ออกซิเดชันของแอลคีนเร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม-ชิฟเบส

นางสาวกรวรรณ หมวกกุล

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ALKENE OXIDATION CATALYZED BY OXOVANADIUM-SCHIFF BASE COMPLEXES

Miss Korawan Muakkul

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Petrochemistry and Polymer Science

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Chulalongkorn University

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Thesis Title	ALKENE OXIDATION CATALYZED BY OXOVANADIUM-SCHIFF BASE COMPLEXES
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Field of Study	Petrochemistry and Polymer Science
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กรวรรณ หมวกกุล : ออกซิเดชันของแอลคีนเร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม-ชิฟเบส (ALKENE OXIDATION CATALYZED BY OXOVANADIUM-SCHIFF BASE COMPLEXES) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ดร.วรินทร ชวศิริ, หน้า.

งานวิจัยนี้มุ่งพัฒนาระบบแอลิลิกออกซิเดชัน โดยใช้ VO(salophen) เป็นตัวเร่งปฏิกิริยา ใช้ไซโคลเฮกซีนเป็นสารต้นแบบ พบว่าทั้งปริมาณของตัวเร่งปฏิกิริยาและปริมาณของออกซิแดนท์มีความจำเป็นต่อการเกิดปฏิกิริยา เมื่อใช้ตัวเร่งปฏิกิริยาร่วมกับเทอร์เชียรีไฮโดรเปอร์ออกไซด์ในแอซิโทไนไทรล์ที่อุณหภูมิรีฟลักซ์หรือเมื่อใช้ร่วมกับไฮโดรเจนเปอร์ออกไซด์ที่อุณหภูมิห้อง เป็นเวลา 4 ชั่วโมง ระบบของตัวเร่งปฏิกิริยานี้แสดงลักษณะเฉพาะในการเกิดแอลิลิกแอลกอฮอล์เป็นผลิตภัณฑ์หลัก และแอลิลิกคีโทนเป็นผลิตภัณฑ์รอง ไม่เกิดอิพอกไซด์ขึ้น สารตั้งต้นอื่น เช่น แอลฟา-ไพนีน ลิโมนีน เมทิล โอเลเอต 1-เมทิลไซโคลเฮกซีนและ 1-โดเดกซีน สามารถเปลี่ยนรูปไปเป็นผลิตภัณฑ์ที่ออกซิไดซ์ได้ในปริมาณปานกลางถึงสูง เมื่อใช้ตัวเร่งปฏิกิริยาร่วมกับไฮโดรเจนเปอร์ออกไซด์ พันธะคู่แบบเทอร์มินัลของแอลฟาเมทิลสไตรีน เกิดการแตกตัวและเกิดผลิตภัณฑ์ในปริมาณปานกลาง ระบบแอลิลิกออกซิเดชันที่พัฒนาขึ้นเชื่อว่าเกิดผ่านกระบวนการฟรีแรดิคัล

สาขาวิชา ปิโตรเคมีและวิทยาศาสตร์พอลิเมอร์ ลายมือชื่อนิสิต .....

ปีการศึกษา 2557 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

5472172923 : MAJOR PETROCHEMISTRY AND POLYMER SCIENCE
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KORAWAN MUAKKUL: ALKENE OXIDATION CATALYZED BY OXOVANADIUM-SCHIFF BASE COMPLEXES. ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., pp.

This research focuses on the development of allylic oxidation system using VO(salophen) catalyst. Cyclohexene was employed as a model substrate. Both amount of catalyst and amount of oxidant are essential in promoting the reaction. Utilizing this catalyst in combination with *tert*-butyl hydroperoxide in acetonitrile at reflux or hydrogen peroxide at room temperature for 4 hours, this catalytic system disclosed the unique characteristics to furnish allylic alcohol as a major product together with allylic ketone as a minor. No sign of epoxide was formed. Other substrates such as **α**-pinene, limonene, methyl oleate, 1-methylcyclohexene and 1-dodecene could be transformed into their oxidized products in moderate to high yield. The use of this catalytic system with hydrogen peroxide, the terminal double bond of **α**-methyl styrene was oxidatively cleaved to form oxidized products in moderate yield. This developed allylic oxidation reaction was believed to undergo *via* a free radical process.

Field of Study: Petrochemistry and Polymer Science Student's Signature .....
Advisor's Signature .....
Academic Year: 2014

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LIST OF ABBREVIATIONS

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)
H_2O_2	hydrogen peroxide
IR	infrared
MB	mass balance
m-CPBA	*meta*-chloroperbenzoic acid
mL	milliliter (s)
mmol	millimole
min	minute
m	multiplet (NMR)
% yield	percentage yield
$\varepsilon/\varepsilon_0$	relative dielectric constants
R_f	retarding factor in chromatography
s	singlet (NMR)
TBHP	*tert*-butyl hydroperoxide
TLC	thin layer chromatography
t	triplet (NMR)
td	triplet of doublets
cm^{-1}	unit of wave number

VO(salophen)	oxovanadiun(IV) (salophen)

CHAPTER I

INTRODUCTION

The oxidation of alkenes is the most fundamental oxygen functionalization of compounds containing double bonds. The products derived from the conversion of alkenes were important intermediates in both academic and industrial point of view [1]. Generally, epoxides can be prepared by epoxidation of alkenes using peroxide [2] or peracid [3] whereas allylic alcohols and ketones can be synthesized via allylic oxidation using for example selenium dioxide (SeO_2) [4]. A mixture of products was normally obtained and a separation was required. Thus, the process that can provide the target product selectively is always searched for. The oxidation of alkenes catalyzed by transition metal complexes has been an area of intense study [5, 6].

1.1 Oxidation of alkenes.

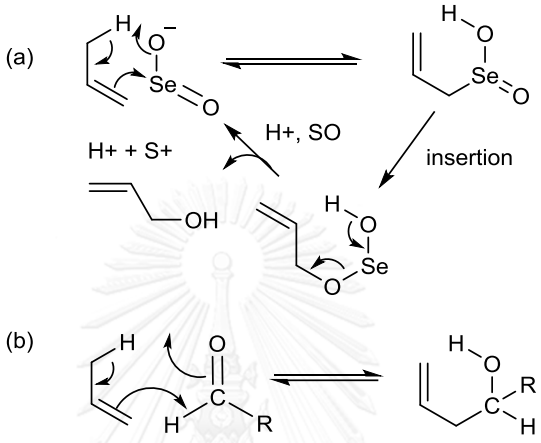
Alkenes were molecules containing a C=C double bond. Oxidation always involves either the addition of oxygen atoms or the removal of hydrogen atoms. Whenever a molecule is oxidized, another molecule must be reduced. Therefore, these reactions require a compound that can be reduced. The oxidation was the most common reaction of alkenes. Several types of reagents adding to alkenes such as water (H_2O), oxidizing agents and halogens were addressed. Those also included allylic oxidation, epoxidation, oxidative cleavage, halogenation, hydration and hydroxylation [7].

Allylic oxidation remains very important reactions for the chemical industries. The products from this oxidation can be divided into two types: reactions which produce allylic alcohols and those which yield α,β-unsaturated aldehydes or ketones [8].

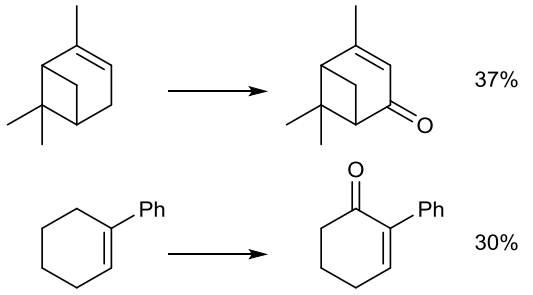
The most valuable method for direct oxidation to allylic alcohols and α,β-unsaturated ketones involves chromium(VI), palladium or selenium reagents. Usually,

homogeneous catalytic systems based on such oxidants as SeO_2, manganese dioxide (MnO_2) or chromium trioxide (CrO_3) are used to allylic oxidations [8-10].

SeO_2 catalyzes the oxidation of alkenes to allylic alcohols in the presence of an oxygen donor such as TBHP [11]. The mechanism is probably (a) concerted or (b) as in the Prins reaction of aldehydes with alkenes.

