การแตกของเทอร์มินัลโอเลฟินแบบออกซิไดซ์เร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนโลหะสเทียเรต

นางสาวสื่อกัญญา จารุพินทุโสภณ

CATALYTIC OXIDATIVE CLEAVAGE OF TERMINAL OLEFINS
BY METAL STEARATE COMPLEXES

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การเปลี่ยนหมู่ฟังก์ชันอย่างเลือกจำเพาะของโอเลฟินไม่เพียงแต่มีความสำคัญต่อ
กระบวนการอุตสาหกรรม แต่ยังมีประโยชน์ต่อการสังเคราะห์อย่างมากในด้านการศึกษา งานวิจัย
นี้มุ่งเน้นที่จะพัฒนาวิธีการสังเคราะห์แบบใหม่เพื่อเตรียมสารประกอบคาร์บอนิลจากปฏิกิริยาการ
แตกของเทอร์มินัลโอเลฟินโดยใช้แอลฟาเมทิลสไตรีนเป็นสารต้นแบบ เมื่อใช้ TBHP เป็นออกซิ
แดนท์ร่วมกับตัวเร่งปฏิกิริยาโครเมียมสเทียเรต สารที่มีพันธะคู่คอนจูเกตกับวงแอโรมาทิกหรือหมู่
คาร์บอนิลสามารถเกิดปฏิกิริยาออกซิเดชันอย่างเลือกจำเพาะได้ปริมาณผลิตภัณฑ์ปานกลางถึงดี
มากภายใต้อุณหภูมิที่เหมาะสมในเวลา 24 ชั่วโมง ทั้งตัวเร่งปฏิกิริยาและ TBHP มีความจำเป็น
ต่อการเกิดปฏิกิริยา ปฏิกิริยาการแตกแบบออกซิไดซ์สามารถเกิดได้ดีในตัวทำละลายประเภท
แอโปรติก เช่น ไอโซออกเทน, แอซิโทไนไทรล์ และ 1,2-ไดคลอโรอีเทน ภายใต้ภาวะที่เหมาะสม
ปฏิกิริยาสามารถเกิดได้กับเทอร์มินัลโอเลฟินอื่นๆ การแตกของอนุพันธ์ของแอลฟาเมทิลสไตรีนที่มี
หมู่ให้อิเลกตรอนมากจะให้ผลิตภัณฑ์ได้ดี และเกิดผลิตภัณฑ์ได้น้อยเมื่ออนุพันธ์ของแอลฟา
เมทิลสไตรีนมีหมู่ดึงอิเลกตรอน ปฏิกิริยาการแตกพันธะคู่ที่มีอิเลกตรอนมากแบบคอนจูเกตกับวง
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สาขาวิชา...ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์...ลายมือชื่อนิสิต..
ปีการศึกษา…….........2547.......................ลายมือชื่ออาจารย์ที่ปรึกษา..............................

SUEKANYA JARUPINTHUSOPHON: CATALYTIC OXIDATIVE CLEAVAGE OF TERMINAL OLEFINS BY METAL STEARATE COMPLEXES. THESIS ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D. 67 pp. ISBN: 974-53-1982-1.

Selective functionalization of olefins is not only an industrially important process, but also has many synthetic utilities in academic point of view. This work focuses on the development of a new synthetic methodology for the preparation of carbonyl compounds from the oxidative cleavage of terminal olefins using α-methylstyrene as a model compound. With the use of TBHP as an oxidant in combination with chromium(III) stearate catalyst, selective oxidation of conjugated double bonds with aromatic ring or carbonyl group was achieved at ambient temperature in 24 hours in moderate to excellent yield. Both the catalyst and TBHP are essential in promoting the reaction. The oxidative cleavage works well in aprotic solvents such as isooctane, acetonitrile, and 1,2-dichloroethane. The optimized condition was accomplishedly applied in the oxidative cleavage of a variety of different terminal olefins. The oxidative cleavage of electron rich α-methylstyrene derivatives proceeds in good to excellent yield. Lower yields were observed in α-methylstyrene derivatives containing an electron withdrawing group. The oxidative cleavage is selective for electron rich conjugated double bond with aromatic ring or carbonyl group. This developed oxidation reaction was believed to undergo *via* free radical process and high valent chromium oxo species.

Field of study Petrochemistry and Polymer Science Student's signature……………...……..

Academic year………….…2004……………… Advisor's signature…..……....…..…

ACKNOWLEDGEMENT

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b	broad (IR)
δ	chemical shift
J	coupling constant
°C	degree celsius
$CDCl_3$	deuterated chloroform
d	doublet (NMR)
dd	doublets of doublet (NMR)
GC	gas chromatography
g	gram (s)
^{1}H NMR	proton nuclear magnetic resonance
h	hour (s)
Hz	hertz (NMR)
IR	infrared
m.p.	melting point
m-CPBA	*meta*-chloroperbenzoic acid
mL	milliliter (s)
mmol	millimole
m	multiplet (NMR)
%yield	percentage yield
%wt	percent by weight
q	quartet (NMR)
R_f	retarding factor in chromatography
s	singlet (NMR)
s	strong (IR)
TLC	thin layer chromatography
t	triplet (NMR)
cm^{-1}	unit of wave number
w	weak (IR)

CHAPTER I

INTRODUCTION

The C=C double bond cleavage is a synthetically important reaction to degrade large compounds or to introduce oxygen functionality into molecules. The cleavage of olefins to ketone, aldehydes or carboxylic acids is useful synthetically. At present, there have been efforts to convert olefins to versatile and valuable raw materials for other chemical industries, for example, production of acetophenone and α-keto acid *(1)*.

Acetophenone is used in fragrance industries as a perfume head. α-Keto acids, especially the α-keto acid analogues of the naturally occurring amino acids, are of major importance in intermediary metabolism. α-Keto acids have been used in the therapy of certain conditions, *e.g.*, uremia and nitrogen accumulation disorders. α-Keto acids are of continuing interest as intermediates in chemical syntheses, in the development of enzyme inhibitors and drugs and as model substrates of enzymes *(2)*.

1.1 Metal stearate catalysts

General concepts of catalysis, a catalyst accelerates the rate of a chemical reaction without being consumed. Many catalytic cycles can be induced by a single catalyst molecule and so stoichiometric quantities of the catalyst are not needed. Catalysis is accomplished in the laboratory by stabilizing the transition state of the rate-determining step of a chemical reaction. This might be done, for example, by providing electrostatic stabilization of partially charged centers that develop as the transition state is formed or by prearranging the reactants into a geometry appropriate for a desired bimolecular reaction or by both methods.

Metal esters complexes have often been examined with the objective of obtaining catalysts soluble in organic media. With this aim, a cheap fatty acid has been generally employed for the ester part. The efficiency of metal stearate and metal acetate have been less investigated while metal trifluoroacetate, metal naphthenate,

and metal octoate have been rarely used. Metal esters have been used mainly in conjunction with oxygen *(3)*.

The most popular reagent for oxidative cleavage double bonds is Jones' reagent *(4)*. A major drawback of this reagent is poor solubility in organic solvents. To increase the solubility of chromium salts, different hydrophobic ligands were investigated. One of the most efffective ligand appears to be stearate. Initially, metal stearate catalysts were screened for C-H activation of saturated hydrocarbon *(5)*. Oxidation of aromatic compounds at benzylic position was also achieved by these catalysts *(6)*. Transition metal stearate catalyst was proved to be effective in the oxidation of alchohol to ketone *(7)* and allylic oxidation of unfunctionalized alkenes *(8)*. In this study, transition metal stearate is developed to study the oxidative cleavage of terminal olefins.

1.2 Oxidative cleavage of double bond

Double bonds are oxidatively cleaved to alcohol, aldehyde, ketones, or acids. The specific product formed depends on the structure of the alkene, that is, the presence or absence of hydrogen atoms at the carbons of the double bonds and on the oxidants used.

The oldest and still very common cleavage is the reaction of unsaturated compounds with ozone and the subsequent treatment of the ozonides formed. But the reaction needs to be careful because the ozonides have violently explosive properties *(9)*.

A much more frequently used reaction is the cleavage of unsaturated compounds. For instance, Oxo-de-alkylidene-bisubstitution *(10)* and so on

$$R_2C{=}CHR \xrightarrow{\text{CrO}_3} R_2C{=}O \ + \ RCOOH$$

Double bonds can be cleaved by many oxidizing agents, the most common of which are neutral or acid permanganate and acid dichromate. The products are generally 2 mol of ketone, 2 mol of carboxylic acid (or 1 mol of each) depending on what groups are attached to the alkene. With ordinary solutions of permanganate or dichromate yields are generally low, and the reaction is seldom a useful synthetic method; but high yields can be obtained by oxidizing with $KMnO_4$ dissolved in

benzene containing the crown ether dicyclohexano-18-crown-6 *(11)*. The crown ether coordinates with K^+, permitting the $KMnO_4$ to dissolve in benzene. A mixture of aqueous $KMnO_4$ and $NaIO_4$ on sand is also effective. Another reagent frequently used for synthetic purposes is the Lemieux-von Rudloff reagent: HIO_4 containing a trace of MnO_4^-. The MnO_4^- is the actual oxidizing agent, being reduced to the manganate stage, and the purpose of the HIO_4 is to reoxidizethe manganate back to MnO_4^-. Another reagent that behaves similarly is $NaIO_4$-ruthenium tetroxide *(12)*.

The Barbier-Wieland procedure for decreasing the length of a chain by one carbon involves oxidative cleavage by acid dichromate ($NaIO_4$-ruthenium tetroxide has also been used), but this is a cleavage of a 1,1-diphenyl alkene, which generally gives good yields *(13)*:

$$RCH_2COOH \xrightarrow[H^+]{EtOH} RCH_2COOEt \xrightarrow{PhMgBr} RH_2C \overset{Ph}{\underset{OH}{\diagdown}} Ph$$

$$\xrightarrow{\triangle} RCH= CPh_2 \xrightarrow[\text{or} \atop NaIO_4\text{-}RuO_4]{CrO_3} RCOOH \quad + \quad Ph_2CO$$
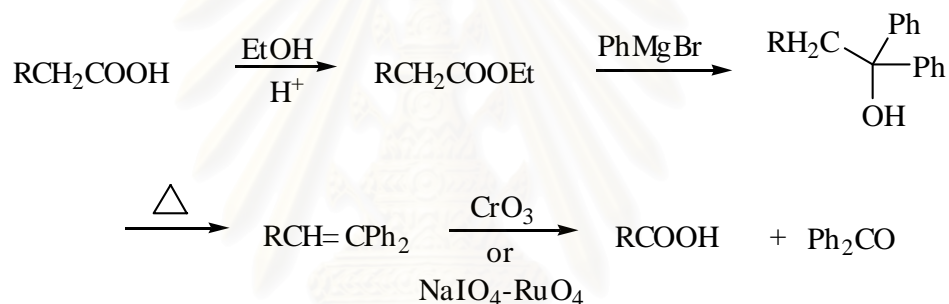
Addition of a catalytic amount of OsO_4 to Jones reagent leads to good yields of the carboxylic acid from simple alkenes. With certain reagents, the oxidation of double bonds can be stopped at the aldehyde stage, and in these cases the products are the same as in the ozonolysis procedure. Among these reagents are *tert*-butyl iodoxybenzene, $KMnO_4$ in tetrahydrofuran-water, and $NaIO_4$-OsO_4. Electrolysis with $LiClO_4$ in aqueous acetonitrile also cleaves alkenes to give the aldehyde. Enol ethers $RC(OR')=CH_2$ have been cleaved to carboxylic esters $RC(OR')=O$ by atmospheric oxygen *(14)*.

The mechanism of oxidation probably involves in most cases the initial formation of a glycol or cyclic ester, and then further oxidation. In line with the electrophilic attack on the alkene, triple-bonds are more resistant to the oxidation than double bonds. Terminal triple-bond compounds can be cleaved to carboxylic acids ($RC\equiv CH \rightarrow RCOOH$) with thallium(III) nitrate or with [bis(trifluoroacetoxy)iodo] pentafluorobenzene, that is, $C_6F_5I(OCOCF_3)_2$, among other reagents *(15)*.

Aromatic rings can be cleaved with strong enough oxidizing agents. An important laboratory reagent for this purpose is ruthenium tetroxide along with co-oxidant such as $NaIO_4$ or $NaOCl$ (household bleach can be used). Examples are the oxidation of naphthalene to phthalic acid and, even more remarkably, of cyclohexylbenzene to cyclohexanecarboxylic acid. The latter conversion was also accomplished with ozone. Another reagent that oxidizes aromatic rings is air catalyzed by V_2O_5. The oxidations of naphthalene to phthalic anhydride and of benzene to maleic anhydride by this reagent are important industrial procedures. Ortho-diamines have been oxidized with nickel peroxide, with lead tetraacetate, and with O_2 catalyzed by $CuCl_2$ *(16)*:
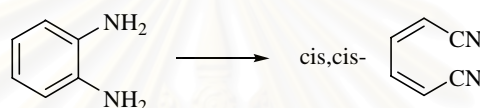
The last-named reagent also cleaves ortho-dihydroxybenzenes (catechols) to give, in the presence of methanol, the monomethylated dicarboxylic acids

$$HOOC\text{-}C\text{=}C\text{-}C\text{=}C\text{-}COOMe$$
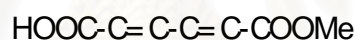
Enamines (R'_2=NR_2) are oxidatively cleaved with potassium in sulfuric acid to the ketone (R'_2C=O) *(17)*.

1.3 Mechanism of the oxidative cleavage

The mechanisms of oxidation and reduction reactions are diverse because the bond changes are different. Therefore, a relatively few mechanisms covered all the reactions. Moreover, the mechanism of a given oxidation or reduction reaction can vary greatly with the oxidizing or reducing agent employed. Very often the mechanism has been studied intensively for only one or a few of many possible agents. Mechanism of oxidative cleavage of double bonds depends on either oxidant or metal catalyst.

1.3.1 The oxidative cleavage of olefins by osmium tetroxide/oxone *(18)*

From previous work in the oxidative cyclization of 1,4-dienes, in which OsO_4 and various cooxidants were used to promote the cyclization pathway. Low yields of cyclized products were attributed to a substantial amount of overoxidized products

resulting from an oxidative cleavage of the olefin functionality. Further investigation into the nature of the overoxidized products and optimization of the reaction has led to a selective oxidative cleavage of olefins to yield carboxylic acids using catalytic OsO_4 and Oxone in dimethyl sulfoxide (Scheme 1.1).
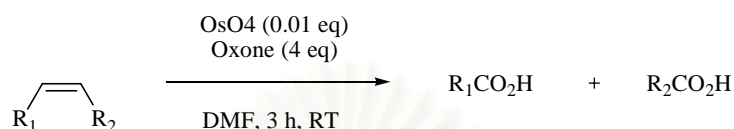
Scheme 1.1 The oxidative cleavage of olefins by OsO_4

Oxidative cleavage of olefins takes place with OsO_4 and Oxone in dimethyl sulfoxide, to provide ketones or carboxylic acids. The mechanism is as follow:
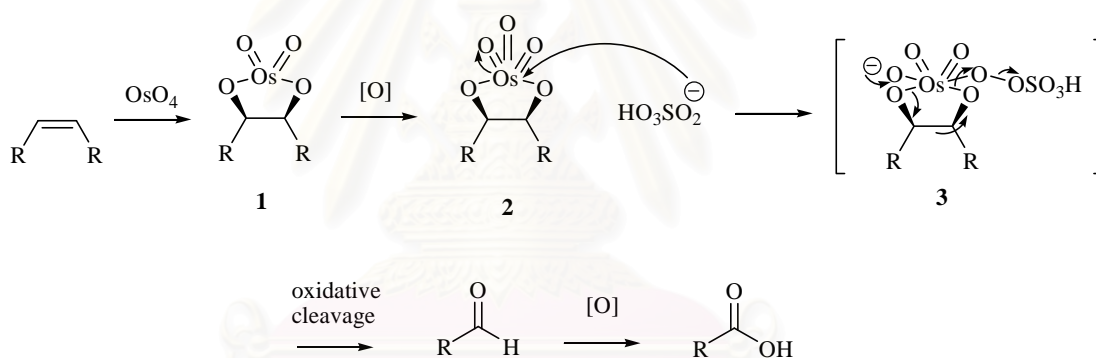
Scheme 1.2 Mechanism of the oxidative cleavage of olefins by OsO_4

Osmium tetroxide adds to the double bond, forming osmate ester **1**. It was oxidized by oxone to furnish **2** which is subsequently attacked by oxone again to yield intermediate **3**. Fragmentation of **3** regenerates OsO_4 and producs two aldehydes, which can undergo further oxidation to yield carboxylic acids (Scheme 1.2). Note that there is no vicinal diol intermediate present in this proposed mechanism as opposed to dihydroxylation of olefins.

1.3.2 The oxidative cleavage of α-methylstyrene by $CoCl_2$/oxygen *(19)*

The application of $CoCl_2$/Oxygen catalyzed oxidation of organic compounds was reported the results using alkene substrates. It was found that, for some classes of

olefin such as α-methylstyrene, the selective cleavage of the carbon-carbon double bond to the corresponding carbonyl compounds can occur under optimal conditions. In addition, the selectivity towards forming cleavage products or polymers is strongly influenced by the electronic and steric properties of the substrate (Scheme 1.3).
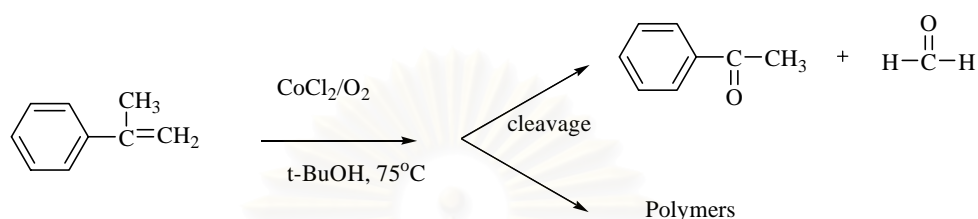
Scheme 1.3 The oxidative cleavage of α-methylstyrene by CoCl$_2$/oxygen

The cobalt(II) chloride-catalyzed oxidative cleavage of α-methylstyrene with oxygen in *tert*-butanol gave acetophenone and formaldehyde in good yield. The proposed mechanism is shown in Scheme 1.4 with α-methylstyrene as a substrate.
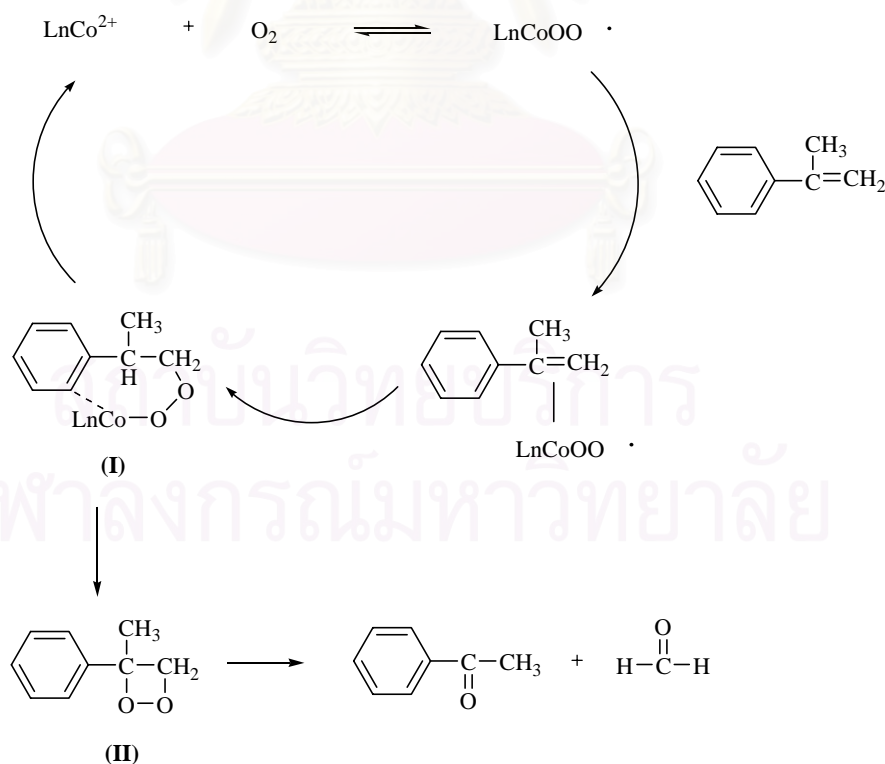
Scheme 1.4 Mechanism of the oxidative cleavage of α-methylstyrene by CoCl$_2$/oxygen

First, cobalt-activated molecular oxygen, in the form of cobalt superoxo complex ($L_nCoOO\cdot$) reacts with the alkene to form an intermediate (**I**) having a benzylic radical centre. The intermediate (**I**) may then collapse to a cyclic peroxide intermediate (**II**) by intramolecular reaction. Then (**II**) is subsequently decomposed to acetophenone and formaldehyde under the reaction conditions. For olefins other than styrenes, the benzylic intermediate cannot be formed. Hence, the reaction is ineffective.

