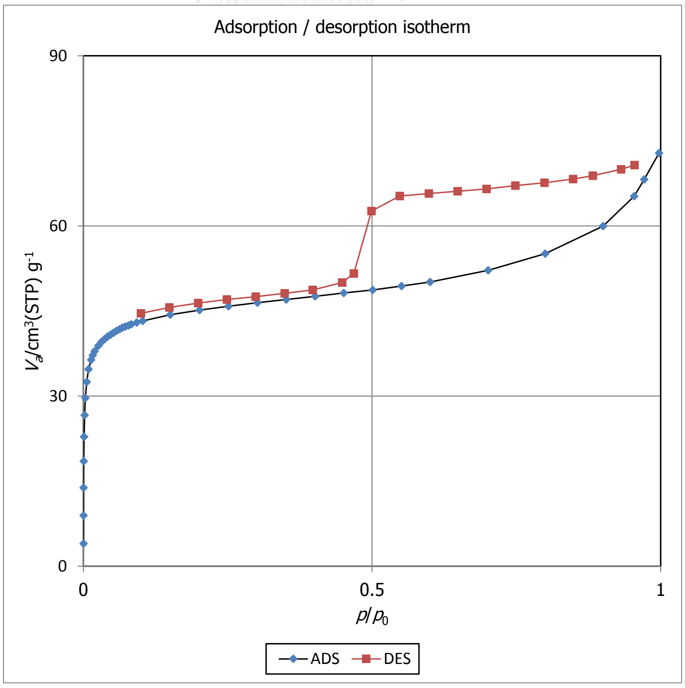

Figure A-4 N_2 adsorption-desorption isotherm of $NdCl_3$/Al-PLM

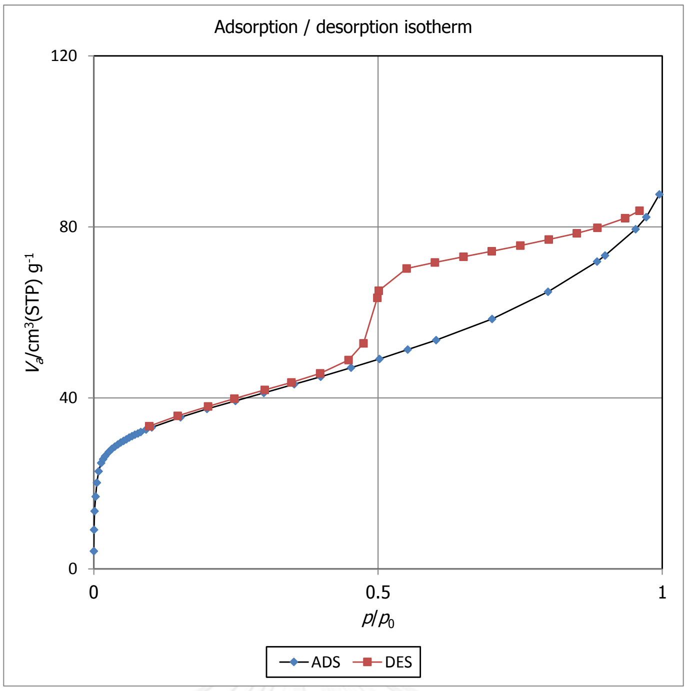

Figure A-5 N_2 adsorption-desorption isotherm of $NdCl_3$/Fe-PLM

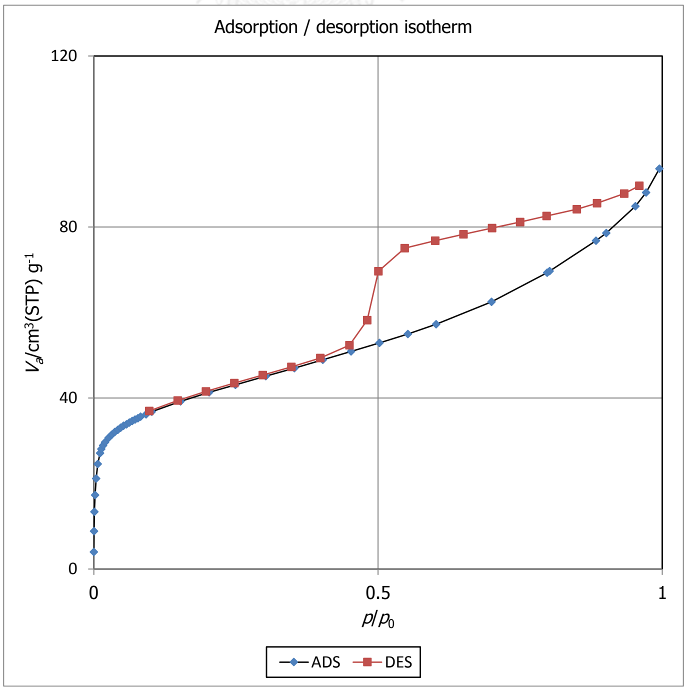

Figure A-6 N_2 adsorption-desorption isotherm of $CrCl_3$/Fe-PLM

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