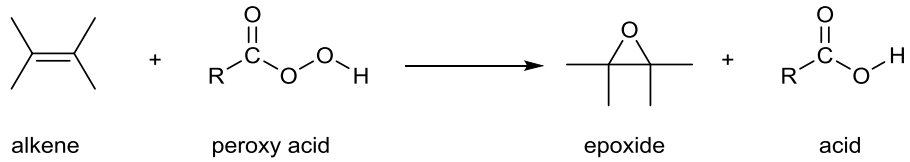


In 1987, Chidambaram and Chandrasekaran [9] used pyridinium dichromate (PDC) in the oxidation of alkenes. For example, α-pinene was converted to verbenone in 37% yield and 1-phenylcyclohexene gave exclusively 2-phenyl- 2-cyclohexenone in 30% yield.

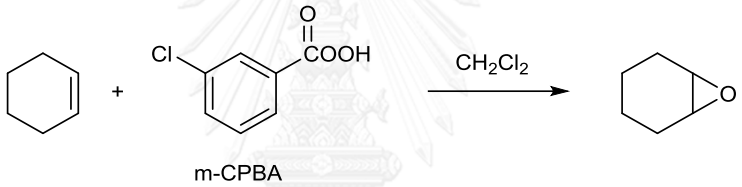


The epoxidation of alkene occurs via the addition to C=C. A general method for preparing epoxides is the reaction with peracids (RCO_3H). The most widely used oxidants such as sodium perborate ($NaBO_3$), peracetic acid (CH_3COOOH), hydrogen

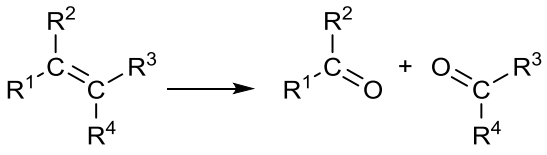
peroxide (H_2O_2), iodosylbenzene (PhIO), *meta*-chloroperbenzoic acid (*m*-CPBA) and molecular oxygen (O_2) [12]. Epoxides are valuable synthetic intermediates in organic chemistry.



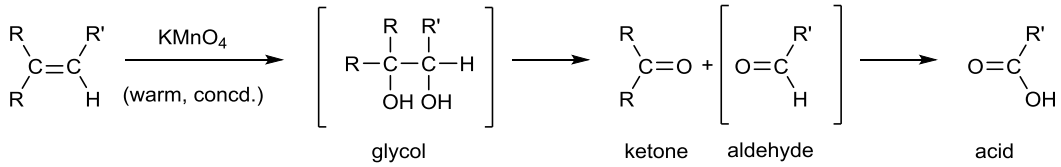
The reaction of alkenes with peroxy acid to produce epoxides has been known for almost 90 years. In 1982, *m*-CPBA was used in cyclohexene epoxidation to obtain the desired epoxide (84 %) in good yield [13].



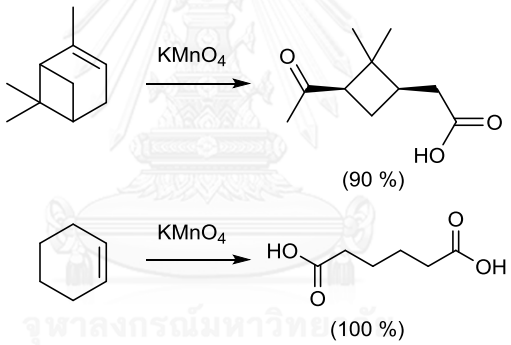
The oxidative cleavage of alkene where the C=C double bond is broken and each of the former alkene carbons becomes a carbonyl. The product formed depends on the structure of alkene, which is the presence of hydrogen atoms at the carbons of the double bonds and on the oxidants used.



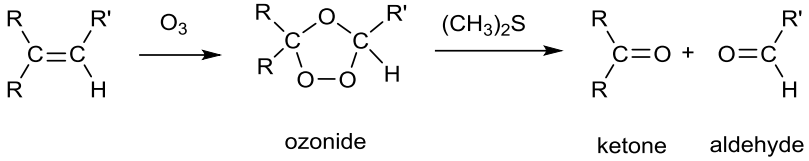
In a potassium permanganate ($KMnO_4$) hydroxylation, if the solution is warm or acidic or too heightened, oxidative cleavage of glycol may occur. A terminal $=CH_2$ group is oxidized to CO_2 and H_2O.



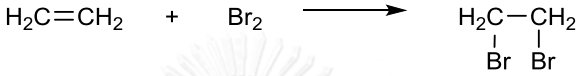
In 1972, Sam and Simmons [14] used $KMnO_4$ in the oxidative cleavage of alkenes. For example, **α**-pinene was converted to pinonic acid in 90% isolated yield and cyclohexene gave exclusively adipic acid in 100% isolated yield.



Ozone (O_3) is a much better behaved reagent than $KMnO_4$, at least at low temperature. O_3 also cleaves alkenes, but it will not oxidize aldehyde groups to carboxylic acids. The reaction of O_3 with an alkene does not directly form carbonyl groups. It is necessary to reduce an intermediate ozonide. The reduction step simply cleaves the relatively weak peroxidic O-O bond in the ozonide, but the reaction needs to be careful because the ozonides have violently explosive properties.

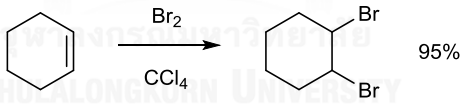


Halogenation was the addition of halogen atoms such as chlorine (Cl_2), bromine (Br_2) and iodine (I_2) to C=C in alkenes. For example, the addition of Br_2 to ethene gave 1,2-dibromoethane.

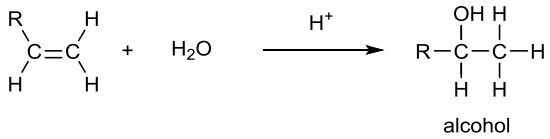


In 1999, Barhate and co-workers [15] studied the halogenation of alkenes with hydrobromic acid (HBr) and H_2O_2. The reaction of cyclohexene and cyclooctene gave 1,2-dibromoalkanes (86 and 82% isolated yield, respectively).

In 2002, Fang and co-workers [16] synthesized 1,2-dibromocyclohexane (95%). The reaction of cyclohexene was oxidized by Br_2 in CCl_4.

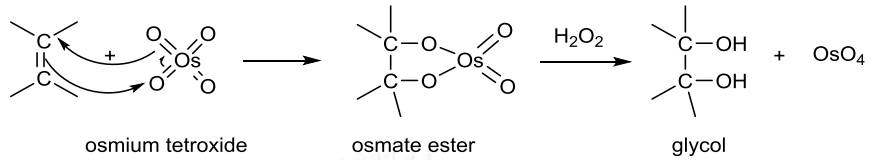


An alkene may react with H_2O in the presence of a strongly acidic catalyst and lead to the formation of alcohols. This reaction is a hydration (the addition of H_2O), with a hydrogen atom adding to one carbon and a hydroxyl group adding to the other. This type of reaction is employed industrially to produce ethanol, *iso*propanol and 2-butanol [17].

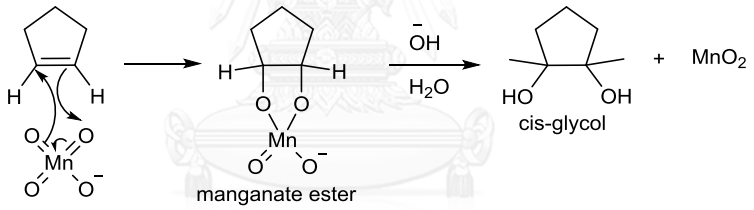


Converting an alkene to a glycol requires adding a hydroxyl group to each end of the double bond (hydroxylation). The hydroxylation can also take place *via* hydrolysis of epoxides, giving *anti*-hydroxylation of the double bond. The two most reagents for this purpose are osmium tetroxide (OsO_4) and $KMnO_4$.

OsO_4 reacts with alkenes in a concerted step to form a cyclic osmate ester. Hydrogen peroxide hydrolyzes the osmate ester and reoxidizes osmium to OsO_4.