1.3.3 The oxidative cleavage of methylidene group by Gif type systems *(20)*

The Gif oxidation systems cleave methylidene olefins into the ketone or aldehyde and formaldehyde. For instance, methylenecyclohexane gave substantial yields of cyclohexanone and α-methylstyrene afforded nearly 30% of the corresponding ketone. The Gif type systems depend for their selectivity on a common iron oxenoid species. This is considered to be a manifestation of an ^VFe oxenoid species. In terms of Barton's theory, the addition of the ^VFe oxenoid species to the double bond followed by cleavage to the ketone and a methylene carbene (**A**). The latter to be oxidized to formaldehyde (Scheme 1.5).

(**A**)
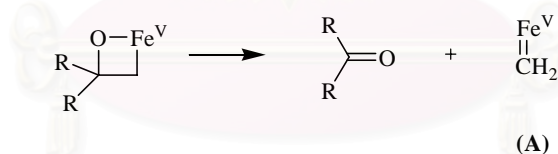
Scheme 1.5 The oxidative cleavage of methylidene group by Gif type systems

1.4 Literature review on the oxidative cleavage of terminal olefins

There are many methods for oxidizing double bonds in organic compounds (1) ozonolysis (2) oxidation with potassium permanganate ($KMnO_4$) (3) with osmium tetroxide (OsO_4) (4) ruthenium tetroxide (RuO_4) and (5) combination of oxidant and a catalyst.

In 1957, Warnell and coworkers reported that ozonolysis of indene in ethanol at 0-5 ^oC for one hour gave 3-hydroxy-4,5-benzo-7-ethoxy-1,2-dioxacycloheptane with 99% selectivity. Subsequent reduction by treating with zinc dust and acetic acid

at room temperature gave homophthalaldehyde with 98% yield *(21)*. In 1966, Pappas and colleagues found that ozonolysis of styrene (a terminal double bond) in dimethyl sulfide-methanol at -10 to 25 ^{o}C gave benzaldehyde (89%) *(22)*.

Similarly, molecular oxygen could be used to oxidize terminal double bonds. In 1997, Lin and coworkers used cobalt chloride in *tert*-butyl alcohol in an oxygen atmosphere at 75 ^{o}C for 20 hour, oxidative cleavage of α-methylstyrene was achieved to produce acetophenone with 74% regioselectivity *(19)*. In 2001, Baucherel and colleagues studied the catalytic system of metal methyl 2-*N*-salicylidene-3-hydroxypropanoate (metal = Mn, Co, V) under oxygen atmosphere in the presence of thiophenols. They reported the oxidative cleavage of olefins by free radical pathway in the conversion from β-pinene to nopinone (68%) and from (S)-(-)-limonene to (S)-(-)-4-acetyl-1-methylcyclo-1-hexene, a perfume head, with 73% yield *(23)*.

In other developments, oxidative cleavage of terminal olefins could be achieved with potassium permanganate immobilized on solid support to prepare aldehydes. In 1993, Lee and colleagues used potassium permanganate on moist alumina to oxidize 1-pentadecene to tetradecanal in 24 hours with 52-60% yield *(24)*.

Oxidation of olefins with osmium tetroxide could be used to generate high quantity of carboxylic acids. In 2002, Travis and coworkers found that styrene could be oxidized with a combination of osmium tetroxide and ozone (O_3) in dimethylformamide at room temperature in 3 hours to benzoic acid (94%) *(18)*.

Oxidative cleavage of terminal olefin by ruthenium tetroxide was reported by Carlsen and colleagues in 1981. 1-Decene was converted to nonanoic acid (89%) by ruthenium tetroxide/sodium periodate ($NaIO_4$) in a solvent mixture (acetonitrile/ carbon tetrachloride/water 2:2:3) at 25 ^{o}C in 2 hours *(25)*. In 1985, Torii and coworkers oxidized enolic olefins such as α-D-glucal triacetate with ruthenium tetroxide/sodium periodate in 1:1 carbon tetrachloride/water. The keto acid product was separated in 96% *(26)*.

The use of oxidant in the presence of a catalyst was also reported. In 1990, Neumann's group used $((C_6H_{13})_4N)_5SiRu^{III}.(H_2O)W_{11}O_{39}$ to convert styrene to benzaldehyde (98%) with high regioselectivity when sodium periodate was used as an oxidant *(27)*. In 1992, Rao and colleagues found that selective oxidation of olefins to methyl ketones could be achieved by employing hydrogen peroxide as an oxidant and

montmorillonite silylpropylethylenediamine palladium as a catalyst. In 30 minutes, 1-octene could be converted to 2-octanone (92%) and styrene to acetophenone (98%) *(28)*. In 1998, Antonelli and coworkers oxidized 1-dodecene to nonanoic acid (80%) by using 40% w/v aqueous hydrogen peroxide in the presence of methyltrioctyl ammonium tetrakis(oxodiperoxotungsto)phosphate as a catalyst at 85°C for 6 hours *(29)*. In 1999, Brooks and colleagues achieved rapid and complete conversion in the oxidative cleavage of olefins to carbonyl compounds. By using aqueous hydrogen peroxide as an oxidant and 6-molybdo-6-tungstophosphoric acid (PMWA, a heteropolyacid) on either magnesium or aluminium or zinc oxide as a catalyst in 2-methylpropan-2-ol as a solvent, 1-octene was stoichiometrically converted to heptanoic acid after 4 hours at 60 $^{\circ}$C *(30)*. In 2001, Yang and colleagues used $RuCl_3$-Oxone-$NaHCO_3$ in acetonitrile/water (1.5:1) to oxidize α-methylstyrene to acetophenone in 78% yield. More recently, $RuCl_3$/$NaIO_4$ in 1,2-dichloroethane/ water (1:1) was shown to cleave cyclohexene to adipaldehyde (70%). Moreover, with this $RuCl_3$/$NaIO_4$ system in acetonitrile/water (6:1), 1-dodecene was oxidized to undecenal with 95% yield within only 1.6 hours *(31)*.

From these literatures, alkenes are one of the most common functionalities in natural products. Conversion of alkenes to carbonyl compound is another important process in petrochemical industry. This was so called "oxidative cleavage" process usually gives carbonyl compound and/or other oxidized products such as epoxides, allylic hydroperoxides alcohols, and polymers. There are transition metal catalyzed oxidation methods for oxidative cleavage. The search for cheap, simple, and selective oxidative cleavage often focuses on the transition metal catalysts. The most successful metal catalyzed cleavage usually employs second or third row transition metal complexes. Amongst the first row transition metal catalysts, only few metals have been studied. An interesting example is the cobalt Schiff base complex catalyst for the selective cleavage of isoeugenol. However, none has focused on oxidative cleavage of terminal olefins by employing metal stearate complex as a catalyst. These metal stearates are inexpensive and easily preparative. Catalytic efficiency of these complexes was screened using the oxidative cleavage of α-methylstyrene as a model reaction. *tert*-Butylhydroperoxide was chosen as an oxidant because it is readily

available and it was reported to affect various oxidations on organic compounds. After the reaction was optimized, it will be applied to a variety of different olefins.

1.5 The goal of this research

The aim of this research can be summarized as follows:

1. To prepare transition metals stearate complexes

2. To develop a new catalytic system for oxidative cleavage of terminal olefins by metal stearate catalyst under mild reaction conditions

3. To apply the optimized condition to a variety of substituted olefins

4. To study the effect of substituents of olefins on the reactivity

CHAPTER II

EXPERIMENTAL SECTION

2.1 General procedure

Melting points (m.p.) were measured on Fisher-Johns melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's, Kieselgel 60G Art 7734 (70-230 mesh)) and aluminium oxide 90 (70-230 mesh ASTM). Gas chromatographic analysis was carried out on a Shimadzu gas chromatograph GC-14A instrument equipped with flame ionization detector (FID) using nitrogen as a carrier gas, the column used for chromatography was a capillary column type of DB-WAX (30 m x 0.250 mm) from J & W Scientific company. Fourier Transform-Infrared spectra (FT-IR) were recorded on Nicolet Impact 410 FT-IR spectrometer. Solid samples were incorporated to potassium bromide (KBr) to form pellet. As a liquid sample, a drop of the liquid was squeezed between flat plates of sodium chloride (transparent through the 625-4000 cm^{-1} region). The ^1H and ^{13}C-NMR spectra were obtained in deuterated chloroform ($CDCl_3$) or otherwise stated, with Bruker model ACF200 and Varian model Mercury 400 spectrometers.

2.2 Chemical reagents

All solvents used in this research were purified prior to use by standard methodology except for those which were reagent grade. The reagents used for synthesizing metal stearate complexes and all organic substrates were purchased from Fluka chemical company and were used without further purification.

2.3 Syntheses of metal stearate complexes

General procedure for the syntheses of metal stearate complexes *(32)*

Stearic acid (22 mmol) was dissolved in 1 M sodium hydroxide solution at 80°C. After the mixture was heated and transmuted homogeneously, a solution of metal(III) chloride (7.3 mmol) dissolved in distilled water 10 mL was added dropwise. The mixture was continued heating at about 80 °C for about 30 min, the precipitate was collected and dried *in vacuo*.

Cr(III) stearate: blue gray solid (86 %), m.p. 100-103 °C. IR (KBr, cm^{-1}): 2856-2921(w), 1720(s), 1569(s), 1461(s) and 723(s).

Mn(II) stearate: white solid (90%), m.p. 108-111 °C. IR (KBr, cm^{-1}): 2856(b), 1569-1720(w), 1461(s) and 718(s).

Fe(III) stearate: orange solid (78%), m.p. 94-96 °C. IR (KBr, cm^{-1}): 2846-2912(w), 1705(s), 1583(s), 1461(s) and 723(s).

Co(II) stearate: pink solid (74%), m.p. 86-90 °C. IR (KBr, cm^{-1}): 2856-2912(w), 1630-1701(b), 1545(s) and 721(s)

Ni(II) stearate: light green solid (87%), m.p. 175-177 °C. IR (KBr, cm^{-1}): 2856-2903(w), 1564-1720(w), 1381(b) and 721(s).

Cu(II) stearate: light blue solid (92%), m.p. 138-145 °C. IR (KBr, cm^{-1}): 2903(s), 2846(s), 1592(s), 1404-1456(w) and 721(s).

Zn(II) stearate: white solid (81%), m.p. 115-120 °C. IR (KBr, cm^{-1}): 2908-2848(w), 1703(s), 1536(s), 1466(w) and 726(s).

2.4 Syntheses of authentic samples

α-methylstyrene oxide

To a solution of α-methylstyrene (9.7 mmol) in 50 mL of dry dichloromethane at 0 °C was added 70% 3-chloroperbenzoic acid (*m*-CPBA) (2.22 mmol) in 40 mL of dry dichloromethane over a period of 30 min. After the solution was stirred for 3-4 hours, the excess peracid was decomposed with 5 mL of 10% sodium sulfite solution and the dry dichloromethane solution was washed carefully with 100 mL of saturated sodium hydrogen carbonate solution, the organic layer was separated, and the aqueous layer was washed twice with dry dichloromethane. The organic layers were combined, washed with brine, dried and evaporated to yield the desired epoxide.

Purification was achieved by chromatography (aluminium oxide 90, CHCl$_3$) to give the compound as a colorless liquid.

α-methylstyrene oxide (33): 38% yield, colorless liquid, R$_f$ 0.36 (CHCl$_3$); ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.23-7.42 (m, 5H), 2.98 (d, *J* = 5.4 Hz, 1H), 2.82 (d, *J* = 5.4 Hz, 1H) and 1.73 (s, 3H).

diethyl oxalacetate

Sulfuric acid was added dropwise to catalyze the diesterification reaction between oxalacetic acid (1 mol) and ethanol (3 mol). The reaction mixture was refluxed until complete consumption of oxalacetic acid (TLC monitored). After this, the reaction mixture was cooled and the crude was washed with saturated sodium hydrogen carbonate. The organic phase was separated, dried, evaporated, and flash column chromatograped by eluting with dichloromethane to afford diester.

diethyl oxalacetate (34): 74% yield, colorless liquid, R$_f$ 0.44 (hexane:ethyl acetate 8:2); IR (NaCl, cm^{-1}): 2980 (s), 2937 (w), 2902 (w), 1727 (s), 1641 (w), 1478 (w), 1369 (w), 1314 (w), 1201 (s), 1144 (w), 1030 (s), 956 (w), 867 (w), 816 (w) and 746 (w); ^{1}H-NMR (CDCl$_3$) δ (ppm): 3.57 (q, *J* = 7.3 Hz, 2H), 3.49 (q, *J* = 7.3 Hz, 2H), 2.97 (s, 2H) and 1.30 (m, *J* = 7.2 Hz, 6H).

methyl pyruvate

Chromium(III) acetyl acetonate (Cr(acac)$_3$, 0.57 mmol), methyl methacrylate (94.19 mmol) and hydrogen peroxide (30% H$_2$O$_2$, 283 mmol) was stirred in acetonitrile (100 mL) at 50 °C for 8 hours. The reaction mixture was poured into 25% sulfuric acid (100 mL) and the product was extracted with ethyl acetate (2 x 100 mL). The combined organic phase was then washed with 25% sulfuric acid (2 x 100 mL), saturated sodium hydrogen carbonate (2 x 100 mL), and distilled water (2 x 100 mL), then dried, evaporated, and flash column chromatograped to give the desired compound as a colorless liquid.

methyl pyruvate (35): 55% yield, colorless liquid, R$_f$ 0.47 (5% methanol in dichloromethane); IR (NaCl, cm^{-1}): 2995 (w), 2960 (s), 1801 (w), 1742 (s), 1446 (s), 1369 (w), 1283 (w), 1213 (w) and 1120 (w); ^{1}H-NMR (CDCl$_3$) δ (ppm): 3.87 (s, 3H) and 2.48 (s, 3H).

2.5 Syntheses of starting materials

diethyl itaconate

Sulfuric acid (3% by weight of alcohol, 3.5 mL) was added dropwise to catalyze the diesterification reaction between itaconic acid (30.0 g, 0.23 mol) and ethanol (4.61 mol, 269 mL). The reaction mixture was monitored by TLC. The mixture was refluxed for 96 hours (4 days) and then allowed to cool and neutralized with saturated sodium hydrogen carbonate. The resulting precipitate was filtered and ethanol was removed under reduced pressure. The concentrated mixture was added 50 mL of saturated sodium hydrogen carbonate. The product was extracted with ethyl acetate (3 x 50 mL) and the combined organic phase was washed with saturated hydrogen carbonate (2 x 50 mL) and distilled water (2 x 50 mL). It was then dried over anhydrous sodium sulfate, filtered, and the solvent was removed under reduced pressure to give a yellow oil as crude product. Purification was achieved by flash chromatography (silica gel, 0-10% ethyl acetate in hexane) to give the desired compound as colorless liquid.

diethyl itaconate (36): 81% yield, colorless liquid, R_f 0.39 (hexane:ethyl acetate 8:2); IR (NaCl, cm^{-1}): 2980 (s), 2937 (w), 2898 (w), 1746 (s), 1625 (w), 1454 (w), 1376 (w), 1302 (w), 1178 (s), 1065 (s), 948 (w), 859 (w) and 773 (w); ^{1}H-NMR (CDCl$_3$) δ (ppm): 6.35 (s, 1H), 5.72 (s, 1H), 4.24 (q, J = 7.3 Hz, 2H), 4.18 (q, J = 7.3 Hz, 2H), 3.35 (s, 2H) and 1.30 (m, J = 7.2 Hz, 6H).

General procedure for the syntheses of α-methylstyrene derivatives

Preparation of methyltriphenylphosphonium iodide

Under an atmosphere of dry nitrogen, triphenylphosphine (52.4 g, 0.2 mol) was added to 500 g of dry diethyl ether in a dried 1000-mL round-bottom flask. After stirring until all solid was dissolved, iodomethane (25.0 g, 0.17 mol) was added and the flask was stoppered. The reaction was then stirred for 24 hours at room temperature. Filtration gave 54.8 g of a white solid and recrystallized from ethanol-ether.

Methyltriphenylphosphonium iodide (37): 78% yield, white solid; ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.66-7.84 (m, 15H) and 3.20 (d, J = 13.0 Hz, 3H).

<u>Preparation of terminal olefins</u> *(38)*

Into a 250 ml three-necked round bottom flask equipped with a magnetic stir bar, condenser with nitrogen inlet, pressure-equalizing addition funnel, and a rubber septum was placed methyltriphenylphosphonium iodide (4.85 g, 12 mmol) suspended in 25 mL dry tetrahydrofuran. The suspension was cooled to 0 °C with an ice bath. The reaction mixture was charged slowly with *n-* butyllithium (1.6 M in hexanes, 7.5 mL, 12.1 mmol) to give an orange solution. After one hour, solution of a carbonyl compound (10 mmol) in 15 mL dry tetrahydrofuran was added slowly to the flask from the addition funnel, the ice bath was removed and the flask was gradually warmed to room temperature. After the reaction mixture was stirred overnight, TLC analysis of a small aliquot of the reaction mixture showed complete consumption of the starting material. Hydrochloric acid (1N) was added to the reaction mixture, and the aqueous layer (pH 5) was extracted with ethyl acetate, washed with brine, dried, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography.

2-nitro-α-methylstyrene: 73% yield, brown liquid, R_f 0.47 (hexane:ethyl acetate 8:2); ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.89 (d, J = 7.1 Hz, 1H), 7.58 (t, J = 6.3 Hz, 1H), 7.43 (t, J = 6.8 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 5.21 (s, 1H), 4.98 (s, 1H) and 2.13 (s, 3H).

3-nitro-α-methylstyrene: 87% yield, brown liquid, R_f 0.43 (hexane:ethyl acetate 8:2); ^{1}H-NMR (CDCl$_3$) δ (ppm): 8.83 (s, 1H), 8.15 (d, J = 8.2, 1H), 7.70 (t, J = 6. 9 Hz, 2H), 7.57 (d, J = 7.4 Hz, 1H), 5.54 (s, 1H), 5.29 (s, 1H) and 2.24 (s, 3H).

4-nitro-α-methylstyrene: 71% yield, brown liquid, R_f 0.39 (hexane:ethyl acetate 8:2); ^{1}H-NMR (CDCl$_3$) δ (ppm): 8.21 (d, J = 8.9 Hz, 2H), 7.57 (d, J = 6.0 Hz, 2H), 5.55 (s, 1H), 5.32 (s, 1H) and 2.22 (s, *3*H).

4-bromo-α-methylstyrene (39): 69% yield, colorless liquid, R_f 0.59 (hexane); ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.48 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 5.40 (s, 1H), 5.14 (s, 1H) and 2.17 (s, 3H).

4-methoxy-α-methylstyrene (40): 95% yield, white solid, R_f 0.48 (hexane:ethyl acetate 9:1); ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.46 (d, J = 8.9 Hz, 2H), 6.91 (d, J = 8.9 Hz, 2H), 5.33 (s, 1H), 5.04 (s, 1H), 3.86 (s, 3H) and 2.18 (s, 3H).

2.6 The general procedure for the oxidative cleavage of terminal olefins

For the oxidative cleavage of terminal olefins, a solution of substrate (5 mmol) in isooctane (5 mL) containing chromium(III) stearate complex (0.2 mmol) in a round bottom flask and 70% TBHP (9 mmol) was added. The mixture was stirred at $70^{o}C$ for 24 hours. After the reaction finished, 1 mL of the reaction mixture was taken and extracted with diethyl ether. The combined extracts were washed with 25% sulfuric acid and saturated solution of sodium hydrogen carbonate, respectively. The organic layer was dried over anhydrous sodium sulfate and analyzed by gas chromatograph (GC) with the addition of an exact amount of appropriate internal standard.

2.7 Study on the optimum conditions for oxidative cleavage of α-methylstyrene

2.7.1 Effect of metal stearate complexes

The oxidation reaction was carried out in the same manner as previously described employing various metal stearate complexes: Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) stearates. In addition, the amount of chromium(III) stearate was varied for oxidative cleavage reaction: 0.02, 0.05, 0.10, 0.15, 0.20, 0.25 and 0.30 mmol.

2.7.2 Effect of type of oxidants

The oxidation reaction was carried out in the same manner as aforementioned, switching from TBHP to H_2O_2, MCPBA, $NaIO_4$, 2-ethylbutylraldehyde and O_2, zinc grit and acetic acid, urea hydrogen peroxide, oxone tetrabutylammonium salt, and ammonium peroxodisulfate. The amount of TBHP was also studied by variation for oxidative cleavage reaction: 0, 3, 6, 9 and 12 mmol.

2.7.3 Effect of solvents

The oxidation reaction was carried out in the same manner as described above except for dimethyl sulfoxide, tetrahydrofuran, dichloromethane, 1,2-dichloroethane, ethanol, methanol, carbon tetrachloride, acetone, chloroform, pyridine and acetonitrile was used as a reaction medium.

2.7.4 Effect of the amount of substrate

The oxidation reaction was carried out as described in the general procedure using chromium(III) stearate as a catalyst with different amount of α-methylstyrene: 5, 10, 15, 20, 25 and 50 mmol.

2.7.5 Effect of temperature

The oxidation reaction was performed according to the general procedure mentioned earlier using chromium(III) stearate as a catalyst, but different reaction temperature was varied: 30, 50, 70 and 90 °C.

2.7.6 Kinetic study on the oxidative cleavage of α-methylstyrene catalyzed by chromium(III) stearate

The general oxidation procedure of α-methylstyrene using chromium(III) stearate as a catalyst was carried out. At different reaction time proceeded an aliquot from the reaction mixture was taken, worked up and analyzed by GC: 0.5, 1, 3, 6, 9, 24, 36 and 48 hours.

2.8 Study on the oxidative cleavage of α-methylstyrene catalyzed by bicatalyst and tricatalyst of metal stearate complexes

2.8.1 Effect of bicatalyst

The oxidation reactions of α-methylstyrene catalyzed by bicatalysts were conducted. These reactions were carried out at 70 ^{o}C, at different ratio of catalyst: Cr(III) stearate and other metal stearates in ratio of 1:1 and 2:1.

2.8.2 Effect of tricatalyst

Tricatalyst was used in these reactions with the ratio of Cr(III) stearate and other metal stearates (1:1:1). Procedures were carried out the same manner as mentioned above. Metal stearate tried in this examination included Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) stearates.

2.9 Oxidative cleavage of selected terminal olefins catalyzed by chromium(III) stearate

The oxidation reaction was carried out as described in the general procedure using chromium(III) stearate as a catalyst and different types of substrate were varied: methyl methacrylate, 4-chloro-α-methylstyrene, diethyl itaconate, camphene, *etc*. The aliquot (1 mL) of the reaction mixture was taken, worked up with 25% sulfuric acid, saturated hydrogen carbonate and dried over anhydrous sodium sulfate, analyzed by GC or ^{1}H-NMR spectrometer.

General isolation procedure.

After the reaction was complete (followed by TLC), the oxidation product was separated as follows: the whole reaction mixture was extracted according to the general procedure and all the solvents were removed. The crude product was purified by silica gel column chromatography using a mixture of hexane-ethyl acetate or chloroform as an eluent. The equivalent fractions monitored by TLC were combined and the solvents were completely evaporated. The residue was recrystallized by an appropriate solvent or chromatographed over silica gel column to yield the desired carbonyl compound.

4-chloroacetophenone: 81% yield, colorless liquid, R_f 0.38 (hexane:ethylacetate 9:1); ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.91 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.5 Hz, 2H) and 2.61 (s, 3H).

benzophenone: 76% yield, white needle, R_f 0.52 (hexane:ethyl acetate 9:1), recrystallized from ether; ^{1}H-NMR (CDCl$_3$) δ (ppm): 7.84 (d, J = 7.3 Hz, 4H), 7.63 (t, J = 7.4 Hz, 2H) and 7.52 (t, J = 7.6 Hz, 4H).

1-acetyl-3-propenylbenzene (41): 43% yield, colorless liquid, R_f 0.34 (hexane:ethyl acetate 9:1); ^{1}H-NMR (CDCl$_3$) δ (ppm): 8.08 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.7, 1H), 5.47 (s, 1H), 5.12 (s, 1H), 2.66 (s, 3H) and 2.22 (s, 3H)

CHAPTER III

RESULTS AND DISCUSSION

Functionalization of olefinic feedstock is one of important processes in petrochemical industry. Among common methods for the preparation of carbonyl compounds, the oxidative cleavage of olefins is well recognized. In addition to the desired carbonyl compounds, other common products from the functionalization of olefins include epoxides, allylic hydroperoxides, alcohols, and polymers.

Many synthetic methods, especially ozonolysis or stoichiometric oxidation are well documented *(42)*. A number of potentially useful selective oxidations of various organic substrates using relatively simple catalytic systems have been reported *(43)*. Metal-catalyzed oxidative cleavage of olefins has been thoroughly investigated, with most success in the use of second- or third-row transition metal complexes *(44)*. Amongst the first row transition metal catalysts, only a few metals such as cobalt Schiff base complexes have been studied as a catalyst for isoeugenol oxidation of a carbon-carbon double bond cleavage *(45)*.

Olefin functionality can be divided into two types according to its reactivity: internal and terminal double bonds. Examples of compounds containing internal double bond are *trans*-stilbene, 2-norbornene, isoeugenol and cyclohexene. Compounds containing terminal double bonds are for instance α-methylstyrene and methyl methacrylate (MMA). While a lot of studies have focused on the internal double bonds and activated or conjugated double bonds, only a few have been directed towards the reactivity of terminal double bonds.

This research was focused on the catalytic oxidative cleavage of terminal olefins by first row transition metal complexes. In this study, the reaction conditions were optimized using α-methylstyrene as a chemical model. Other substrates such as styrene, MMA, 4-chloro-α-methylstyrene, 4-vinyl-1-cyclohexene, 2-nitro-α-methylstyrene and 4-methoxy-α-methylstyrene were selected for examining the scope of this developed oxidation system. In order to find the optimum conditions for the

oxidative cleavage reaction, various factors were needed to be considered, for example, concentration of catalyst, type of oxidizing agent, amount of oxidant and substrate, solvent, temperature and reaction time.

3.1 Syntheses and identification of metal stearate complexes

Metal stearate complexes were prepared by reacting stearic acid with the corresponding metal chlorides under basic conditions according to encyclopedia of chemical technology *(32)*. The complexes studied in the catalysis screening are of chromium(III), manganese(II), iron(III), cobalt(II), nickel(II), copper(II), and zinc(II) stearates. Their identities were confirmed by comparison both physical properties (color and melting point) and IR spectroscopic data with those reported *(46)*. Major peaks from the IR spectrum of stearic acid were a broad COOH peak at 2700-3400, 1703 for asymmetric stretching of COO, and 1471 for symmetric stretching of COO. The IR spectra of metal stearate catalysts prepared showed C=O bands at 1600-1700 and 1400-1450 cm^{-1} for asymmetric and symmetric stretching of (COO)$^-$, respectively. The COO peak shifts are indicative of the complex formation. Both the free acid and the complexes showed a significant $(CH_2)_n$ skeletal vibration peak at 720 cm^{-1}*(47)*. The instance of IR spectrum of chromium(III) stearate complex is shown in Fig 3.1.

Figure 3.1 IR spectrum of chromium(III) stearate complex.

From Fig 3.1, the IR spectrum of chromium(III) stearate complex exhibited C=O bands at 1710 cm^{-1} and 1541-1461 cm^{-1} for asymmetric and symmetric stretching of (COO)$^{-}$, respectively together with (CH$_2$)$_n$ skeletal vibration peak at 723 cm^{-1}.

3.2 Study on the optimum conditions for oxidative cleavage of α-methylstyrene

In order to obtain appropriate parameters that could promote the transformation of α-methylstyrene to acetophenone in high yield, the reaction was optimized by varying the amount of catalyst, solvent and oxidant. The optimized conditions were then applied to the oxidation of other terminal olefins.

3.2.1 Effect of metal stearate complexes

The effects of metal stearate complexes on the oxidative cleavage of α-methylstyrene in the presence of TBHP and isooctane as a solvent were explored. The results are addressed in Table 3.1 and Fig 3.2.

Table 3.1 The effect of metal stearate complexes on the oxidative cleavage of α-methylstyrene

Entry	Metal stearate	% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
1	Chromium(III)	85	2	9	96
2	Manganese(II)	57	2	40	99
3	Iron(III)	59	4	37	100
4	Cobalt(II)	71	18	9	98
5	Nickel(II)	66	15	19	100
6	Copper(II)	63	3	31	97
7	Zinc(II)	42	10	46	98

reactions conditions: α-methylstyrene (5 mmol), metal stearate (0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ℃ for 24 h.
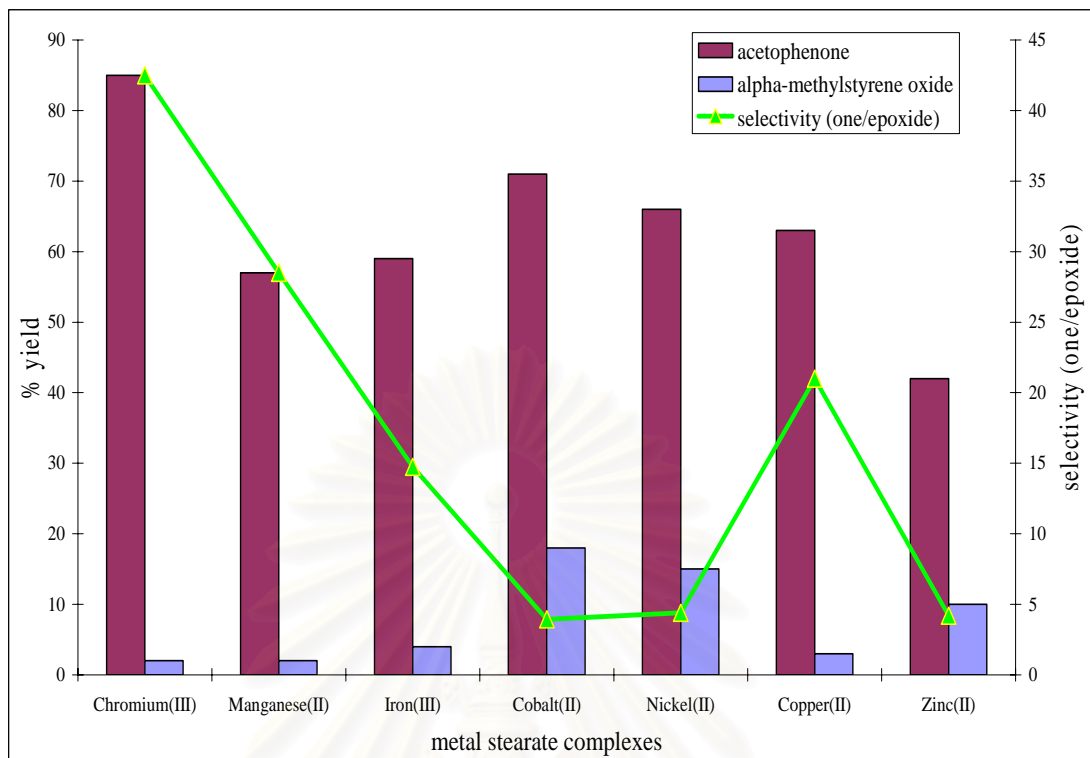
Figure 3.2 The effect of metal stearate complexes on the oxidative cleavage of α-methylstyrene.

Oxidative cleavage of α-methylstyrene was performed in isooctane in the presence of different metal stearates. TBHP was chosen as the oxidant since it has been claimed as a versatile oxidizing agent for functionalization of hydrocarbons. From Table 3.1 and Fig 3.2, the condition employing chromium(III) stearate as a catalyst gave the best yield of acetophenone (85%, entry 1). In all cases, the only by-product was the corresponding epoxide and some unreacted α-methylstyrene was observed. With cobalt(II) or nickel(II) stearates as a catalyst, the reaction could be proceeded to give acetophenone in good yield; nonetheless being a significant amount of by product α-methylstyrene oxide was detected (entries 4 and 5). The reactions employing copper(II) and zinc(II) stearates gave somewhat less conversion (entries 6 and 7). Good yield of acetophenone was however achieved with copper(II) stearate. Among seven metal stearates examined, zinc(II) stearate gave the poorest yield of product mixture with approximately 50% conversion.

According to the literatures, a variety of catalysts have been reported to promote the transformation of α-methylstyrene to acetophenone. Henry and Weinreb

(4) have found that a combination of a catalytic amount of OsO_4 with a stoichiometric amount of Jones reagent could be used to oxidize α-methylstyrene to acetophenone in acetone at room temperature with almost quantitative yield (98% isolated yield). Though high yield was reported, poor solubility in organic solvent was a major drawback of this method as well as the high cost of OsO_4. Another example could be seen from the oxidative carbon-carbon double bond cleavage of α-methylstyrene induced by $VO(OEt)Cl_2$ to furnish acetophenone in only a moderate yield (54%) *(48)*.

Based on this present study, two major products, acetophenone and α-methylstyrene oxide, were observed. The best product selectivity for the formation of acetophenone over α-methylstyrene oxide was visualized when chromium(III) stearate was used as a catalyst. When the reaction was performed with other metal stearate complexes, much lower selectivity was observed. Therefore, chromium(III) stearate effectively promotes the oxidative cleavage of double bonds leading to a single, clean ketone product in high yield.

To ensure that acetophenone did not stem from the conversion of α-methylstyrene oxide, α-methylstyrene oxide was thus subjected to the oxidative cleavage condition. It was observed that none of acetophenone was detected. Therefore, acetophenone and α-methylstyrene oxide were formed *via* a different route. It is likely that two reactions were taken place concomitantly: α-methylstyrene oxide was formed by epoxidation, while acetophenone was formed by an oxidative cleavage reaction.

According to the above results, these first row transition metal catalysts successfully promote the oxidative cleavage of carbon-carbon double bond of α-methylstyrene to acetophenone. The most suitable catalyst disclosed was chromium(III) stearate; therefore, this metal complex would be utilized as a catalyst to optimize the conditions for oxidative cleavage of α-methylstyrene.

To show that the oxidative cleavage reactions depend on both catalyst and oxidant, the oxidation was performed with and without chromium(III) stearate and TBHP. The results are displayed in Table 3.2.

Table 3.2 The effect of chromium(III) stearate and TBHP on the oxidative cleavage
of α-methylstyrene

Entry	chromium(III) stearate (mmol)	TBHP (mmol)	% Yield		α-methylstyrene recovery (%)	Mass balance
			acetophenone	α-methylstyrene oxide		
1	0.2	9	85	2	9	96
2	0.2	0	3	trace	93	96
3	0	9	7	trace	95	102
4	0	0	1	trace	99	100

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0-0.2 mmol),
isooctane (5 mL) and TBHP (0-9 mmol) at 70 ℃ for 24 h.

From Table 3.2, in the absence of chromium(III) stearate, the oxidation with
only TBHP gave a small amount of acetophenone (entry 3). Addition of 4 mol% (0.2
mmol) of chromium(III) stearate raised the yield to 85% (entry 1). This observation
strongly supported the concept of metal catalysis in the oxidation reaction. TBHP is
no doubt essential for the reaction as the reaction with 4 mol% (5 mmol)
chromium(III) stearate gave only tiny amount of acetophenone (entry 2). In the
present study, it was found that both chromium(III) stearate and TBHP affected on
the oxidative cleavage of α-methylstyrene to acetophenone.

In the case of catalyst, chromium(III) stearate gave the best result among
metal stearate complexes investigated. Therefore, the amount of chromium(III)
stearate was further investigated for oxidative cleavage reaction. The results of the
effect of the amount of chromium(III) stearate on the oxidative cleavage of α-
methylstyrene could be visualized in Table 3.3.

Table 3.3 The effect of the amount of chromium(III) stearate on the oxidative cleavage of α-methylstyrene

Entry	chromium(III) stearate (mmol)	% Yield		α-methylstyrene recovery (%)	Turnover number[*]
		acetophenone	α-methylstyrene oxide		
1	0.01	48	trace	54	240
2	0.02	69	2	19	178
3	0.05	61	5	37	66
4	0.10	80	trace	9	40
5	0.15	72	6	21	26
6	0.20	85	2	9	22
7	0.25	84	trace	12	17
8	0.30	64	trace	11	11

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0.01-0.30 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ℃ for 24 h.