$KMnO_4$ adds to the C=C to form a cyclic ester. The solution hydrolyzes the manganate ester, liberating the glycol and producing a brown precipitate of MnO_2.



In 2013, Antonetti and co-workers [18] reported the synthesis of 1,2-cyclohexanediol. The one-pot dihydroxylation of cyclohexene to *trans*-1,2-cyclohexanediol was achieved with 97.4% yield, in the absence of a solvent using an aqueous solution of H_2O_2, a phase-transfer-agent (PTA) and a tungstic acid (H_2WO_4)/phosphoric acid (H_3PO_4) catalytic system.

1.2 Literature review on metal catalyzed oxidation of alkenes.

Catalysts for oxidation is a key technology for converting petroleum-based feed stocks to useful chemicals of a high oxidation state such as alcohols, carbonyl compounds, and epoxides. These compounds are annually produced worldwide and

find applications in all areas of chemical industries, ranging from pharmaceutical to large-scale commodities.

Recent review on chemical literatures found that the metal catalysts for oxidation of C=C bonds have been developed. There are many methods for the oxidation of alkenes using the combination of homogeneous or heterogeneous catalysts and oxidizing agents.

In oxidative cleavage development, the use of oxidant in the presence of homogeneous catalysts was reported. In 1999, Brooks and colleagues [19] reported the oxidative cleavage of alkenes to carbonyl compounds. By using H_2O_2 and 6-molybdo-6-tungstophosphoric acid (PMWA, a heteropolyacid) on magnesium or aluminium or zinc oxide as a catalyst in 2-methylpropan-2-ol after 4 h at 60 ºC, 1-octene was converted to heptanoic acid. In 2002, Travis and co-workers [20] researched the oxidative cyclization of alkenes in which OsO_4 and O_3 in DMF. Oxidative cleavage of alkenes provided ketones or carboxylic acids. The oxidative cleavage of *trans*-, *cis*-stilbenes and styrene led to benzoic acid (95, 95, and 94% isolated yield, respectively). In 2008, Ranu and co-workers [21] studied the oxidative cleavage of alkenes and alkynes using TBHP and indium(III) chloride ($InCl_3$) as catalyst in H_2O at 90ºC to produce the carboxylic acids or ketones. Cyclohexene and cyclooctene produced adipic and suberic acids (92 and 94% isolated yield), respectively.

In development of halogenation, the use of catalyst was reported. In 2006, Mellegaard-Waetzig and co-workers [22] reported **α**-halogenation of Se(II)- and Se(IV)-halogen reagents with cyclohexene in CH_2Cl_2 and pyridine with *N*-chlorosuccinimide (NCS) to produce 3-chlorocyclohex-1-ene (68%), 1-chlorocyclohexene (20%) and 1,2 dichlorocyclohexane (12%). In 2009, Pawluc´ and colleagues [23] studied bromination and iodination of styrene using trimethylvinylsilane and $RuHCl(CO)(PPh_3)_3$ in toluene with *N*-iodosuccinimide (NIS) or *N*-bromosuccinimide (NBS) for 6 h at 100 ºC. The reactions gave (*E*)-**β**-iodostyrene and (*E*)-**β**-bromostyrene in 95 and 92% isolated yield, respectively. In 2011, Zheng and co-workers [24] used $FeBr_3$ for bromination of styrene with NBS and NaBr at 60ºC under N_2 to give styrene dibromide (88% isolated yield).

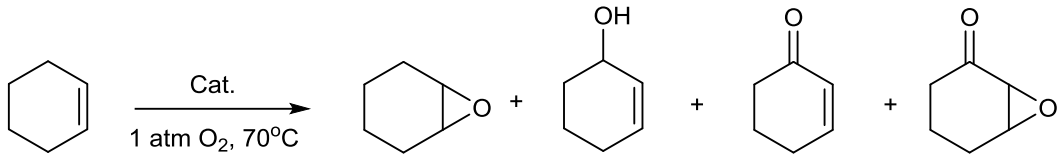
The hydroxylation using catalysts in reaction was also reported. In 2012, Santi and co-workers [25] used L-selenocysteine for dihydroxylation of (+)-*para*-menth-1-ene with H_2O_2 at RT for 168 h. The reaction gave 88% yield of *anti*-diol.

For the epoxidation, the use of oxidant in the presence of homogeneous catalysts was reported. In 1997, Kesavan and Chandrasekaran [26] used ruthenium–bisoxazole complex for oxidation of cyclooctene in CH_2Cl_2 at 25 ºC for 6 h in the presence of O_2 and *iso*butyraldehyde as the co-reductant, excellent yields of epoxides were obtained. In 2013, Shabashov and Doyle [27] researched the epoxidation of *trans*-stilbene and cyclooctene with $Rh_2(OAc)_4$ in the presence of *iso*butyraldehyde in acetone under O_2 at RT to obtain epoxides (88 and 78% isolated yield, respectively). In 2004, Rinaldi and co-workers [28] found that hexaaquoaluminum nitrate ($Al(NO_3)_3.9H_2O$) was able to catalyze the epoxidation of cyclooctene with high epoxide yields using 70 wt% H_2O_2 in THF for 12 h.

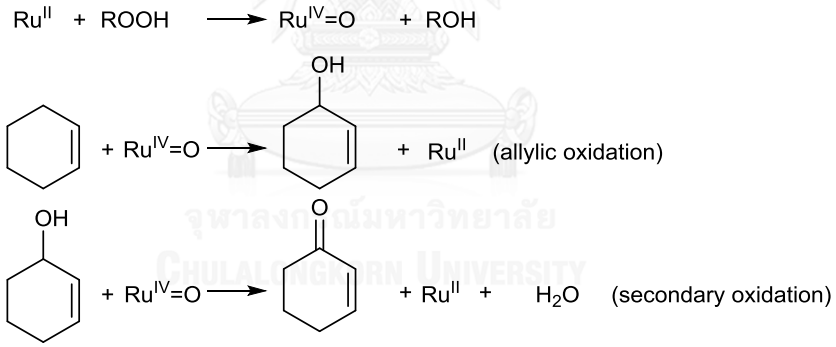
For allylic oxidation, those systems used the combination of transition metal complex as a catalyst and an oxidant. In 1969, Daube and co-workers [29] presented allylic oxidation of cyclohexene using chromium trioxide pyridine complex [CrO_3-$(pyridine)_2$] in CH_2Cl_2 at RT for 24 h. The oxidation afforded cyclohexan-2-en-1-one in 21% yield.

Molecular oxygen (O_2) is the most interesting oxidizing agent, since it is readily available, environmentally benign, easy to remove, clean and cheap. O_2 could be used to oxidize alkenes. In 1995, Birnbaum and colleagues [30] used 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetrakis(pentafluorophenyl)porphyriato-iron(III) chloride, [Fe(TFPPBr_8)Cl], catalyzed the oxidation of cyclohexene with O_2 for 3 h, produced mainly allylic oxidation products (49 and 44% of alcohol and ketone, respectively) and epoxidation product.

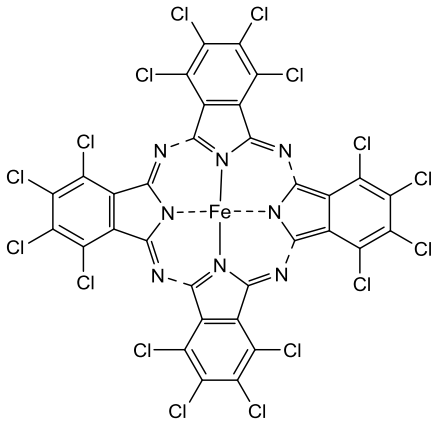
In 2004, Yang and co-workers [31] used six dendritic PAMAMSA-Mn (II) complex under 1 atm of O_2 at 70 ºC for 6 h to oxidize cyclohexene to cyclohexene oxide, cyclohexan-2-en-1-ol, cyclohexan-2-en-1-one and 7-oxabicyclo[4,1,0]heptan-2-one as the major product.