[*] turnover number (TON): moles of products produced per moles of chromium(III) stearate.

From Table 3.3, at low catalyst loading (0.4-1 mol%, entries 2 and 3), though the reaction gave a fair yield of acetophenone (69% and 61% respectively), incomplete conversion was observed along with the detection of a small amount of α-methylstyrene oxide. The optimum catalyst loading was 4 mol% (entry 6). When the amount of catalyst was increased to 6 mol% (entry 8), the yield was lowered to 64%. This may be occurring from the over oxidation being taken place. Accounting on turnover number (TON), using the catalyst 0.01 mmol provided interesting result to gain over 200 TON.

From all above results, it was observed that not only type of catalyst but also amount of catalyst affected the production of the desired product.

3.2.2 Effect of type of oxidants

Oxidative cleavage of carbon-carbon double bonds is a fundamental and important transformation in synthetic organic chemistry *(49)*. Ozonolysis *(50)* and oxidation by stoichiometric oxidants such as osmiun tetraoxide *(51)*, ruthenium tetraoxide *(52)* and potassium permanganate *(53)* are frequently used for this purpose.

However, these reagents have the obvious drawbacks as being toxic and expensive, a number of catalytic systems using H_2O_2 *(54)*, NaOCl *(55)*, $NaIO_4$ *(56)* and peracetic acid *(57)* as oxidants have thus been later developed. Among these aforementioned oxidants, aqueous H_2O_2, a cheap and environmentally benign oxidant, has attracted much interest in recent years. However, the transformation of olefins to the corresponding compounds *via* oxidative cleavage is rarely explored because of the difficulty in controlling the oxidation at the stage of the formation of desired products: ketone, aldehyde, epoxide, methyl ketone, alcohol, polymer, *etc. (58)*

In this study, TBHP was a primary oxidant used for the oxidative cleavage of α-methylstyrene to acetophenone. Various oxidants such as H_2O_2, aldehyde under oxygen atmosphere were also tried in this oxidation reaction. The effects of various oxidants on the oxidative cleavage of α-methylstyrene are presented in Table 3.4.

Table 3.4 The effect of oxidants on the oxidative cleavage of α-methylstyrene

Entry	Oxidant	% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
1	TBHP	85	2	9	96
2	H_2O_2	14	trace	85	99
3	MCPBA	trace	7	89	96
4	$NaIO_4$	18	trace	82	100
5	2-ethylbutyraldehyde / O_2	2	trace	101	103
6	2-ethylbutyraldehyde / O_2[*]	3	14	84	101
7	zinc grit / acetic acid[*]	trace	trace	99	99
8	zinc grit / acetic acid[*,**]	trace	trace	100	100
9	urea hydrogen peroxide	5	trace	94	99
10	oxone tetrabutylammonium salt	5	trace	95	100
11	ammonium peroxodisulfate	11	trace	86	97

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0.2 mmol),

isooctane (5 mL) and oxidant (9 mmol) at 70 ºC for 24 h.

[*] under the oxygen atmosphere at room temperature.

[**] catalyzed by $FeCl_2 \cdot 4H_2O$ (0.2 mmol).

From Table 3.4, the reactions were proceeded in very good yield (entry 1) employing TBHP as an oxidant. MCPBA and 2-ethylbutyraldehyde/O_2 gave α-methylstyrene oxide as a major product (entries 3 and 6), however with very small amount of the desired product. By employing $NaIO_4$ and ammonium peroxodisulfate, the reaction gave acetophenone in poor yield (entries 4 and 11). Other common oxidizing agents such as urea hydrogen peroxide and oxone tetrabutylammonium salt failed to give a reasonable amount of either acetophenone or α-methylstyrene oxide (entries 9 and 10) under this particular conditions studied.

Therefore, TBHP was chosen as an oxidant for the oxidative cleavage reaction. The effect of the amount of TBHP on this reaction was examined and the results are shown in Table 3.5.

Table 3.5 The effect of the amount of TBHP on the oxidative cleavage of α-methylstyrene

Entry	TBHP (mmol)	% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
1	0	3	trace	94	97
2	3	25	trace	74	99
3	6	38	trace	62	100
4	9	85	2	9	96
5	12	83	11	8	102

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0.2 mmol), isooctane (5 mL) and TBHP (0-12 mmol) at 70 ºC for 24 h.

Reactions with a low amount of TBHP resulted in incomplete conversion (entries 1-3). 1.8 Equivalents of TBHP based on the starting material were sufficient to promote the reaction (entry 4). It is interesting to note that higher amounts of TBHP (2.4 eq) resulted in marked increase of α-methylstyrene oxide by-product (entry 5). This probably was another indirect evidence to show that these two attained products were derived from different routes.

3.2.3 Effect of solvents

Solvents always play an important role in catalysis. The effect of various solvents on the oxidative cleavage reaction of α-methylstyrene was investigated and the results are displayed in Table 3.6.

Table 3.6 The effect of solvents on the oxidative cleavage of α-methylstyrene catalyzed by chromium(III) stearate

Entry	Solvents	% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
1	isooctane	85	2	9	96
2	dichloromethane[*]	31	4	67	102
3	acetonitrile	80	6	18	104
4	chloroform	17	trace	81	98
5	methanol	7	trace	90	97
6	ethanol	10	trace	83	93
7	pyridine	34	trace	51	85
8	acetone[*]	59	2	12	73
9	carbontetrachloride	12	trace	97	109
10	acetonitrile:pyridine 3:1	61	trace	13	74
11	pyridine:acetic acid 3:1	97	trace	trace	97
12	dimethylsulfoxide	31	4	68	103
13	*N,N-*dimethylformamide	3	0	95	98
14	n-butanol	70	2	26	98
15	1,2-dichloroethane	77	4	16	97
16	tetrahydrofuran	trace	0	99	99

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0.2 mmol), solvent (5 mL) and TBHP (9 mmol) at 70 ℃ for 24 h.

[*] refluxing temperature of solvent.

Isooctane and acetonitrile (entries 1 and 3) were found to be ideal solvents. Reactions in acetone, acetonitrile/pyridine 3:1, butanol, and 1,2-dichloroethane all gave acetophenone in good yield (entries 8, 10, 14 and 15). It was very interesting to note that the reaction carried out in pyridine/acetic acid 3:1 resulted in almost quantitative amount of product with excellent selectivity. However, the workup of reaction was quite complicated and highly exothermic. Thus, isooctane is the solvent of choice because of the availability, cheapness and being able to solubilize chromium(III) stearate catalyst.

3.2.4 Effect of the amount of substrate

Effects of the amount of α-methylstyrene were explored and the results are tabulated in Table 3.7.

Table 3.7 The effect of the amount of α-methylstyrene on the oxidative cleavage reaction

Entry	α-methylstyrene (mmol)	Product (mmol)		% Yield of acetophenone	
		acetophenone	α-methylstyrene oxide	based on α-methylstyrene	based on TBHP
1	5	4.25	0.10	85	47
2	10	7.92	trace	79	88
3	15	8.19	0.36	55	91
4	20	8.28	0.63	41	92
5	25	7.83	0.72	31	87
6	50[*]	6.39	trace	13	71

reactions conditions: α-methylstyrene (5-50 mmol), chromium(III) stearate (0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ºC for 24 h.
[*] no isooctane was used.

When total volume of the reaction was less than 4 mL, isooctane was added in the reaction (entries 1-5). The use of α-methylstyrene 5 mmol and TBHP 9 mmol (entry 1, α-methylstyrene is a limiting agent) gave high yield of acetophenone (85%). In addition, the reactions with increasing amount of α-methylstyrene 10 – 25 mmol (entries 2-5, TBHP is a determining agent) gave high yield of acetophenone based on TBHP (88, 91, 92 and 87%, respectively). Surprisingly, high α-methylstyrene content leads to poorer selectivity (one/oxide ratio) (entries 3-5, 22%, 13% and 10% respectively).

In the case of the reaction being performed without any extra solvent, the reaction gave exclusive acetophenone in moderate yield (entry 6, based on TBHP). The use of excess amount of substrate is in a similar condition with continuous flow reactor where the starting material is recycled back to the reactor.

These results explicitly show that a batch reactor would be more suitable if isooctane is used as solvent while a continuous flow reactor could also be utilized without the need of any solvent.

3.2.5 Effect of temperature

Temperature is another important factor for condition optimization on the oxidative cleavage reaction. The temperature in the reaction was varied from 30-90 ℃ in order to find the most appropriate temperature that provided the highest yield of acetophenone. The results are presented in Table 3.8.

Table 3.8 The effect of temperature on the oxidative cleavage of α-methylstyrene

Entry	Temperature (℃)	% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
1	30	57	trace	41	98
2	50	61	4	30	95
3	70	85	2	9	96
4	90	41	trace	11	52

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate (0.2 mmol),
isooctane (5 mL) and TBHP (9 mmol) at room temperature (30
℃) - 90 ℃ for 24 h.

The highest yield of acetophenone was accomplished at 70 ℃ as shown in Table 3.8 (entry 3). Therefore, the optimum temperature for this reaction is 70 ℃. According to the literlatures, both Barton and Chavez reported that TBHP gave good yield of desired product when it was used at 70 ℃ (59).

At lower temperature, conversion was incomplete and around a half of starting material was recovered. This was probably because TBHP was not homolytically dissociated to form radical to initiate oxidation reaction. At higher temperature (90 ℃), there were many unidentified by-products detected by GC resulting in a very complicated reaction mixture.

3.2.6 Kinetic study on the oxidative cleavage of α-methylstyrene catalyzed by chromium(III) stearate

Chromium(III) stearate was used for kinetic study on the oxidative cleavage of α-methylstyrene to examine the appropriate time of the reaction. The kinetic analysis results of this reaction is presented in Fig 3.3.
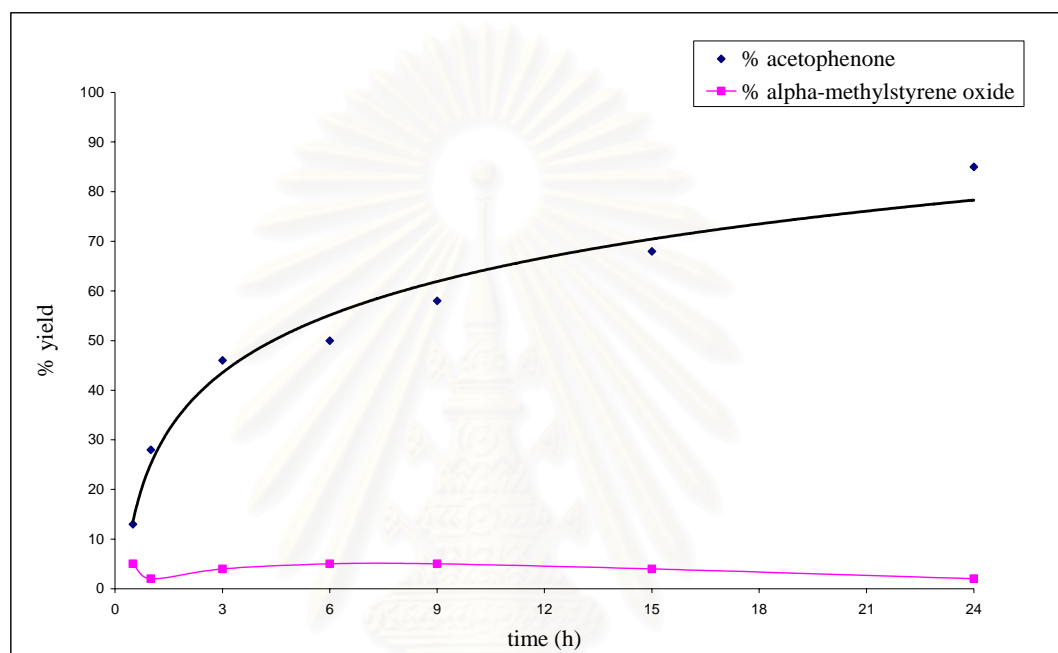
Figure 3.3 The kinetic study of the oxidative cleavage of α-methylstyrene.

Kinetic study of the oxidative cleavage of α-methylstyrene is shown in Fig 3.3. Half-life of this reaction – the time at which the starting material was half-consumed – was determined to be 3 hours and the reaction reached completion after 24 hours. If the reaction was left on for 48 hours, the yield deteriorated. The product acetophenone may be further oxidized by TBHP resulting in lower yield.

The decrease of α-methylstyrene follows a second-order reaction (Fig 3.4), indicating that there may be two species involved in the rate determining step *(60)*. According to the literatures, Barton *(61)* found the rate of the catalytic reaction was dependent on type of catalyst. This could be visualized by the determination of the quantity of product and time used for reaction to complete.
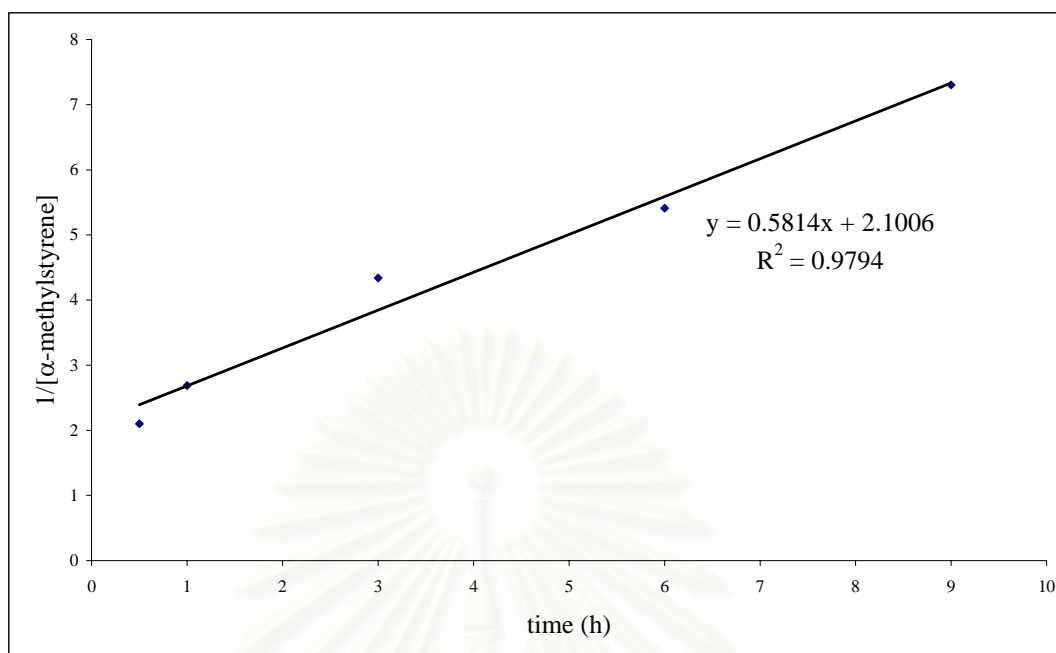
Figure 3.4 The kinetic study of the oxidative cleavage of α-methylstyrene (second-order).

According to aforementioned results, the optimized conditions for the oxidative cleavage of α-methylstyrene could be summarized as follows: the mixture of α-methylstyrene (5 mmol), TBHP (9 mmol) and chromium(III) stearate (4 mol%) was stirred in isooctane (5 ml) at 70 °C for 24 h.

3.3 Study on the oxidative cleavage of α-methylstyrene catalyzed by bicatalyst and tricatalyst of metal stearate complexes

Based upon the results gained in previous sections, other metal stearate complexes could also be employed within the oxidative cleavage reaction, for instance, cobalt(II), nickel(II), copper(II) stearate, *etc*. In order to minimize the amount of chromium catalyst in this reaction and to observe the outcome of the reaction utilizing a combination of catalyst, a series of experiment were carried out.

3.3.1 Effect of bicatalyst

From previous results, chromium(III) stearate provided the highest yield of the desired product with excellent selectivity. The use of mixed catalyst between

chromium(III) stearate and other metal stearates at two different ratios (1:1 and 2:1) was therefore investigated to explore the similarity and the difference of the reaction employing chromium(III) stearate alone. The results are presented in Table 3.9 and Fig 3.5.

Table 3.9 The effect of bicatalyst on the oxidative cleavage of α-methylstyrene

Fraction	Metal stearate		% Yield		α-methylstyrene recovery (%)	Mass balance
			acetophenone	α-methylstyrene oxide		
1 : 0	Cr(III)	-	85	2	9	96
1 : 1	Cr(III)	Mn(II)	52	11	35	98
		Fe(III)	42	trace	57	99
		Co(II)	61	3	29	93
		Ni(II)	57	7	29	93
		Cu(II)	52	1	46	99
		Zn(II)	14	8	77	99
2 : 1	Cr(III)	Mn(II)	58	2	30	90
		Fe(III)	31	trace	66	97
		Co(II)	69	2	19	90
		Ni(II)	43	4	42	89
		Cu(II)	71	1	18	90
		Zn(II)	27	15	51	93

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate and other metal stearate (0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ºC for 24 h.

Figure 3.5 The effect of bicatalyst on the oxidative cleavage of α-methylstyrene
(Chromium(III) + orther metal stearate complexes, 1:1 and 2:1).

The results presented in Table 3.9 and Fig 3.5 expressed that the best
combination of catalyst in 1:1 ratio was chromium(III) and cobalt(II) stearates
yielding 61% yield of acetophenone while a 2:1 ratio gave 69% of the product. The
obtained selectivity was also explored and compared with the result derived from
only chromium(III) stearate was used. Both combination of 1:1 and 2:1
chromium(III) with copper(II) stearate gave the best selectivity of acetophenone per
α-methylstyrene oxide (20 and 35, respectively). However, the yield was still less
than using only the chromium(III) stearate catalyst.

3.3.2 Effect of tricatalyst

Furthermore, the system of tricatalyst was examined on the oxidative cleavage
of α-methylstyrene using 1:1:1 ratio of chromium(III) stearate and other two metal
stearates. The effects of tricatalyst are observed in Table 3.10 and Fig 3.6.

Table 3.10 The effect of tricatalyst on the oxidative cleavage of α-methylstyrene

Metal stearate		% Yield		α-methylstyrene recovery (%)	Mass balance
		acetophenone	α-methylstyrene oxide		
Mn(II)	Fe(III)	32	4	61	97
	Co(II)	58	2	36	96
	Ni(II)	27	4	54	85
	Cu(II)	67	11	19	97
	Zn(II)	32	8	52	92
Fe(III)	Co(II)	19	4	76	99
	Ni(II)	16	9	73	98
	Cu(II)	22	1	70	93
	Zn(II)	7	trace	91	98
Co(II)	Ni(II)	81	3	12	96
	Cu(II)	35	1	61	97
	Zn(II)	44	19	27	90
Ni(II)	Cu(II)	76	7	12	95
	Zn(II)	8	1	87	96
Cu(II)	Zn(II)	17	15	63	95

reactions conditions: α-methylstyrene (5 mmol), chromium(III) stearate and other two metal stearates (1:1:1, 0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ºC for 24 h.
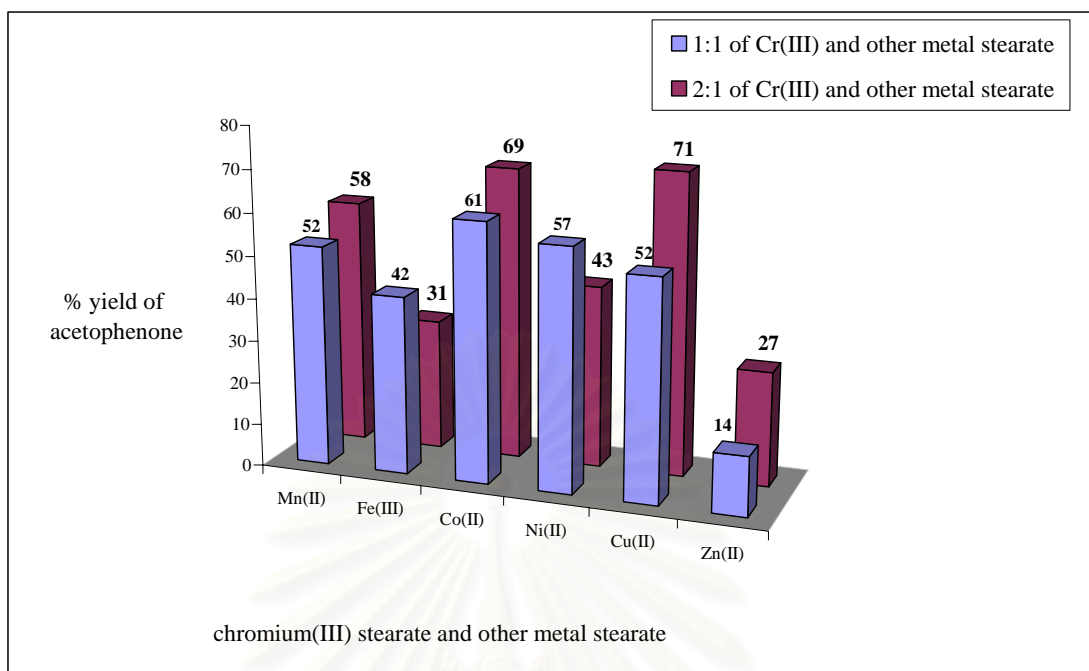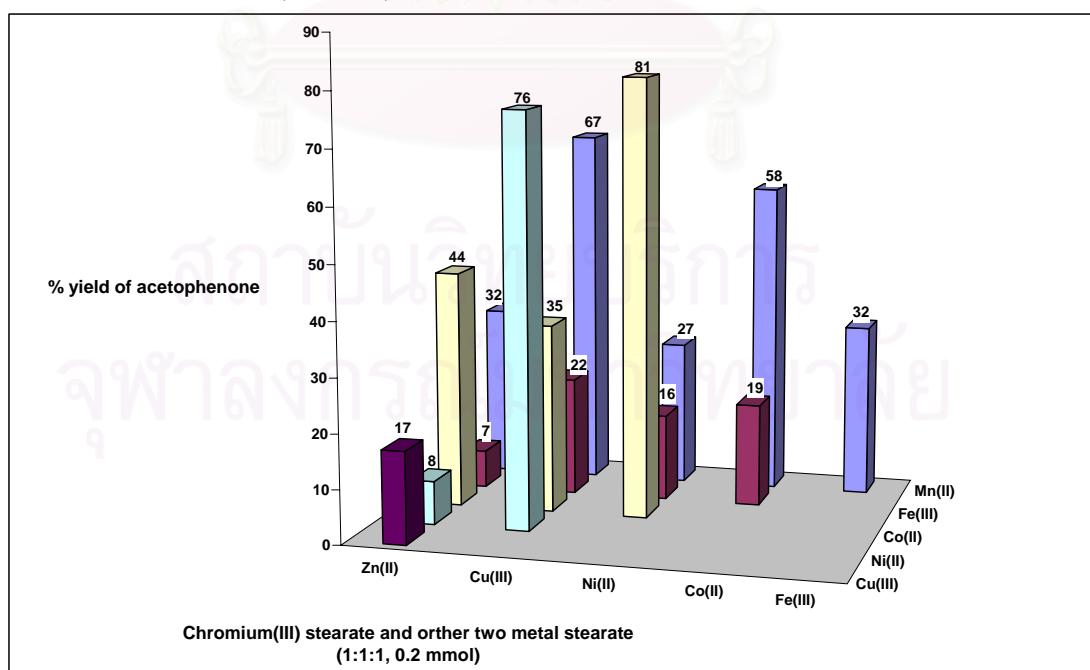

Figure 3.6 The effect of tricatalyst on the oxidative cleavage of α-methylstyrene (Chromium(III) + orther two metal stearate complexes, 1:1:1).

Results from the use of a mixture of three catalysts in the reaction are shown in Table 3.10 and Fig 3.6. The best combination of 1:1:1 mixture could be observed from chromium(III), cobalt(II), and nickel(II) stearates furnishing 81% yield of the product which is comparatively the same as the optimum condition for chromium(III) stearate catalyst.

3.4 Oxidative cleavage of selected terminal olefins catalyzed by chromium(III) stearate

After the reaction conditions were optimized using α-methylstyrene as a chemical model, the extended study, the oxidative cleavage of other substrates terminal olefins was conducted. Those terminal olefins: MMA, 4-chloro-α-methylstyrene, styrene, diethyl itaconate, camphene, 4-vinyl-1-cyclohexene, 1,1-diphenylethylene, 1,3-diisopropenylbenzene, 2-nitro-α-methylstyrene, 3-nitro-α-methylstyrene, 4-nitro-α-methylstyrene, 4-methyl-α-methylstyrene, 4-ethyl-α-methylstyrene and 4-methoxy-α-methylstyrene were selected for examining the scope of this developed oxidation system.

3.4.1 Oxidative cleavage of MMA

Pyruvic acid, an important metabolite of lactic acid, is widely found in muscle. Generally, synthetically ethyl pyruvate has been obtained by the oxidation of ethyl lactate with $KMnO_4$ *(62)*. However, the disadvantage of $KMnO_4$ was the need to employ with a stoichiometric amount. Therefore, the new route for the preparation of pyruvic acid and its derivatives was still called for. The oxidative cleavage from methacrylic acid esters to pyruvic acid esters is thus another attractive pathway. The results of the oxidative cleavage of MMA using the developed reaction are given as shown in Table 3.11.
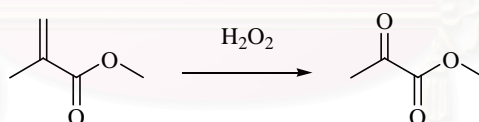
Table 3.11 The oxidative cleavage of MMA

Entry	Catalyst (mmol)		Oxidant(mmol)		Solvent (mL)		% Yield methyl pyruvate
	Cr(III) stearate	Cr(acac)$_3$	TBHP	H$_2$O$_2$	isooctane	acetonitrile	
1	-	0.03	-	15	-	10	38
2	-	0.03	15	-	-	10	27
3	0.03	-	9	-	5	-	15
4[*]	0.03	-	9	-	5	-	34
5	0.2	-	9	-	5	-	19
6[*]	0.2	-	9	-	5	-	55
7[*]	0.2	-	9	-	-	5	51
8	0.2	-	-	9	5	-	42
9[*]	0.5	-	9	-	5	-	36
10[*]	0.2	-	18	-	5	-	61

reactions conditions: methyl methacrylate (5 mmol) at 50 ºC for 24 h.

[*] at 70 ºC.

A relevant literature was addressed by Inoue concerning the procedure for oxidative cleavage of MMA to methyl pyruvate by using catalytic amount of 0.03 mmol Cr(acac)$_3$ with 15 mmol of 60% H$_2$O$_2$ in CH$_3$CN 10 mL *(63)*.

MMA   methyl pyruvate

The condition for the oxidative cleavage of MMA as Inoue and coworkers reported was repeated but using 30% H$_2$O$_2$ instead of 60% H$_2$O$_2$ (because of availability). The obtained yield however could not reproduce 96% conversion quoted in the paper. Apparently, concentrated H$_2$O$_2$ which is not commercially available plays a very important role in that published procedure. Based on this optimum conditions studied, MMA was subjected to 0.2 mmol chromium(III) stearate, 18 mmol TBHP oxidation condition in isooctane 5 mL at 70 ºC for 24 h, methyl pyruvate was observed as the major product in 61% yield.

This present method nonetheless proves to be superior to the existing method in two aspects: (1) the use of more readily available TBHP as an oxidizing agent and

(2) use of more hydrophobic reagents minimize the possibility of two-phase system which could compromise the yield of the reaction.

It is also worth noting here that the oxidative cleavage of MMA under these conditions could not give a good mass balance. For instance (entry 6), the mass balance of methyl pyruvate and recovery of MMA was 69% yield. This probably was occurred from the over oxidation of methyl pyruvate.

From Table 3.11, entries 6 and 10 gave the best yield of methyl pyruvate. When the double amount of TBHP was used, methyl pyruvate gave a little increasing yield. The kinetic study on the oxidative cleavage of MMA was investigated and the results are displayed in Fig 3.7.
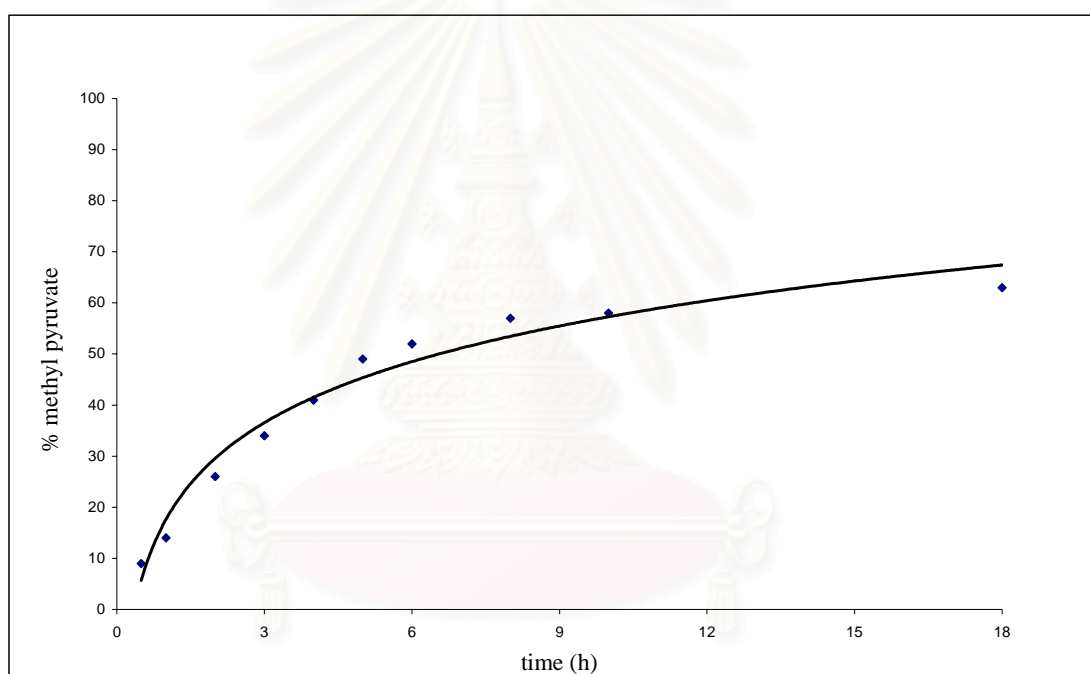
Figure 3.7 Kinetic study of the oxidation of MMA.

From kinetic study, the reactions were carried out in isooctane 5 mL at 70 ℃, with MMA (5 mmol), chromium(III) stearate (0.2 mmol), and TBHP (9 mmol). %Yield of MMA was decreased when the reaction times were more than 18 hours. For instance, the reactions performed for 24 and 48 hours gave 55 and 37 % yield of MMA, respectively. This may be because the product, methyl pyruvate may be over oxidized by the remained oxidant. From kinetic study with variation of time presented in Fig 3.7, it was found that 18 hours was the appropriate reaction time for oxidative cleavage of MMA and the result displayed that the half-life of the reaction was determined to be 3 hours.

From kinetic studies of the oxidation of MMA, the rate was shown to be second-order with k 0.2328. The decrease of MMA follows the second-order reaction (Fig 3.8), determining that there may be two species involved in the rate determining step.
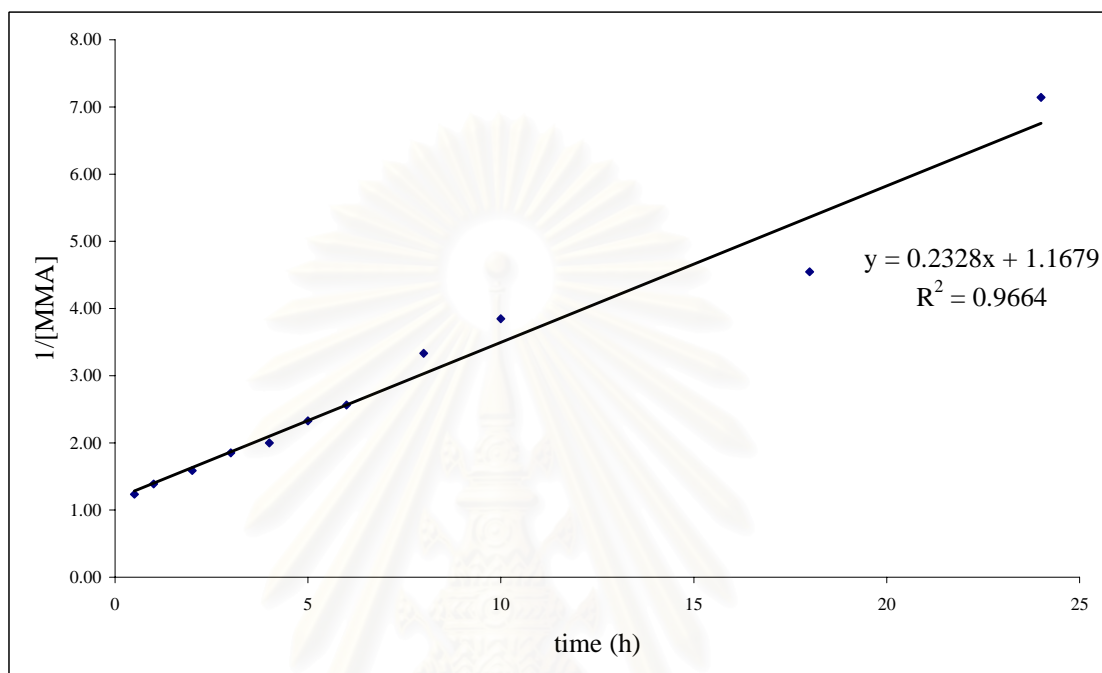
Figure 3.8 Kinetic study of the oxidation of MMA (second-order).

3.4.2 Oxidative cleavage of 1,3-diisopropenylbenzene

The oxidative cleavage of terminal olefins to carbonyl compounds is useful in natural product synthesis *(64)*. Several procedures have been reported using molecular oxygen *(65)*, transition metals *(66)* or sensitizers *(67)*. 1,3-Diisopropenylbenzene containing two sites of terminal olefin was selected as another chemical model. In order to explore the oxidative cleavage of this particular substrate, the reaction was optimized by varying the amount of catalyst, oxidant and time. The results are tabulated in Table 3.12.

1,3-diisopropenylbenzene   1-acetyl-3-isopropenylbenzene   1,3-diacetylbenzene

Table 3.12 The oxidative cleavage of 1,3-diisopropenylbenzene

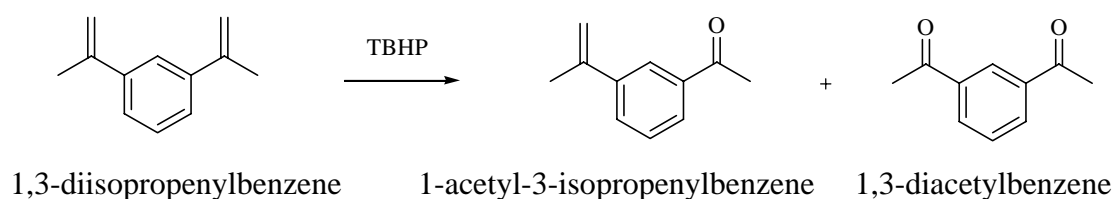| Entry	chromium(III) stearate (mmol)	TBHP (mmol)	time (h)	% Yield		Mass balance
				1-acetyl-3-isopropenylbenzene	1,3-diacetylbenzene	
1	0.1	9	12	21	trace	97
2	0.1	9	18	39	trace	95
3	0.1	9	24	71	12	101
4	0.1	9	48	60	19	103
5	0.1	18	24	47	35	96
6	0.2	9	12	32	trace	100
7	0.2	9	18	44	16	101
8	0.2	9	24	46	29	99
9	0.2	18	24	41	48	97
10	0.2	18	48	23	57	95
11	0.25	18	48	13	62	99

reactions conditions: 1,3-diisopropenylbenzene (5 mmol), chromium(III) stearate (0.1 - 0.25 mmol), isooctane (5 mL) and TBHP (9 - 18 mmol) at 70 ℃ for 12 - 48 h.