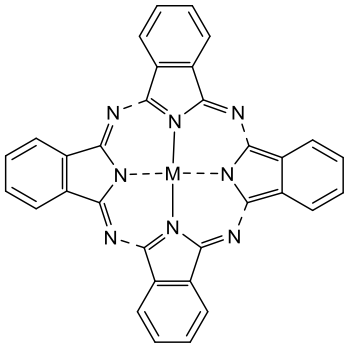
In other developments, the uses of oxidant such as TBHP or H_2O_2 in the presence of homogeneous and heterogeneous catalysts were also reported. In 1999, Kanmani and Vancheesan [32] reported the selective homogeneous oxidation of alkenes with TBHP or H_2O_2 by ruthenium(II) perchlorate complexes. Cyclohexene on oxidation with TBHP could be transformed to cyclohexan-2-en-1-ol, cyclohexan-2-en-1-one and 1-(*tert*-butylperoxy)-2-cyclohexene.1-(*tert*-Butylperoxy)-2-cyclohexene was generated through a radical intermediate. Cyclohexene on oxidation with H_2O_2 gave the allylic oxidation products. The oxidation of cyclohexene to the allylic oxidation products proceeded through a ruthenium(IV)-oxo intermediate.



In 2004, Sehlotho and Nyokong [33] prepared iron(II) polychlorophthalocyanine (Cl16PcFe), iron(II) phthalocyanine (PcFe) and cobalt(II) phthalocyanine (PcCo). These catalysts were used for the oxidation of cyclohexene using TBHP or *m*-chloroperoxybenzoic acid (*m*-CPBA). In the presence of Cl16PcFe using TBHP for 8 h led to 3.5% yield in cyclohexene oxide, 9.1% yield in cyclohexan-2-en-1-ol, and 32.7% yield in cyclohexan-2-en-1-one as a major product.



Iron Perchlorophthalocyanine,(Cl16PcFe)



Metallophthalocyanine (M= Fe(II) or Co(II)), (PcFe), (PcCo)

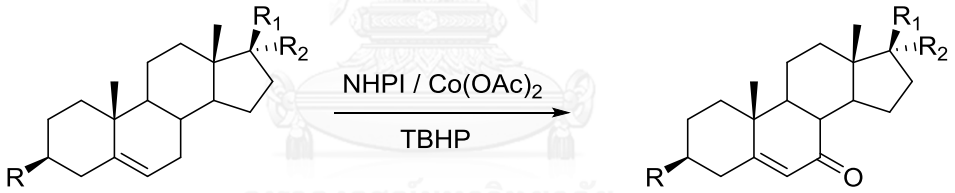
The use of oxidant such as TBHP and O_2 in the presence of a catalyst was also reported. In 2006, Shing and co-workers [34] used manganese(III) acetate ($Mn_3O(OAc)_9$) catalyzed allylic oxidation of alkenes. The reactions with TBHP in decane in EtOAc at RT under O_2 atm for 24 h provided ketone product. The oxidation of 1-dodecene by palladium(II) chloride with TBHP in CH_3CN at 40°C for 2 h was reported by Escola and colleagues in 2008 [35]. 1-Decene was converted to 40% yield of 2-dodecanone as a major product and other ketones. The reaction temperature showed a key role as the selectivity towards 2-dodecanone increased at lower temperature due to the lower extent of the competing isomerization reaction.

In 2009, Chutia and co-workers [36] synthesized Co(II) and Cu(II) complexes of 2-pyrazinecarboxylic acid ligand in zeolite–Y, alumina and organically modified silica supports. The Cu(II) of 2-pyrazinecarboxylic acid ligand in zeolite–Y ($[Cu(N\hat{}O)_2]$–Y), (N^O = η^2-(N,O) coordinated 2-pyrazinecarboxylic acid) complex was used for the heterogeneous oxidation of cyclohexene using H_2O_2. The oxidation afforded 91% cyclohexene conversion with 51% selectivity of cyclohexan-2-en-1-one, 42% selectivity of cyclohexan-2-en-1-ol and 7% selectivity of 1,2-cyclohexanediol. In the same year, Yang and co-workers [37] synthesized and used ionic liquids:$[Bpy]PF_6$ and $[Epy]PF_6$ as solvent for the allylic oxidation of α- and β-ionones. The 70% yield of 3-oxo-α-ionone was obtained with $CuCl_2{\cdot}2H_2O$ as catalyst, TBHP as oxidant and $[Bpy]PF_6$ as solvent for 4 h at 60°C.

In 2011, Khare and Chokhare [38] used iron(III)salen intercalated α-zirconium phosphate (α-ZrP·Fe(Salen)) in benzene with TBHP at 80ºC in 5 h to oxidize cyclohexene to 13.5% yield of cyclohexan-2-en-1-one as a major product, 3.5% yield of cyclohexan-2-en-1-ol and 1% yield of cyclohexene oxide.

In 2013, Skobelev and colleagues [39] synthesized Fe- and Cr-containing metal-organic frameworks of the MIL-101 (Fe-MIL-101 and Cr-MIL-101) as heterogeneous catalysts. This research developed heterogeneous catalysts for the allylic oxidation of alkenes. The allylic oxidation of cyclohexene with TBHP and O_2 as oxidants in CH_3CN at 40-60 ºC for 16 h produced cyclohexan-2-en-1-one and cyclohexan-2-en-1-ol. Cr-MIL-101 provided the formation of α,β-unsaturated ketones, while Fe-MIL-101 could produce higher amounts of allylic alcohols.

In 2015, Zhao and co-workers [40] investigated the allylic oxidation of steroids using $Co(OAc)_2$ and *N*-hydroxyphthalimide (NHPI) and TBHP at RT for 12 h. The oxidized product of 25-hydroxycholesterol acetate was an allylic ketone product.

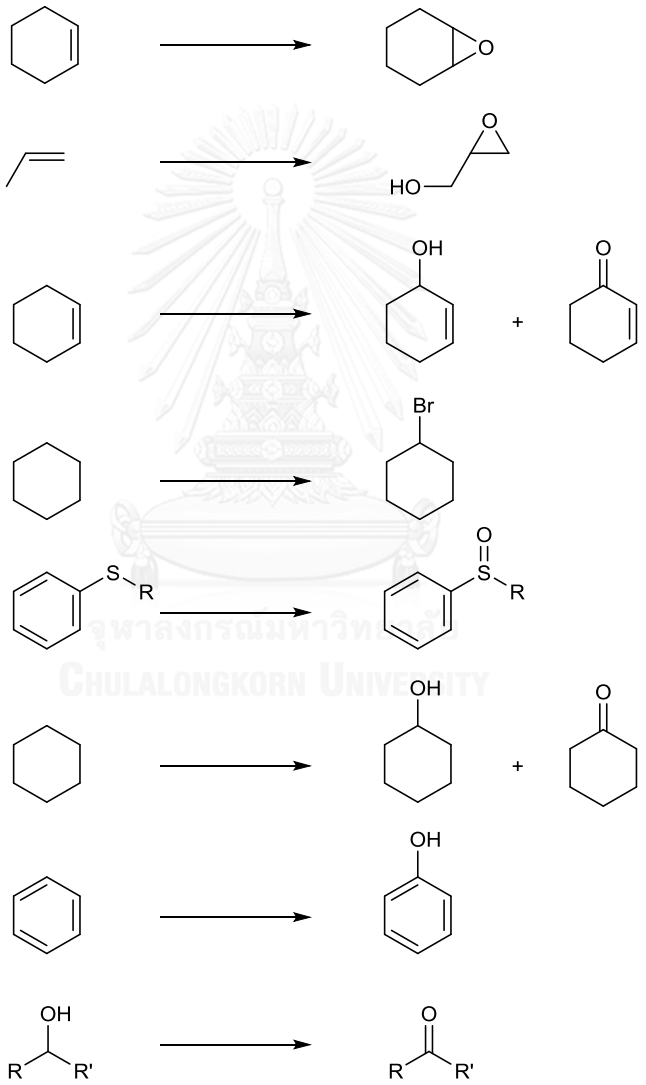


1.3 Vanadium complexes.

Vanadium complexes, including organovanadium compounds, exist in a variety of configurations depending on their oxidation states and coordination numbers. The common oxidation states of vanadium are from +2, +3, +4 and +5. Under ordinary conditions, the +4 and +5 oxidation states are the most stable. Vanadium complexes act as good active catalysts in oxidation of alkenes by O_2 [41, 42]. The oxidation chemistry of vanadium(V) derivatives shares some common features with that of other do transition metal species, e.g. Ti(IV), Mo(VI) and W(VI) [43]. The coordination chemistry of vanadium is experiencing a development with

significance in important fields of biological [44, 45], medicinal [46-48], material and synthetic chemistries.