The oxidative cleavage of 1,3-diisopropenylbenzene furnished exclusively two products, depending upon the reaction conditions utilized. Whereas 1,3-diacetylbenzene is commercially available, 1-acetyl-3-isopropenylbenzene could be gained from the direct isolation from the reaction mixture. By purifying with silica gel column chromatograph, the latter was achieved as colorless liquid. The structure was verified by ^{1}H-NMR spectrum (Fig 3.9). The methyl protons adjacent to a carbonyl group could be detected at δ 2.66 (s, 3H). Methyl protons adjacent to double bond were visualized at δ 2.22 (s, 3H). Terminal protons could be manifestly detected at δ 5.47 (s, 1H) and 5.12 (s, 1H). A singlet signal of aromatic proton between carbonyl group and double bond were appeared at δ 8.08 (s, 1H). The rest of aromatic protons could be observed at δ 7.88 (d, J = 7.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H) and 7.46 (t, J = 7.7, 1H).
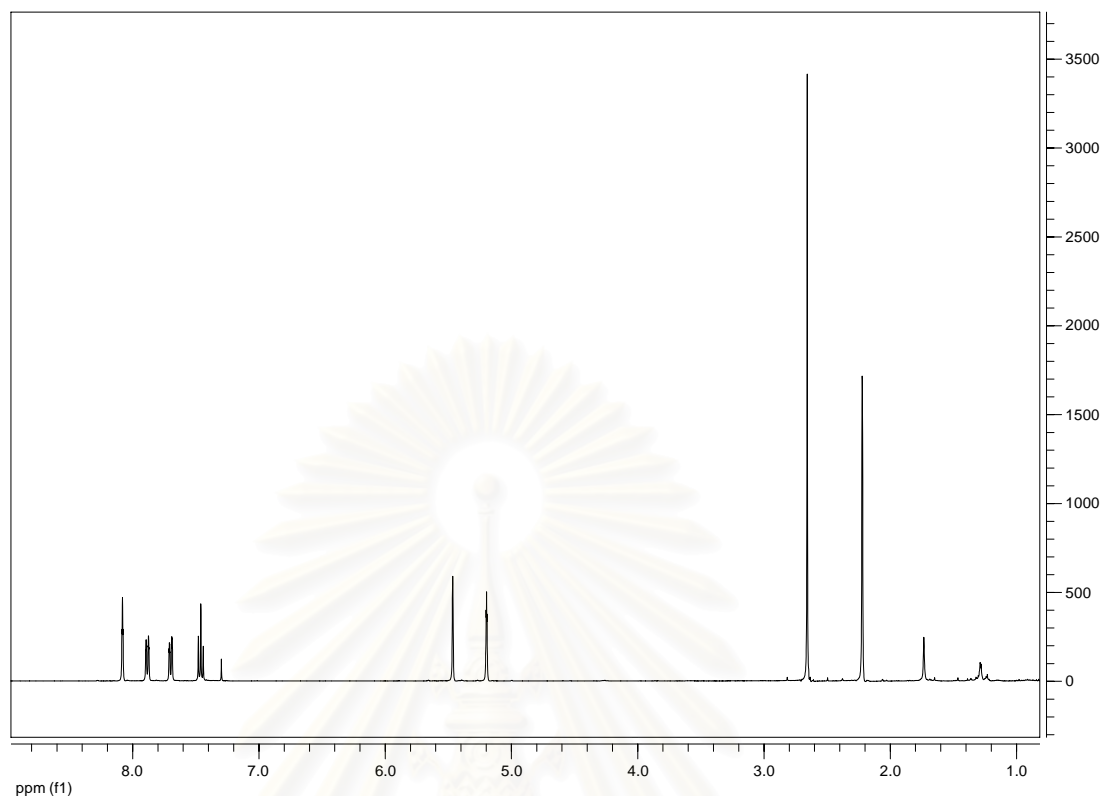
Figure 3.9 The ^{1}H-NMR spectrum of 1-acetyl-3-isopropenylbenzene.

When 1,3-diisopropenylbenzene was treated with 0.1 mmol chromium(III) stearate and 9 mmol TBHP in isooctane 5 mL at 70 ℃ for 24 h, 1-acetyl-3-isopropenylbenzene was formed in 71% (GC) yield. In entries 1-4, the effect of reaction time was explored in order to improve the yield. It was found that the longer the reaction time, the more 1,3-diacetylbenzene was produced. This was indicative of the further oxidation of 1-acetyl-3-isopropenylbenzene was taken place. On the other hand, 1,3-diacetylbenzene could be obtained as a major product when the reaction was carried out with 0.25 mmol chromium(III) stearate and 18 mmol TBHP in isooctane 5 mL at 70 ℃ for 48 h (entry 11). Therefore, the oxidative cleavage conditions could be controlled by appropriate reaction time and amount of TBHP for the production of either 1-acetyl-3-isopropenylbenzene or 1,3-diacetylbenzene.

3.4.3 Oxidative cleavage of α-methylstyrene derivatives

α-Methylstyrene with various substituents on an aromatic ring was the next chemical models to be explored to investigate the scope of the oxidative cleavage reaction. The aim was to (a) test the versatility of this method and (b) observe the changes in reactivity of the substrate due to subtle changes in the electronic effects from the substituents.
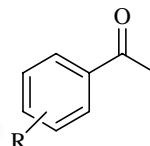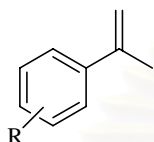
R = Electron donating and electron withdrawing groups

1 R = 4-CH$_3$O	**9** R = 4-CH$_3$O
2 R = 4-Br	**10** R = 4-Br
3 R = 4-Cl	**11** R = 4-Cl
4 R = 4-CH$_3$CH$_2$	**12** R = 4-CH$_3$CH$_2$
5 R = 4-CH$_3$	**13** R = 4-CH$_3$
6 R = o-NO$_2$	**14** R = o-NO$_2$
7 R = m-NO$_2$	**15** R = m-NO$_2$
8 R = p-NO$_2$	**16** R = p-NO$_2$

α-Methylstyrene derivatives used in this study could not be obtained as commercially available. These substrates were therefore synthesized employing Wittig reaction. Methyltriphenylphosphonium iodide was prepared in the first step in order to react with acetophenone derivatives to yield the corresponding terminal olefins. It was purified by recrystallization from ethanol-ether. All prepared compounds were verified the structures by ^{1}H-NMR spectrum. The ^{1}H-NMR spectrum of methyltriphenylphosphonium iodide visualized the methyl protons adjacent to a phosphorus atom could be detected at δ 3.20 (d, J = 13 Hz, 3H) and aromatic protons could be visualized at around δ 7.66-7.84 (m, 15H) (Fig 3.10). Moreover, the ^{1}H-NMR spectrum of terminal olefins exhibited the significant terminal protons as singlet peak around δ 5 (s, 1H); methyl protons adjacent to double bond being visualized around δ 2 (s, 3H) and aromatic protons could be detected at

around δ 7. The ^{1}H-NMR spectrum of a instance of the prepared α-methylstyrene derivative, 4-methoxy-α-methylstyrene is presented in Fig 3.11.
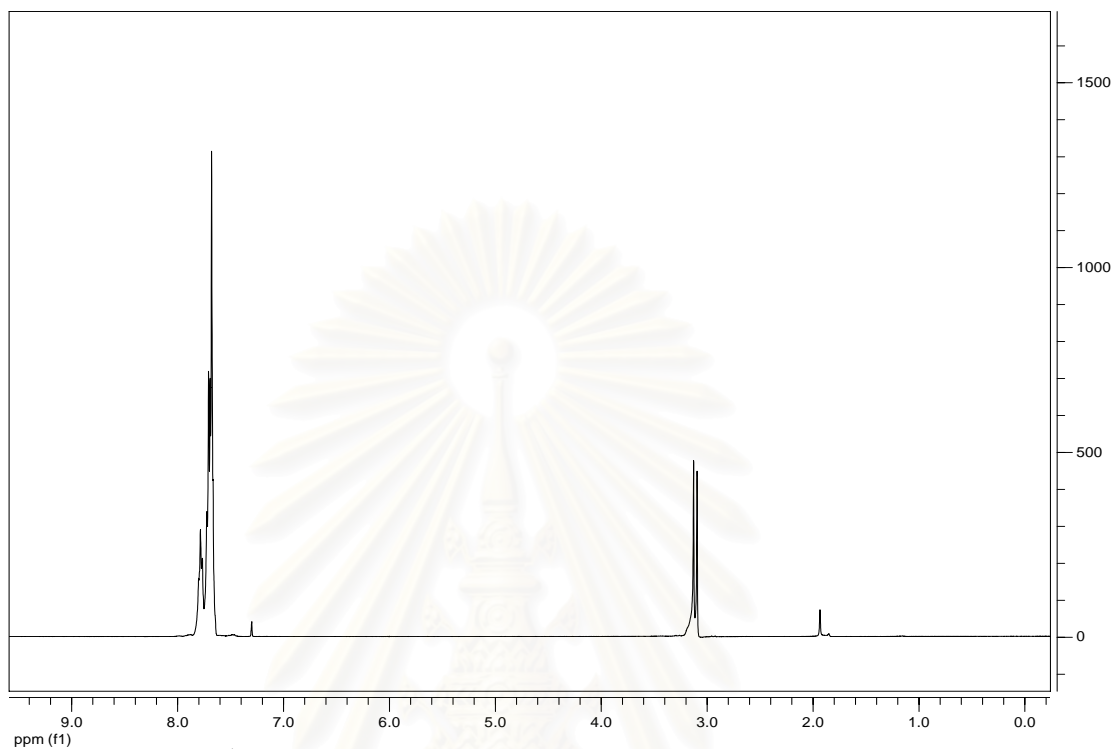

Figure 3.10 The ^{1}H-NMR spectrum of methyltriphenylphosphonium iodide.

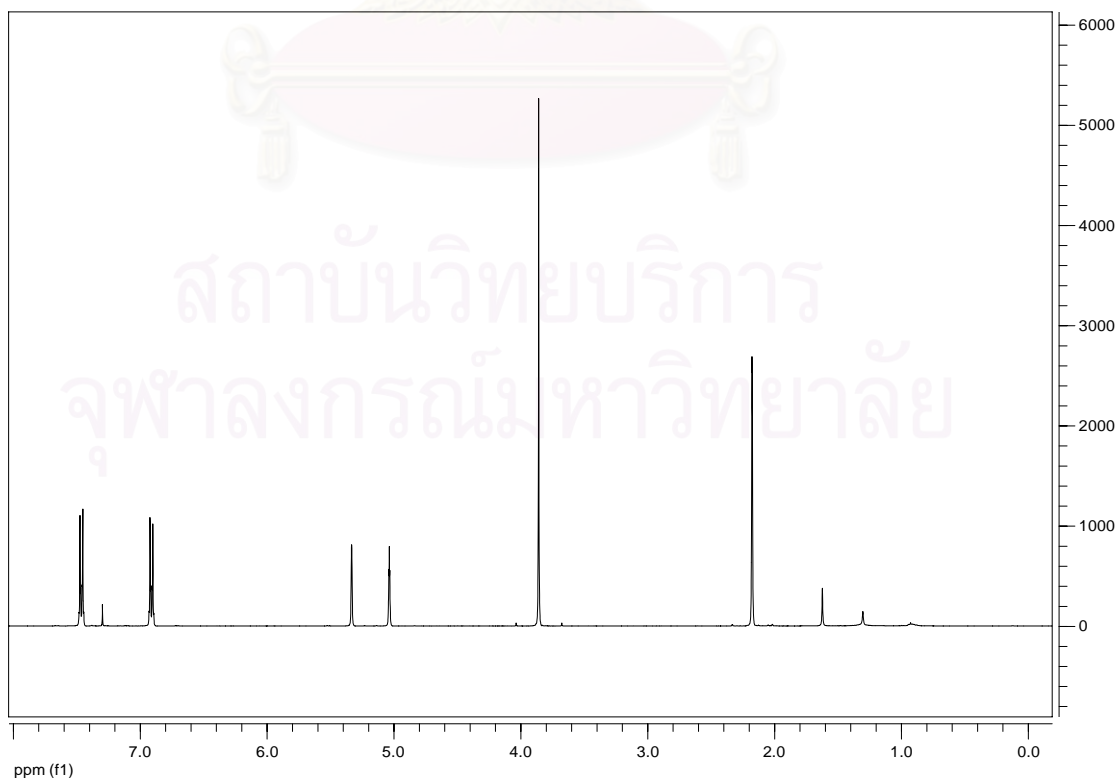**Figure 3.11** The ^{1}H-NMR spectrum of 4-methoxy-α-methylstyrene.

All α-methylstyrene derivatives synthesized were subjected to the oxidative cleavage reaction under the same reaction conditions generally used and the results are summarized in Table 3.13.

Table 3.13 The oxidative cleavage of α-methylstyrene derivatives

Entry	Substrate	acetophenone derivative (% Yield)	Substrate recovery (%)	Mass balance
1	α-methylstyrene	acetophenone (85)	9	96
2	**1**	**9** (89)	9	98
3	**2**	**10** (85)	11	96
4	**3**	**11** (81)	11	92
5	**4**	**12** (67)	30	97
6	**5**	**13** (65)	36	101
7	**6**	**14** (32)	67	99
8	**7**	**15** (46)	50	96
9	**8**	**16** (41)	57	98

reactions conditions: substrate (5 mmol), chromium(III) stearate (0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ºC for 24 h.

Apparently, it was found that the oxidative cleavage of monosubstituted α-methylstyrene gave a good mass balance. α-Methylstyrene containing electron donating groups cleanly produced good yield of the corresponding acetophenone slightly increasing with the electron donating ability of the substituent (81% for *p*-Cl < 85% for *p*-Br < 89% for *p*-OMe). These derivatives showed similar reactivity to the unsubsituted α-methylstyrene.

For alkyl substituted α-methylstyrenes, the oxidative cleavage surprisingly gave a somewhat lower yield (65% for *p*-Me and 67% for *p*-Et). This lower product yield was not the direct result of the alkyl group on the electronic property of α-methylstyrene. Instead, it should be from the presence of a new benzylic carbon which could be readily oxidized, giving out other products from a competitive reaction.

To investigate the effect of electron-withdrawing substituents, *o*-, *m*-, and *p*-NO$_2$ substituted α-methylstyrene was separately subjected to the oxidative cleavage.

The lowest yield in this series (32%) was observed for *o*-NO$_2$. The *p*-NO$_2$ substituted substrate gave a slightly higher yield (41%). This observed difference may be the result of the *ortho* electronic effect. Oxidative cleavage of *m*-NO$_2$-α-methylstyrene gave the desired product in 46% yield. The *m*-substituent obviously has less deactivating effect than *o*- and *p*-ones because it was not conjugated to the ethylene, therefore, deactivation occurred by inductive effect.

3.4.4 Oxidative cleavage of 4-chloro-α-methylstyrene

The oxidative cleavage of the carbon-carbon double bond of substituted α-methylstyrene derivatives was proceeded under optimum conditions to afford the corresponding ketones in high yield. In this study, 4-chloro-α-methylstyrene was examined comparing with α-methylstyrene. It was found that the best yield of 81 % 4-chloroacetophenone was obtained after 24 hours. The kinetic analysis of the oxidative cleavage of 4-chloro-α-methylstyrene was investigated compared with that of α-methylstyrene. The results are displayed in Fig 3.12.
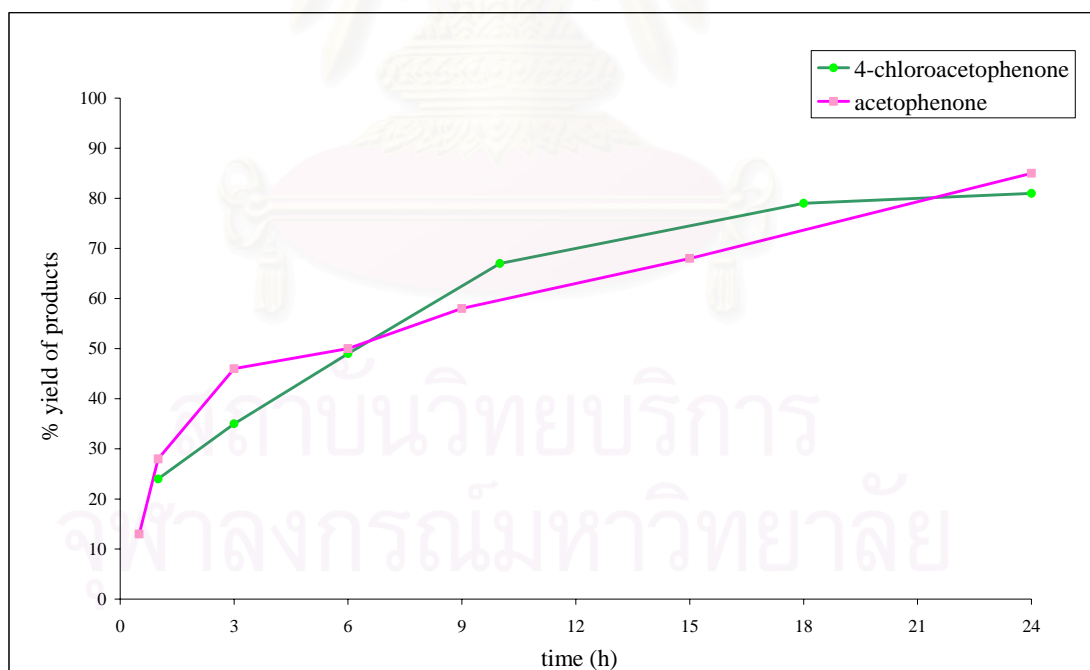
Figure 3.12 Kinetic study of the oxidation of 4-chloro-α-methylstyrene and α-methylstyrene.

Similar reaction kinetic was observed in the oxidation of 4-chloro-α-methylstyrene. The reaction was completed within 24 hr. The rate was shown to be second order with k 0.3234 and a half-life of 6 hr (Fig 3.13). Therefore, two species should be involved in the rate determining step.

$y = 0.3234x + 0.6396$
$R^2 = 0.9653$

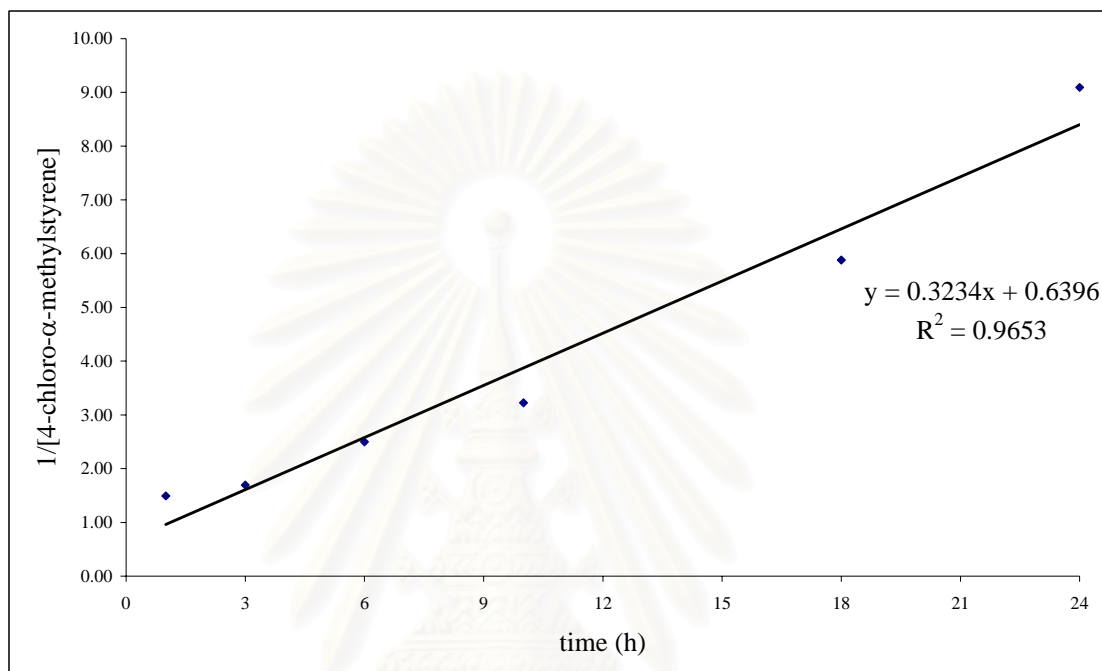**Figure 3.13** Kinetic study of the oxidation of 4-chloro-α-methylstyrene and α-methylstyrene (second-order).

By purifying with silica gel column chromatograph, the structure was verified by ^{1}H-NMR spectrum (Fig 3.14). The methyl protons adjacent to carbonyl group being visualized at δ 2.61 (s, 3H) and aromatic protons could be detected at δ 7.45 (d, J = 8.5 Hz, 2H) and 7.91 (d, J = 8.5 Hz, 2H).
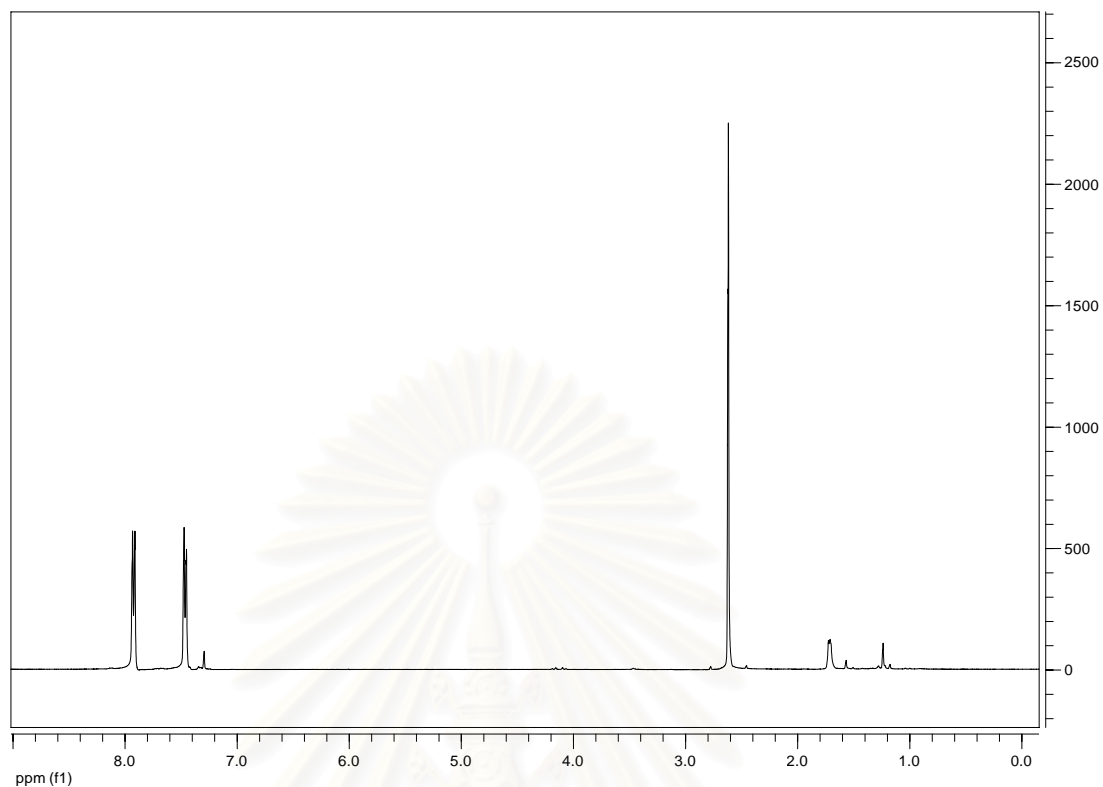
Figure 3.14 The ^{1}H-NMR spectrum of 4-chloroacetophenone.

3.4.5 Oxidative cleavage of other selected terminal olefins

To shed some light on the applicability of this reaction, further study on the oxidative cleavage reaction of other terminal olefins were examined. The results are shown in Table 3.14.

17 X = CH$_2$ **19** X = CH$_2$ **21** X = CH$_2$ **23** X = CH$_2$

18 X = O   **20** X = O   **22** X = O   **24** X = O

25   **26**   **27**

28   **29**   **30**

Table 3.14 The oxidative cleavage of other selected terminal olefins

Entry	Substrate	Product	% Yield	Substrate recovery (%)	Mass balance
1	**17**	**18**	69	28	97
2	**19**	**20**	76	24	100
3	**21**	**22**	55	14	69
4	**23**	no reaction	-	100	100
5	**25**	no reaction	-	100	100
6	**26**	no reaction	-	100	100
7	**27**	**28**	17	43	60

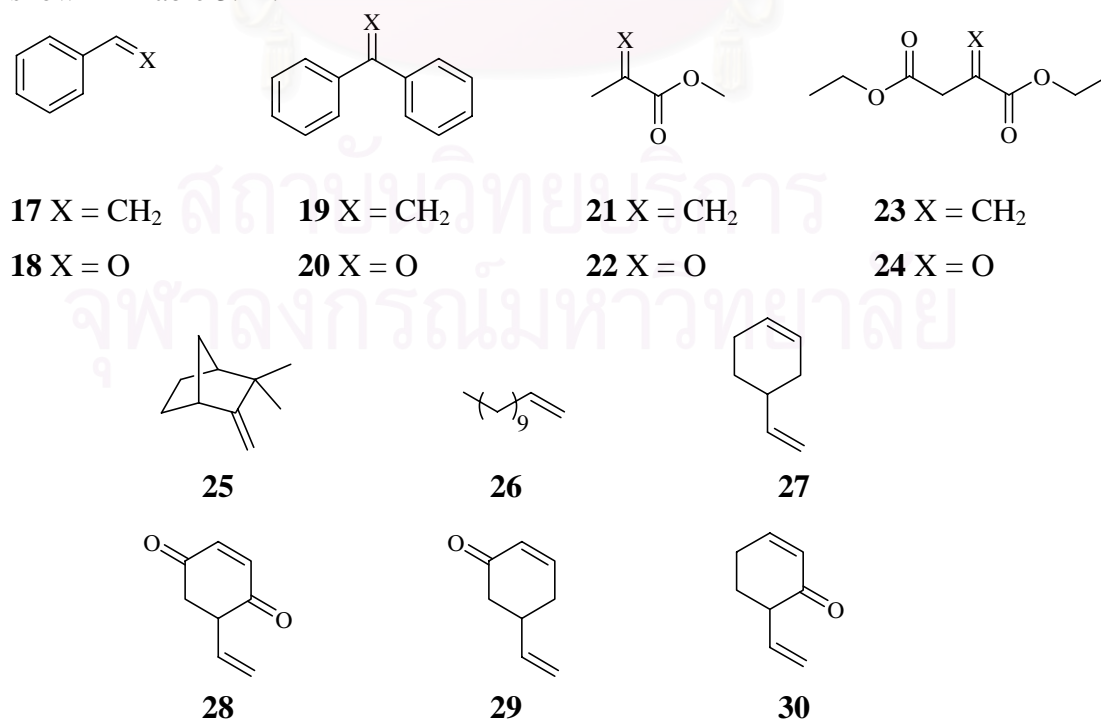reactions conditions: substrate (5 mmol), chromium(III) stearate (0.2 mmol), isooctane (5 mL) and TBHP (9 mmol) at 70 ºC for 24 h.

The oxidative cleavage of styrene **17** gave benzaldehyde **18** in 69% yield. It is slightly lower than the reaction of α-methylstyrene of which methyl group helped stabilization of the intermediate (see mechanism, Topic 3.5). The reaction of 1,1-diphenylethylene **19** gave the benzophenone **20** in good isolated yield (76%). The structure of the obtained product **20** was verified by ^{1}H-NMR spectrum (Fig 3.15). The aromatic protons could be observed at δ 7.52 (t, J = 7.6 Hz, 4H), 7.63 (t, J = 7.4 Hz, 2H) and 7.84 (d, J = 7.3 Hz, 4H). For the oxidative cleavage of 1,1-diphenylethylene **19** a drop in the product yield is probably the result from steric congestion in the cyclization of Cr^V=O species into the proposed intermediate. The reaction of MMA **21** as discussed in 3.4.1 proceeded to give methyl pyruvate **22** in 55% yield. By purifying with silica gel column chromatograph, the structure was verified by ^{1}H-NMR spectrum (Fig 3.16). The methyl protons adjacent to carbonyl group being visualized at δ 2.48 (s, 3H) and the methyl protons adjacent to a carboxylate group could be detected at δ 3.87 (s, 3H).
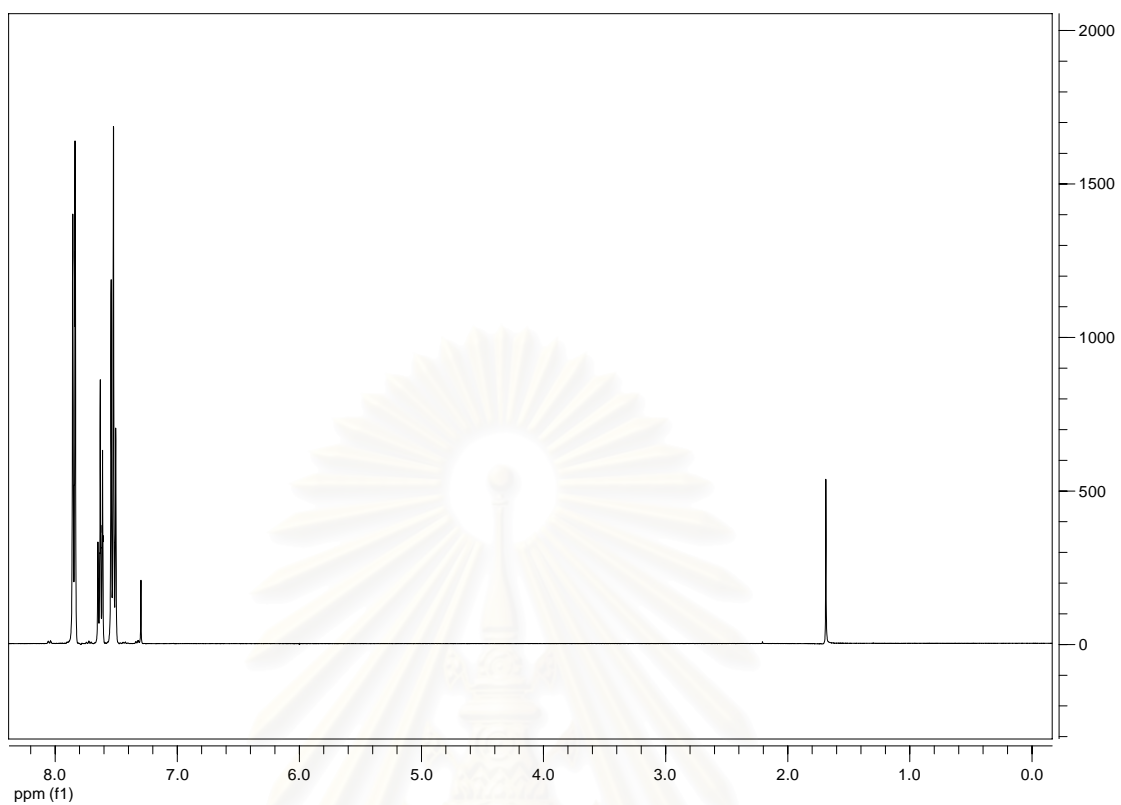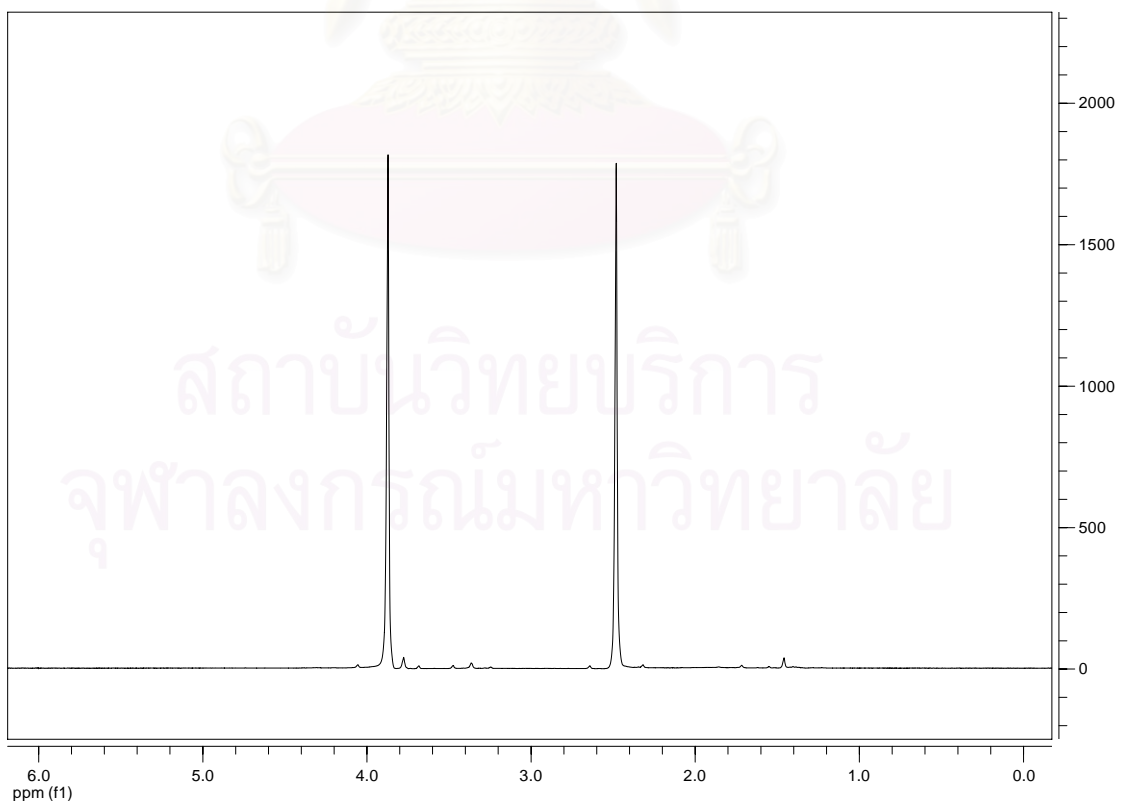
Figure 3.15 The ^{1}H-NMR spectrum of benzophenone.

Figure 3.16 The ^{1}H-NMR spectrum of methyl pyruvate.

Surprisingly, diethyl itaconate **23** did not give the corresponding oxidative cleavage product, diethyl oxalacetate **24** and the starting material **23** was recovered quantitatively from the reaction mixture (entry 4). Camphene **25** and 1-dodecene **26** were also unreactive towards this oxidation. The oxidation of 4-vinyl-1-cyclohexene **27** resulted in an unexpected allkylic oxidation to give a diketone product **28** in 17% yield. This obtained product **28** could be gained from the direct isolation from the reaction mixture. By purifying with silica gel column chromatograph, the structure was verified by ^{1}H-NMR spectrum (Fig 3.17). The methylene protons adjacent to a carbonyl group could be detected at δ 2.35 (m, 2H). The proton adjacent to methylene protons and another carbonyl group was visualized at δ 2.46 (m, 1H). The terminal protons could be appeared at δ 5.14 (d, J = 17.6 Hz, 1H) and 5.25 (d, J = 10.6 Hz, 1H). The proton adjacent to the internal double bond was appeared at δ = 5.88 (dd, J = 10.9, 17.6 Hz, 1H). The protons adjacent to double and carbonyl group could be detected at δ 6.03 (d, J = 10.3 Hz, 1H) and 6.90 (d, J = 11.3 Hz, 1H). From the reaction mixture was monitored by ^{1}H-NMR spectrum, the product **29** could also be detected in low yield. From ^{1}H-NMR spectrum (Fig 3.18), the methylene protons adjacent to double bond could be detected at δ 2.30 (m, 2H). The methylene protons adjacent to carbonyl group could be appeared at δ 2.55 (m, 2H). The terminal protons could be visualized at δ 5.07 (d, J = 5.5 Hz, 1H) and 5.11 (d, J = 12.4 Hz, 1H). The proton adjacent to terminal double bond was detected at δ 5.86 (m, 1H). The protons adjacent to internal double bond could be appeared at δ 6.07 (d, J = 10.1 Hz, 1H) and 7.00 (m, 1H). Furthermore, the reaction mixture could be received the product **30** in very low yield. ^{1}H-NMR spectrum could be detected the significant quartet proton at δ 3.40. This proton is belonging to the proton adjacent to between methylene protons and carbonyl group in structure the product **30**.
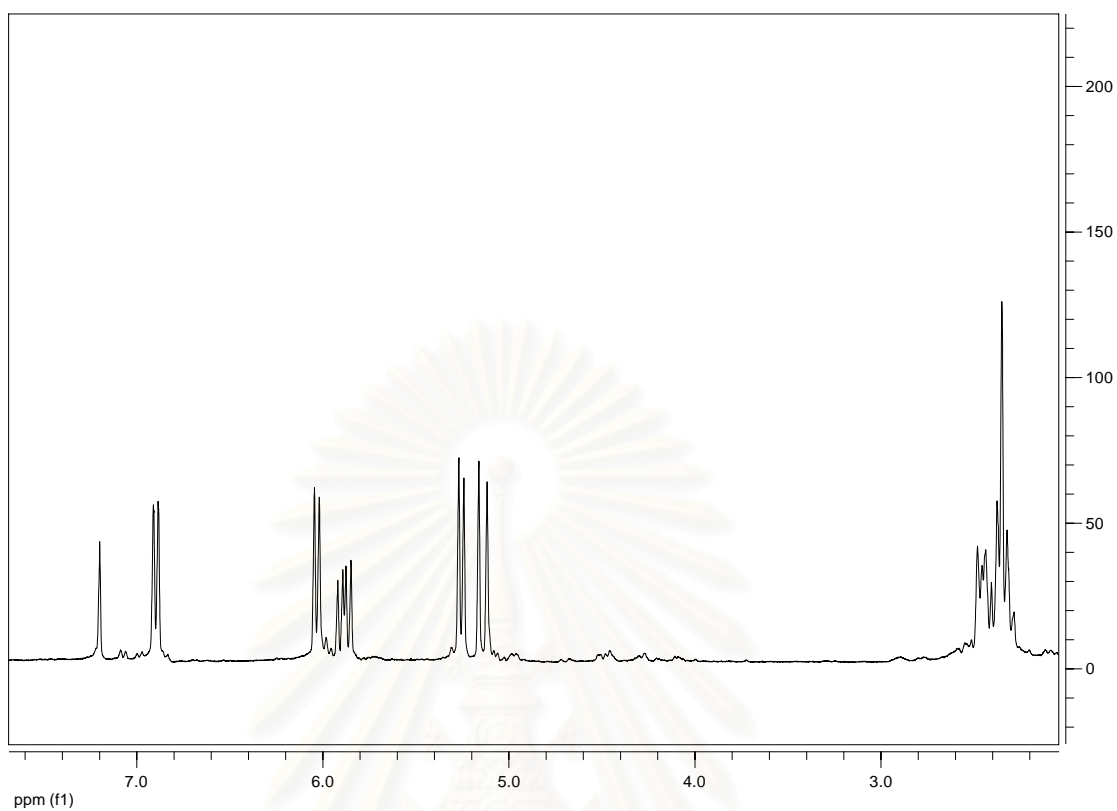
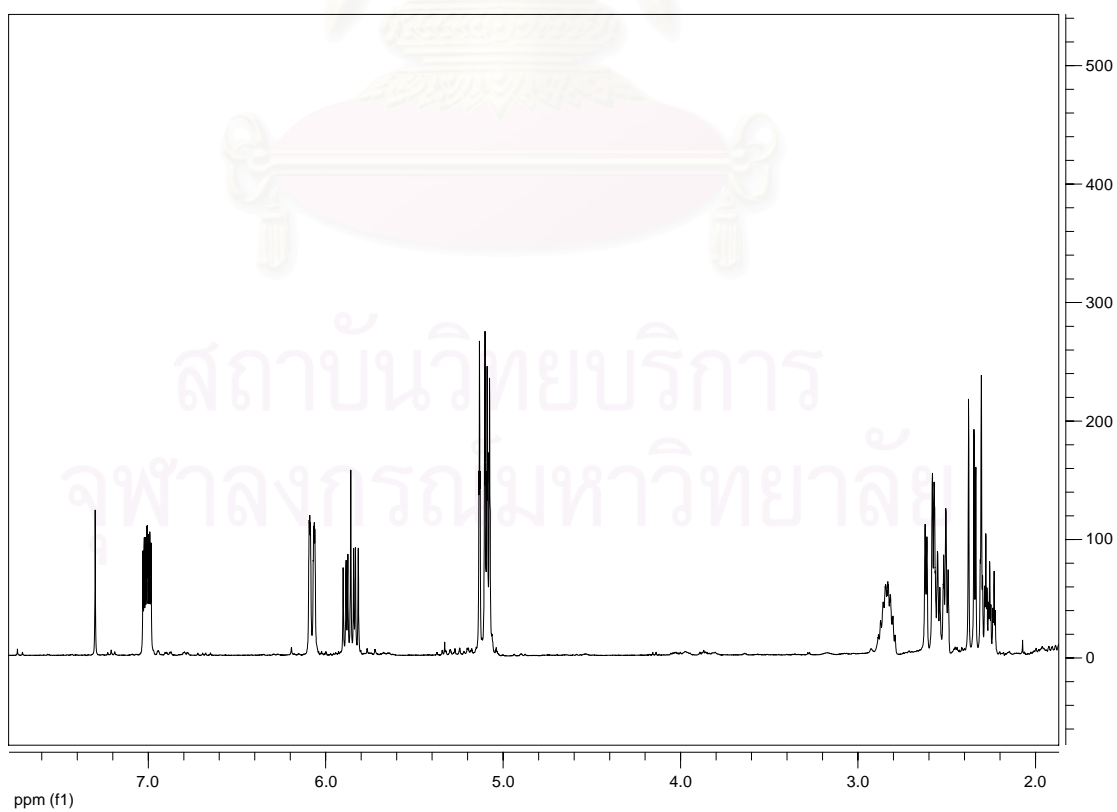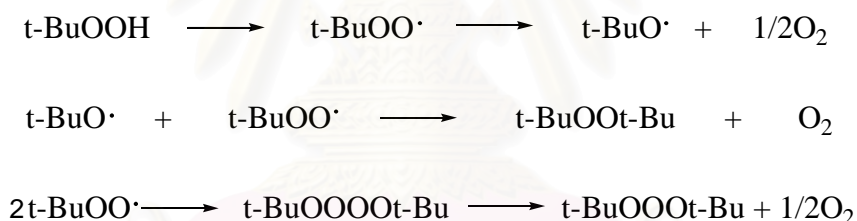**Figure 3.17** The ^{1}H-NMR spectrum of diketone product **28**.