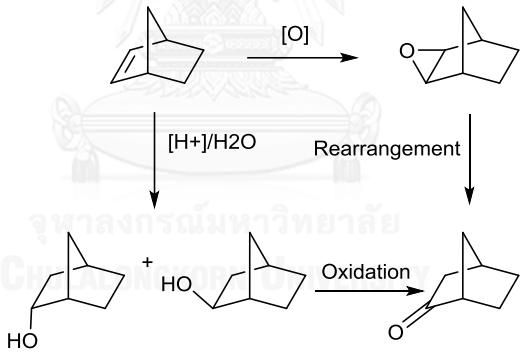
Accordingly, vanadium complexes have been found to perform as catalyst in various oxidation reactions such as epoxidations of alkenes, and allylic alcohols, allylic oxidation of alkenes, bromination of alkanes, oxidation of sulfides, hydroxylation of alkanes, hydroxylation of arenes and oxidation of alcohols.



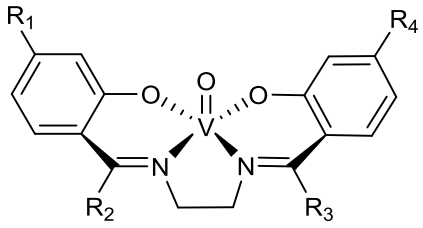
1.4 Literature review on vanadium-catalyzed oxidation of hydrocarbons.

In recent years much attention has been devoted to the vanadium catalyzed oxidation of hydrocarbons. In 2005, Mohebbi and co-workers [49] studied the catalytic system of oxovanadium(IV) complexes with tetradentate Schiff base ligands under 1 atm of O_2 at 79-81ºC for 24 h. In the presence of O_2, vanadyl catalyst in CH_3CN or DMF, cyclohexene was oxidized to a mixture of cyclohexene oxide (60%) as a major product, cyclohexan-2-en-1-ol (30%) and cyclohexan-2-en-1-one (10%).

In 2005, Kala Raj and co-workers [50] synthesized mono-, di- and tri-vanadium substituted phosphomolybdic acid catalysts ($H_4[PV_1Mo_{11}O_{40}]\cdot 19H_2O$, $H_5[PV_2Mo_{12}O_{40}]\cdot 14H_2O$ and $H_5[PV_3Mo_9O_{40}]\cdot 14H_2O$) for oxidation of norbornene. The reactions with H_2O_2, urea-hydrogen peroxide adduct (UHP) and TBHP in CH_3CN at 60ºC for 2 h yielded 2,3-epoxynorbornene (40.6%), norborneols (12%) and 2-norbornanone (17.5%).



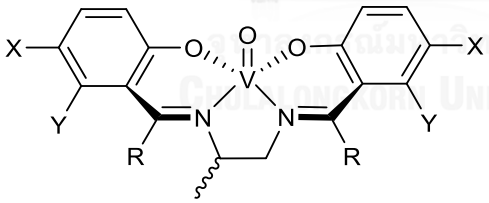
In 2006, Mohebbi and Sarvestani [41] synthesized oxovanadium(IV) complexes with tetradentate Schiff base ligands as catalyst. These catalysts were used for the oxidation of cyclooctene by O_2 in CH_3CN at 75-78ºC for 12 h. The complex (VOL_2) oxidized cyclooctene to cyclooctene oxide, cyclooctenol and cyclooctenone in 28.9, 15.3 and 14.8%, respectively.



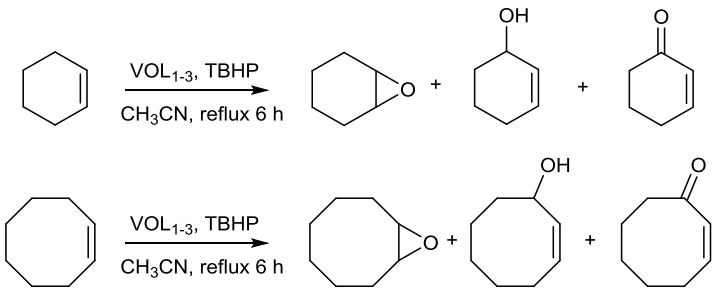
Complex	R_1	R_2	R_3	R_4
VOL^1	H	H	H	H
VOL^2	H	H	CH_3	H
VOL^3	H	H	CH_3	OH
VOL^4	H	CH_3	CH_3	OH
VOL^5	H	CH_3	CH_3	H
VOL^6	OH	CH_3	CH_3	OH

In 2007, Moriuchi and colleagues [51] reported the bromination of cyclohexene using NH_4VO_3 combined with H_2O_2 and $CHCl_3$, HBr and KBr. The bromination products were 1,2-dibromocyclohexane, 2-bromocyclohexan-1-one and 2-bromo-cyclohexan-1-ol (46, 24 and 20% isolated yield, respectively).

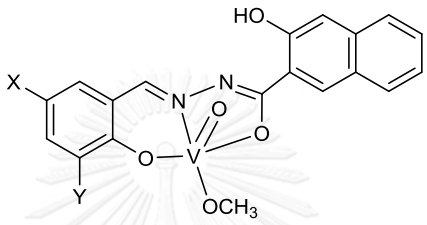
In 2008, Rayati and co-workers [52] synthesized oxovanadium (IV) tetradentate Schiff base complexes and used for oxidation of cyclohexene and cyclooctene by TBHP in CH_3CN at reflux for 6 h. The epoxidation product was 23% yield for cyclohexene oxide and 70% yield for cyclooctene oxide in case of complex VOL_3. The allylic oxidation products were cyclohexan-2-en-1-ol (2.3%), cyclohexan-2-en-1-one (12.1%), cyclooctenol (3.1%) and cyclooctenone (1.8%) in case of complex VOL_3.



Complex	R	X,Y
VOL^1	H	X,Y:-CH=CH-CH=CH
VOL^2	H	X: Br Y: H
VOL^3	Me	X,Y: H



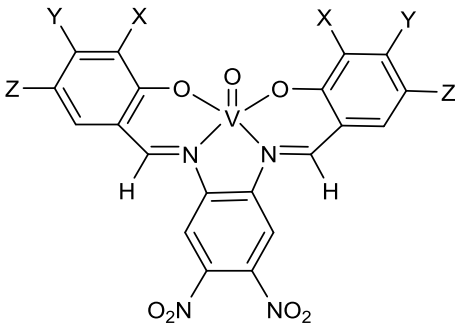
In 2010, Monfared and co-workers [53] synthesized three mono oxovanadium(V) complexes of tridentate Schiff base ligands obtained by monocondensation of 3-hydroxy-2-naphthohydrazide and aromatic *o*-hydroxyaldehydes. These complexes have been tested for the oxidation of cyclohexene using H_2O_2 in CH_3CN at 60ºC for 4 h. For cyclohexene, in addition to cyclohexene oxide (29%), allylic oxidation products (cyclohexan-2-en-1-ol, 55% and cyclohexan-2-en-1-one, 8%) were also formed.



(1): X = H, Y = OCH_3
(2): X = H, Y = H
(3): X = Br, Y = H

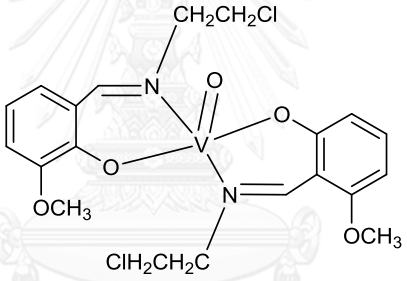
In 2010, Kikushima and co-workers [54] used vanadium-catalyzed (NH_4VO_3) oxidative bromination of arenes, alkenes and alkynes. Bromination of 1-decene was performed in the presence of $AlBr_3$ and Bu_4NBr in CH_3CN under atmospheric O_2 at 50 ºC for 18 h. 1-Decene proceeded well to afford the dibromide in 99% isolated yield.

In 2011, Rahchamani and co-workers [55] synthesized oxidovanadium(IV) complexes of tetradentate Schiff base ligands derived from the condensation of 4,5-dinitro-1,2-phenylenediamine and various salicylaldehydes and examined the oxidation of cyclooctene with TBHP or H_2O_2 in CH_3CN at reflux for 6 h. In system of $VOLig^4$ ([*N,N'-bis*(5-bromoysalicylaldiminato)]oxidovanadium(IV)) and TBHP, cyclooctene oxide was produced upto 64% yield.



Complex	Z	Y	X
VOLig[1]	H	H	H
VOLig[2]	H	OCH_3	H
VOLig[3]	H	H	OCH_3
VOLig[4]	Br	H	H

In 2013, Grivani and co-workers [56] synthesized vanadium(IV) Schiff base complexes VOL_2, L = 2-[(*E*)-[2-chloroethyl)imino]methyl]-6-methoxy phenol. The use of VOL_2 as a catalyst for epoxidation of cyclooctene with TBHP at reflux in $CHCl_3$ within 114 min furnished the only product 86% yield of cyclooctene oxide.



VOL_2

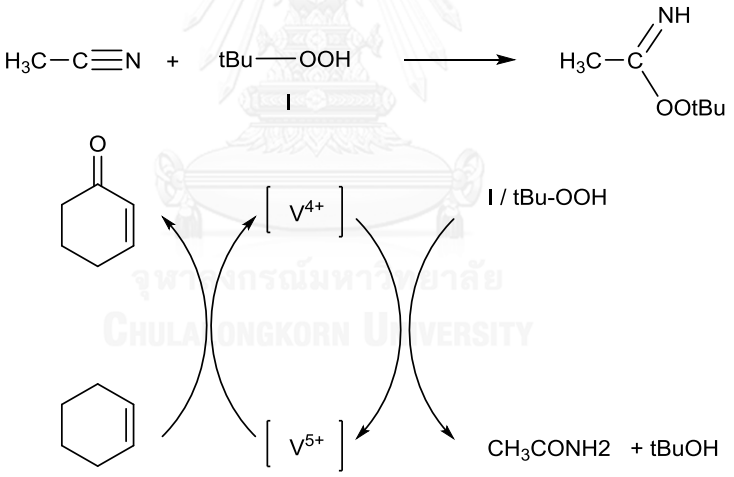
In 2014, Romanowski and co-workers [57] synthesized vanadium(V) complexes derived from Schiff base ligands, monocondensation products *o*-hydroxycarbonyl compounds with 1*S*,2*R*(+)-2-amino-1,2-diphenylethanol. The μ-oxido-*bis*([1*S*,2*R*(+)-2-[(1-oxido-1,2-diphenylethyl)iminomethyl]-6-methoxyphenolato-k^3N,O,O′])
oxidovanadium(V) complex was used for the oxidation of cyclohexene using TBHP in CH_3CN at 80 °C for 6 h. Using TBHP, the excellent conversion (89.6%) and 16.5% selectivity in cyclohexene oxide, 1.0% selectivity of 1,2-cyclohexanediol, 3.5% selectivity in cyclohexan-2-en-1-one and 79% selectivity in cyclohexan-2-en-1-ol as the main reaction products have been noted. They reported sulfoxidation of using

thioanisole as a model substrate with H_2O_2 in CH_2Cl_2 and MeOH at RT for 30 min to produce 82% methyl phenyl sulfoxide.

In 2015, Pisk and co-workers [58] synthesized vanadium(V) complexes with Schiff bases derived from pyridoxal and pyridoxal hydrochloride, and used for epoxidation of cyclooctene by TBHP under solvent-free conditions to give cyclooctene oxide.

1.5 Literature review on vanadium-catalyzed allylic oxidation of alkenes.

In 2011, Liu and co-workers [59] studied the allylic oxidation of cycloalkene. Vanadium phosphorus oxide modified by silver doping (Ag-VPO) as heterogeneous catalyst was synthesized. The reaction using TBHP under Ar atm at 82ºC for 6 h in CH_3CN produced ketone.



According to the literature review, the oxidation of alkenes can either lead to the formation of allylic oxidation products and epoxidation product depending upon transition metal complex catalyst used coupled with TBHP or H_2O_2. The allylic oxidation was very important reactions for chemical industries. However, there was no report on the use of VO(salophen) complex as catalyst for the allylic oxidation of alkenes. This present work focuses on the development of a catalytic system using VO(salophen) for allylic oxidation of alkenes.

1.6 The goal of this research.

The aim of this research can be summarized as follows:

1. To synthesize and characterize VO(salophen) complex
2. To study and develop the catalytic system for oxidation of alkenes using VO(salophen) catalyst under optimized reaction conditions
3. To apply the optimized conditions for oxidation of various selected alkenes

CHAPTER II

EXPERIMENTAL SECTION

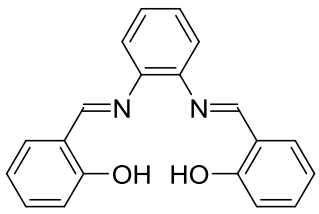
2.1 General procedure.

The reactants and products were confirmed their identities by different spectroscopic techniques. The FT-IR spectra were recorded on a Fourier transform infrared spectrophotometer on Nicolet Impact 410 FT-IR spectrometer. The ^{1}H NMR spectra were obtained in deuterated chloroform ($CDCl_3$) or otherwise stated as an internal reference on a Varian 400 or Bruker 400. Gas chromatographic analysis was carried out on a Varian CP-3800GC equipped with flame ionization detector (FID) using N_2 as a carrier gas. The column used was a capillary column type of BP21 (30m×0.25mm×0.25μm) from VertiBond.

2.2 Chemical reagents.

All solvents used in this research were purified prior to use by standard methodology except for those which were reagent grades. The reagents for synthesizing H_2(salophen), VO(salophen) and all organic substrates, *e.g.* cyclohexene, α-pinene, limonene, 1-methylcyclohexene, 1-dodecene and α-methylstyrene *etc*., were purchased from Fluka and Merck chemical companies.

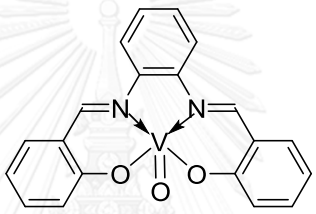
2.3 Preparation of H_2(salophen) ligand [60].



H_2(salophen)

H_2(salophen) was synthesized by condensation of salicyladehyde (2.13 mL, 20 mmol) and 1,2-phenylenediamine (1.08 g, 10 mmol) in MeOH 40 mL. The yellow solution was stirred at RT for 30 min. A yellow precipitate was filtered off, washed with EtOH and dried in dessicator to give yellow solid 2.97 g (94%); R_f 0.53 (CH_2Cl_2); ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.92 (*t*, *J* = 7.5 Hz,2H), 7.04 (*d*, *J* = 11.7 Hz,2H), 7.24 (*m*, 4H), 7.36 (*m,* 2H), 8.64 (*s*, 2H) and 13.06 (*s*, 2H), IR (ATR, cm^{-1}) 3400, 3050, 2950-2870, 1610, 1560-1485, 1275 and 1190.

2.4 Preparation of VO(salophen) complex [61].

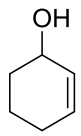


VO(salophen)

H_2(salophen) (0.72 g, 2.3 mmol) was dissolved in EtOH, $VOSO_4.5H_2O$ (0.58 g, 2.3 mmol) and $NaOAc.3H_2O$ (0.81 g) in water were added. The reaction mixture was refluxed for 3 h. After the reaction was cooled down to RT, the green solution was further stirred overnight. The green precipitate was filtered off, washed with water, EtOH and Et_2O and dried in dessicator to give green solid (0.70 g, 80%); R_f 0.79 (30% CH_2Cl_2 in EtOH), IR (ATR, cm^{-1}) 3010, 2890, 1610 and 978.