Figure 3.18 The ^{1}H-NMR spectrum of product **29**.

In a control experiment, the oxidative cleavage was attempted with aliphatic substrates. Diethyl itaconate and camphene were chosen as representative examples. However, the products could not be observed from the reaction mixture. Therefore, this developed oxidative cleavage was selective for conjugated double bonds and could not be reacted with the substrate contains a nonconjugated methyl or methylene proton, respectively (see mechanistic implications, Topic 3.5.2).

3.5 Proposed mechanism for the oxidative cleavage of terminal olefin compounds catalyzed by chromium(III) stearate

The oxidative cleavage of activated double bonds by TBHP is promoted by the addition of a catalytic amount of metal stearate. By using chromium(III) stearate as a catalyst, a reasonably clean product was isolated in high yield. The reaction is believed to proceed *via* radical mechanism. The proposed mechanism for this conversion was illustrated as shown below.

$$t\text{-BuOOH} \longrightarrow t\text{-BuOO}^{\cdot} \longrightarrow t\text{-BuO}^{\cdot} + 1/2 O_2$$

$$t\text{-BuO}^{\cdot} + t\text{-BuOO}^{\cdot} \longrightarrow t\text{-BuOOt-Bu} + O_2$$

$$2 t\text{-BuOO}^{\cdot} \longrightarrow t\text{-BuOOOOt-Bu} \longrightarrow t\text{-BuOOOt-Bu} + 1/2 O_2$$
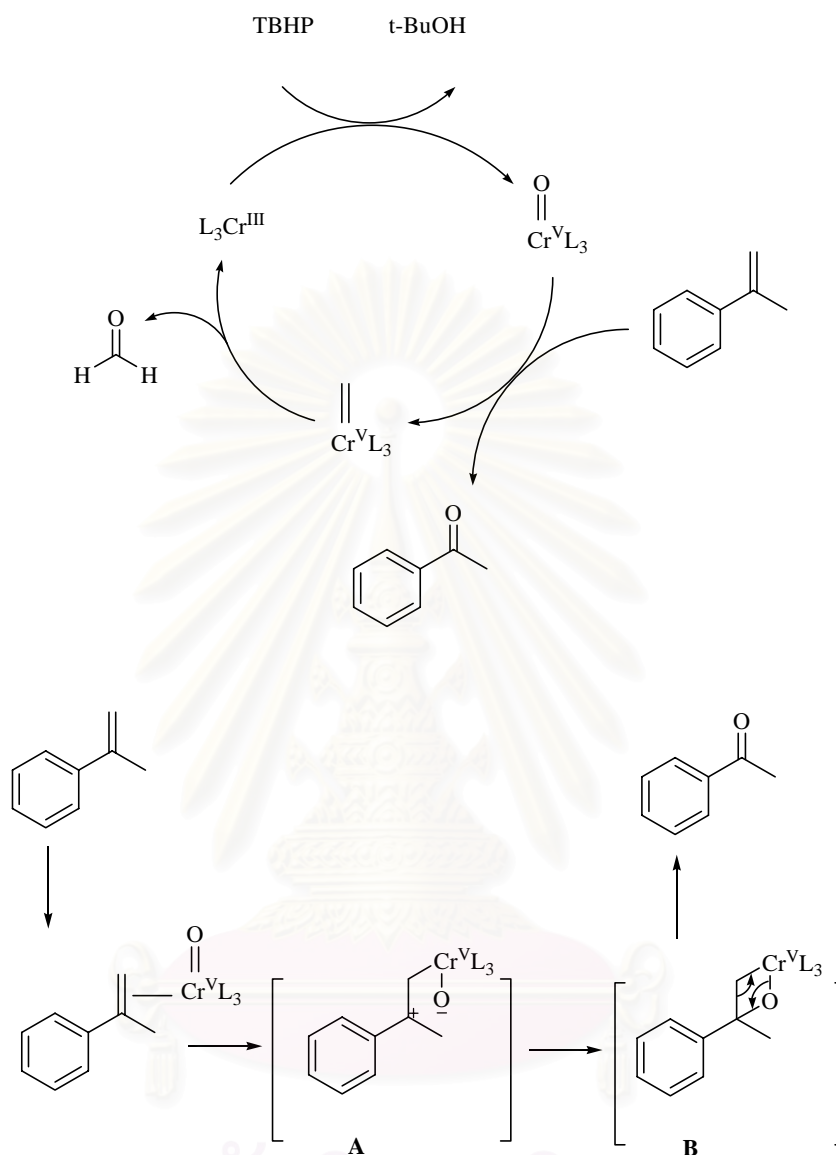
Scheme 3.1 Proposed mechanism for the oxidative cleavage of terminal olefins catalyzed by chromium(III) stearate.

The chromium(III) complex was transformed to the corresponding high valent (formally) Cr^V=O species by interaction with TBHP. In similar fashion of Barton's theory for the formation of high valent iron oxo species, the addition of the Cr^V=O species to the double bond followed by cleavage to the ketone and a methylene carbene. There are experiments which confirmed the detection of formaldehyde *(20)*.

3.5.1 Reactivity of substrates

From the proposed mechanism, any substituent that could stabilize intermediate **A** would promote the reaction. The effects of both electron donating and electron withdrawing groups as aromatic substituents are considered as follows:

A
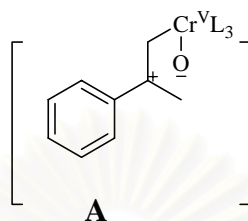
Electron donating group: A representative example for electron donating group is *p*-OMe. The resulting intermediate **A** can be drawn with five canonical forms. Electron donating groups would therefore stabilize the intermediate and thus facilitate the reaction. Other electron donating groups such as *p*-Br and *p*-Cl would have similar effect but in a smaller extent.

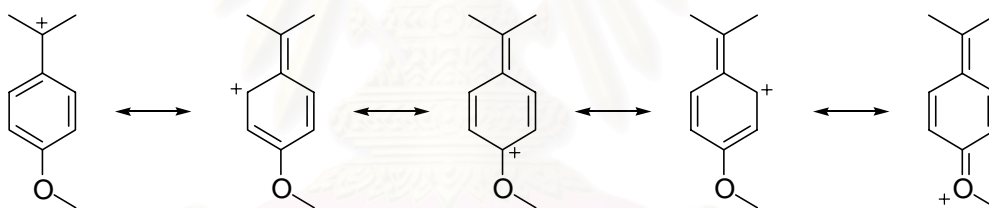*Electron withdrawing group:* A representative example for electron withdrawing group is *o*-NO₂. Unlike electron donating group, the substituent can no longer delocalize to contribute to any new canonical forms. Only four canonical forms can be drawn. Moreover, one of them contains a positive centre which is very unlikely due to charge repulsion. Electron withdrawing groups would destabilize the intermediate and, therefore, does not facilitate the reaction.
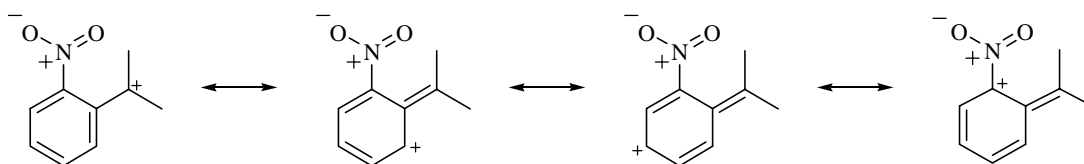
Alkyl groups would have minor effect on the reactivity although it can be viewed as electron donating *via* hyperconjugation. Electron withdrawing group on meta position e.g. *m*-NO$_2$ would destabilize the intermediate by inductive effect. Effect of aromatic substituent on reactivity was therefore believed to be in the order: *p*-OMe > *p*-Br > *p*-Cl > *p*-CH$_3$ ~ *p*-CH$_2$CH$_3$ > *m*-NO$_2$ > *p*-NO$_2$ > *o*-NO$_2$.

### 3.5.2 Mechanistic implications from reactivity of substrates

A new method for the oxidative cleavage of substituted olefins was developed by using TBHP in the presence of a catalytic amount of metal stearate. It was found that this method works well with activated double bonds. Simple alkyl substituted olefins was not oxidized. The best substrate for this reaction is electron rich α-methylstyrene derivative. However, the method also works well with conjugated double bond, albeit giving a somewhat lower yield.

There are some conflicting results from the oxidative cleavage of conjugated double bonds. While the reaction of methyl methacrylate proceeds to give the product in fair yield (55 %), the reaction of diethyl itaconate did not give any separable oxidized product and diethyl itaconate was recovered. This can be explained by the presence of active methylene protons. Any radical species approaching diethyl itaconate will abstract this hydrogen. In other words, diethyl itaconate effectively inhibits the formation of radicals. This parallels the observation from the oxidative cleavage of α-methylstyrene where a *p*-substituted methyl group lowers the yield of the cleaved product by about 25% (from 85% to 60%). Thus, the presence of any active methyl or methylene group in the substrate would disrupt the cleavage
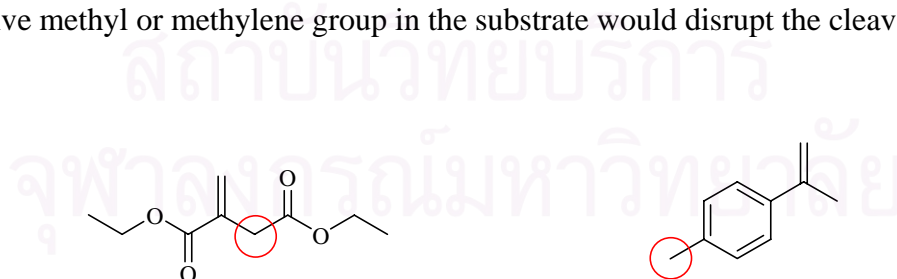
Another limitation of this method is the observation that the yield deteriorates when it was applied to electron poor aromatic substituted olefins. Oxidative cleavage of *o*-, *m*-, and *p*-nitro-α-methylstyrenes gave the product in only a fair yield.

All the observations agree well with the cleavage of the double bonds by radical mechanism:

1. No reaction was observed from non-conjugated double bonds.
2. α-Methylstyrene derivatives with electron rich aromatic substituents gave good yields.
3. The yield deteriorates if the substrate contains an active methyl or methylene proton.

CHAPTER IV

CONCLUSION

Considerable progress has been made in the field of catalytic olefin oxidation since the advent of industrial production of acetaldehyde and ethylene oxide. Therefore, selective functionalization of double bond is an industrially important process. In addition, these reactions have many synthetic utilities. Carbonyl compounds can be prepared from the oxidative cleavage of olefins. Typically, this can be achieved by either ozonolysis or transition metal catalysis, for example, catalytic amount of OsO_4 with stoichiometric amount of Jones' reagent. The aim of this work is to establish a new methodology for the oxidative cleavage of double bonds by the use of a cheap transition metal salt of stearic acid as a catalyst in combination with an oxidant.

The metals of choice are chromium(III), manganese(II), iron(III), cobalt(II), nickel(II), copper(II) and zinc(II). Stearic acid salts of these metals are easily prepared and characterized by infrared spectroscopy. The absence of a broad COOH peak between 2700 and 3400 cm^{-1} and physical properties clearly show the formation of these complexes.

The condition for oxidative cleavage of olefins was optimized by using the oxidation of α-methylstyrene to acetophenone as a model reaction. Initially, TBHP was used as an oxidant. Each metal stearate was screened for the ability to promote the reaction. α-Methylstyrene oxide was frequently observed as a by-product. Zinc(II) stearate gave the poorest yield amongst the catalysts with the highest amount of α-methylstyrene oxide by-product. Cobalt(II) and nickel(II) stearates gave moderate yield of acetophenone while α-methylstyrene oxide by-product was also present. Manganese(II), iron(III) and copper(II) stearates gave moderate yield of acetophenone with a clean reaction mixture. The best catalyst was found to be chromium(III) stearate. Both the catalyst and TBHP are essential in promoting the reaction; control reactions in the absence of either metal or TBHP did not show any significant

conversion. Mixing the metal stearate catalysts together in combination with TBHP did not improve the yield of the product.

The best catalyst and oxidant pair was shown to be a mixture of chromium(III) stearate and TBHP. This system can be used in a variety of common solvents including isooctane, acetonitrile, 1,2-dichloroethane and pyridine/acetic acid (3:1). In pyridine/acetic acid, α-methylstyrene was converted to acetophenone in an almost quantitative yield. However, this solvent system is hard to handle while the toxicity of pyridine limits its use in large scale and the workup of reaction was quite complicated and highly exothermic. Therefore, it was not chosen for further study. Isooctane became the solvent of choice instead.

The optimized condition for oxidative cleavage of 5 mmol α-methylstyrene is as follows: chromium stearate catalyst (4 mol%), TBHP 1.8 equivalent, isooctane as a solvent with a concentration of 1 mmol/ml, temperature 70°C and reaction time 24 h.

With the global concern on the environments, minimal use of organic solvent is encouraged. A solvent-free oxidative cleavage of α-methylstyrene was attempted. It was encouraging that the product acetophenone was achieved in 71% yield. Although the yield was lower than using solvent, a solvent-free reaction may be suitable for a continuous-flow reactor if a large scale is desired.

Reaction kinetics of the oxidative cleavage of three different compounds were studied, namely, methylmethacrylate (MMA), α-methylstyrene and 4-chloro-α-methylstyrene. All these reactions are shown to be second-order. It could be implied from these results that two species are involved in the rate-determining step of this reaction.

The scope and limitation of the oxidative cleavage by chromium(III) stearate and TBHP were studied on a variety of substrates. The reactions of α-methylstyrene, 4-methoxy-α-methylstyrene, 4-chloro-α-methylstyrene, 4-bromo-α-methylstyrene, styrene and 1,1-diphenylethylene gave the desired product in good to excellent yields. The oxidative cleavage of 4-methyl-α-methylstyrene, 4-ethyl-α-methylstyrene, MMA and 1,3-diisopropenylbenzene gave the ketone products in moderate yields. Similar reaction on the *o*-, *m*- and *p*-nitro-α-methylstyrene gave the product in poor yields. No reaction was observed in the reaction of diethyl itaconate, camphene and 1-dodecene. These results show that the cleavage is selective for conjugated double bonds with

aromatic ring or carbonyl group. Clearly from these results, aromatic substituents have a large influence on the reactivity of the α-methylstyrene derivatives. Compounds that contain electron donating substituents on the aromatic ring are more reactive towards oxidative cleavage while those that contain electron withdrawing substituents are unreactive. Another limitation of this methodology is that the presence of any "active" methyl or methylene group in the substrate causes a sharp drop in the product yield.

A mechanism was proposed for the oxidative cleavage reaction. This involves the metal catalyzed generation of the corresponding high valent (formally) $Cr^V=O$ species by interaction with TBHP. The addition of the $Cr^V=O$ species to the double bond followed by cleavage to the ketone and a methylene carbene.

It was demonstrated that oxidative cleavage of double bonds can be achieved by using a catalytic amount of chromium(III) stearate and TBHP. Some of the advantages of this methodology over the existing one are:

1. Use of readily available TBHP.
2. Use of hydrophobic reagents would minimize the possibility of two-phase systems which would compromise the yield due to immiscibility.
3. A solvent-free process is possible.
4. The oxidative cleavage is selective for conjugated double bonds with aromatic ring or carbonyl group.

Propose for the future work

This research concerned with development for the oxidative cleavage of terminal olefins catalyzed by chromium(III) stearate. The outcome opened many possibilities to deal with future exploration. As discussed earlier, metal stearate complex has never been utilized as an olefin oxidative catalyst in organic transformation, therefore the variation of metal from chromium to cobalt or copper *etc*. may provide other intriguing results in terms of product yield and selectivity. The developed system could certainly be used as an alternative to prepare some fine chemicals. Moreover, application of this methodology could be used in the synthesis of a complicated natural product. This present examination is a profitable example for the catalytic olefin oxidation methodology in crucial chemical reaction nowadays, and may be the one of valuable chemical literature data in the near future.

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