2.5 Preparation of authentic samples.

Cyclohexan-2-en-1-ol [62]



Cyclohexan-2-en-1-ol

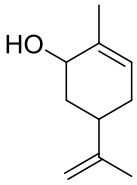
Cyclohexan-2-en-1-one (1.94 mL, 20 mmol) in 25 mL of Et_2O was added $LiAlH_4$ (0.38 g, 10 mmol) in 100 mL of Et_2O, stirred and refluxed for 30 min. Water was slowly added to the cooled mixture until H_2 gas was no longer evolved, followed by 10%H_2SO_4 until the precipitated $Al(OH)_3$ dissolved (pH~3). The aqueous layer was washed with saturated NaCl solution and washed twice with Et_2O. The combined organic layers were washed with saturated $NaHCO_3$, saturated NaCl solutions and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* and the residue was distilled to give colorless oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.20-2.22 (6H, *m*), 3.50 (1H, *s*), 4.17 (1H, *m*) and 5.79 (2H, *m*).

Verbenol [63]

Verbenol

Verbenone (300 mg, 2 mmol) was dissolved in 1 mL EtOH and $NaBH_4$ (38 mg, 1 mmol) was slowly added. The reaction was stirred at RT for 2 h. H_2O was added and the reaction mixture was extracted three times with Et_2O. The organic layer was washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was distilled *in vacuo* to give colorless oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.10 (*s*, 6H), 1.28 (*d*, *J* = 9.0 Hz, 1H), 1.36 (*s*, 3H), 1.72 (*t*, *J* =1.7 Hz, 1H), 1.96 (*t*, *J* =5.5 Hz, 1H), 2.28 (*m*, 1H), 2.44 (*m*, 1H), 4.45 (*s*, 1H) and 5.37 (*s*, 1H).

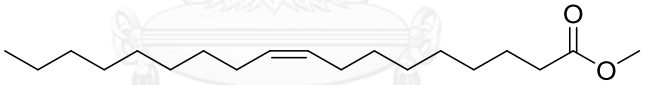
Carveol [64]



Carveol

$NaBH_4$ (25 mg, 0.67 mmol) was added to a stirred solution of (-)-carvone (101 mg, 0.67 mmol) in 10 mL MeOH and $CeCl_3.7H_2O$ (250 mg, 0.67 mmol). The reaction was stirred for 10 min at RT. H_2O (20 mL) and Et_2O (20 mL) were added and the aqueous layer was extracted three times with Et_2O. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was distilled *in vacuo* to give colorless oil. ^{1}H NMR ($CDCl_3$) δ (ppm): 1.46-1.54 (*td*, *J* =12.1, 9.7 Hz, 1H), 1.72 (*s*, 3H), 1.74 (*s*, 3H), 1.92–2.30 (*m*, 4H), 4.19 (*s*, 1H), 4.72 (*s*, 2H) and 5.50 (*s*, 1H).

Methyl oleate [65]



Methyl oleate

Oleic acid (29.94 g, 0.106 mol) in 260 mL MeOH and H_2SO_4 (50.40 mL, 0.946 mol) was added slowly at 0°C. The reaction was refluxed for 24 h, allowed to cool down and then poured into 1.5 L of iced water. The aqueous layer was extracted three times with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* to afford methyl oleate (27.51 g, 92%yield). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.82 (*t, J* =7.1 Hz, 3H), 1.23 (*m*, 20H), 1.56 (*t*, *J* =7.1 Hz, 2H), 1.96 (*m*, 4H), 2.24 (*t*, *J* =7.7 Hz, 2H), 3.60 (*s*, 3H) and 5.28 (*m*, 2H).

2.6 The general procedure for the oxidation of cyclohexene with TBHP catalyzed by VO(salophen).

To a 25 mL round bottom flask equipped with a magnetic stirring fitted with a water circulated condenser was added 10 mL CH_3CN, 2.53 mL (25 mmol) of cyclohexene, 0.62 mL (4.5 mmol) of TBHP and 0.0381 g (0.1 mmol) of VO(salophen) catalyst. The reaction mixture was refluxed for 6 h. After the reaction was completed, 1 mL of the reaction mixture was acidified with cold 25%H_2SO_4 and extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of an appropriate internal standard.

2.7 Study on the optimum conditions for oxidation of cyclohexene with TBHP.

2.7.1 Effect of the amount of VO(salophen).

The oxidation reaction of cyclohexene was carried out according to the general procedure, but the amount of VO(salophen) was varied to 0, 0.05, 0.10 and 0.30 mmol.

2.7.2 Effect of the amount of TBHP.

The oxidation reaction of cyclohexene was carried out in the same manner as general procedure, but the amount of TBHP was varied to 0, 4.5, 9.0, 13.5 and 18.0 mmol.

2.7.3 Effect of solvents.

The oxidation reaction of cyclohexene was carried out according to the general procedure, but the solvent was changed to toluene, 1,2-dichloroethane (DCE), isooctane, chloroform, acetonitrile (CH_3CN), methanol and ethanol.

2.7.4 Effect of reaction time.

The oxidation reaction was carried out in the same fashion as general procedure. At different reaction time proceeded: 1, 4, 6, 18, 24 and 48 h, 1 mL of the

reaction mixture was collected, worked up and dried over anhydrous Na_2SO_4 and analyzed by GC.

2.8 The general procedure for oxidation of cyclohexene with H_2O_2 catalyzed by VO(salophen).

VO(salophen) (0.0381 g, 0.1 mmol), cyclohexene (2.53 mL, 25 mmol), 30%H_2O_2 (0.46 mL, 4.5 mmol) and 10 mL CH_3CN were placed in a 25 mL round bottom flask. The reaction mixture was stirred at RT for 4 h. After the reaction was completed, 1 mL of the reaction mixture was acidified with cold 25%H_2SO_4 and extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$ solution, dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of an appropriate internal standard.

2.9 Study on the optimum conditions for oxidation of cyclohexene with H_2O_2.

2.9.1 Effect of the amount of H_2O_2.

The oxidation reaction was carried out in the same manner as previously described using VO(salophen) as a catalyst with different amount of the oxidant: 0, 2.0, 4.5, 9.0, 13.5 and 18 mmol.

2.9.2 Effect of reaction time.

The oxidation of cyclohexene catalyzed by VO(salophen) catalyst was carried out at RT. At different reaction time proceeded: 0.5, 1, 2, 4, 6, 8 and 16 h, 1 mL of the reaction mixture was collected, worked up and dried over anhydrous Na_2SO_4 and finally analyzed by GC.

2.9.3 Effect of solvents.

The oxidation reaction was carried out in the same fashion as previously described but the solvent was changed to toluene, DCE, isooctane, chloroform, CH_3CN, methanol, ethanol, pyridine:acetic acid, *N,N*-dimethylformamide (DMF) and tetrahydrofuran (THF).

2.9.4 Effect of the amount of catalyst.

The oxidation reaction was carried out in the same manner as previously described using VO(salophen) as a catalyst, but the amount of catalyst was varied: 0, 0.1, 0.25 and 0.5 mmol.

2.9.5 Effect of the amount of cyclohexene.

The oxidation reaction was carried out in the same manner as previously described using VO(salophen) as a catalyst with different amount of cyclohexene: 5, 10, 25 and 50 mmol.

2.10 Effect of type of oxidant.

The oxidation reaction of cyclohexene was carried out according to the general procedure, but type of oxidants was changed to 30%H_2O_2, TBHP and 2-ethyl butylraldehyde/O_2.

2.11 Comparative study of the oxidizing agents on cyclohexene oxidation.

According to the general oxidation procedure, VO(salophen) was used as a catalyst and cyclohexene (25 mmol) was used as a substrate in the reaction using either TBHP or 30%H_2O_2 as oxidizing agents.

2.12 Study on the alkene oxidation catalyzed by VO(salophen).

Under optimum conditions, selected alkenes namely **α**-pinene, limonene, methyl oleate, 1-methylcyclohexene and 1-dodecene were oxidized employing the general oxidation procedure.

2.13 The general procedure for the oxidative cleavage of α-methylstyrene.

For the oxidative cleavage of **α**-methylstyrene, a solution of **α**-methylstyrene (5 mmol) in CH_3CN (10 mL) containing VO(salophen) complex (0.0381 g, 0.1 mmol) in

a round bottom flask and 30%H_2O_2 (0.920 mL, 9 mmol) was added. The mixture was stirred at RT for 4 h. After the reaction finished, 1 mL of the reaction mixture was acidified with cold 25%H_2SO_4 and extracted with Et_2O. The combined extracts were washed saturated $NaHCO_3$ solution, respectively. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of appropriate internal standard.

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

2.14.1 Effect of type of oxidants.

The oxidation reaction was carried out in the same manner as previously described using VO(salophen) as a catalyst, but the type of oxidants was varied: 30% H_2O_2 and TBHP.

2.14.2 Effect of the amount of H_2O_2.

The oxidation reaction was carried out in the same manner as previously described using VO(salophen) as a catalyst with different amount of the oxidant: 0, 4.5, 9, 13.5 and 18 mmol.

2.14.3 Effect of solvents.

The oxidation reaction was carried out in the same manner as described procedure, but the varied solvents (DCE, chloroform, CCl_4, isooctane, toluene, CH_3CN, methanol and ethanol) were employed.

2.14.4 Effect of the amount of α-methylstyrene.

The oxidation reaction was carried out as described in the general procedure using VO(salophen) as a catalyst with different amount of α-methylstyrene: 1, 5, 10 and 25 mmol.

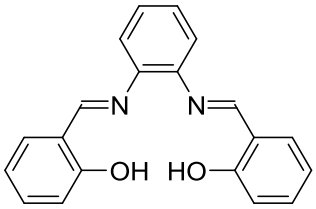
CHAPTER III

RESULTS AND DISCUSSION

This research was focused on the development of the catalytic system for the oxidation of alkenes using VO(salophen). The reaction conditions including the amount oxidant, the amount of catalyst, reaction time, solvent, and the amount substrate were optimized using cyclohexene as a model. Other substrates such as **α**-pinene, limonene, 1-methylcyclohexene, 1-dodecene and **α**-methylstyrene were selected to observe the scope of this system. In addition, three types of oxidants namely 70%TBHP, 30%H_2O_2 and 2-ethyl butylraldehyde/O_2 were investigated.

3.1 Syntheses and identification of H_2(salophen) ligand.

H_2(salophen) was synthesized by condensation salicyladehyde with 1,2-phenylene-diamine. The attained ligand was identified by IR and ^{1}H NMR. The IR spectrum (Figure 3.1) reveals a broad OH peak at 3300-3400 cm^{-1} and 1000-1300 cm^{-1} for C-O stretching vibration. The absorption peak at 1610 cm^{-1} was attributable to azomethine group (C=N) vibration [66]. The ^{1}H NMR ($CDCl_3$) spectrum (Figure 3.2) displays the aromatic protons at δ_H 6.92 (*t*, *J* = 7.5 Hz, 2H), 7.04 (*d*, *J* = 11.7 Hz, 2H), 7.24 (*m*, 4H) and 7.36 (*m,* 2H), the imine proton at δ_H 8.64 (*s*, 2H) and the hydroxyl proton at δ_H 13.06 (*s*, 2H).



H_2(salophen)

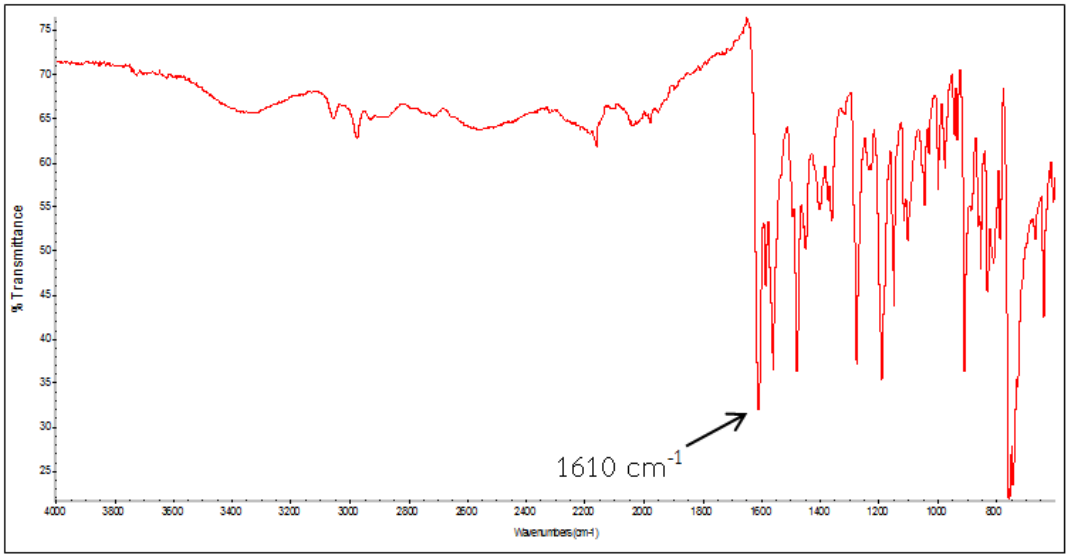


Figure 3.1 IR spectrum of H_2(salophen)

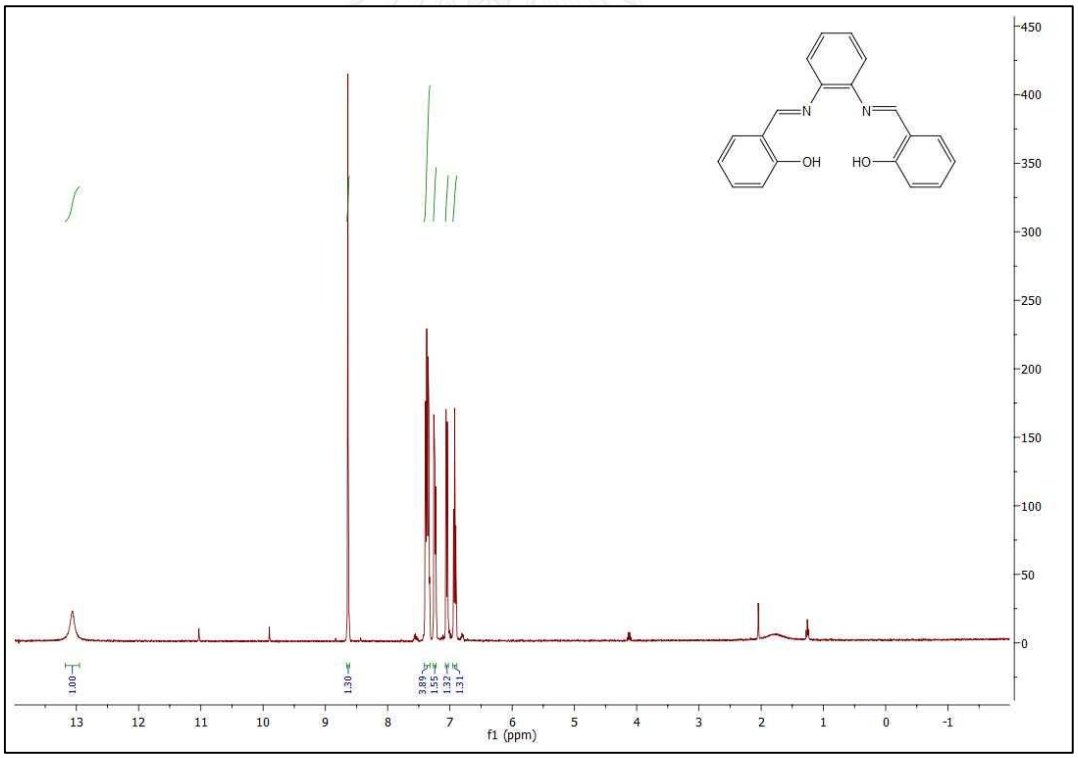


Figure 3.2 ^{1}H NMR spectrum of H_2(salophen)

3.2 Syntheses and characterization of VO(salophen) complex.

The VO(salophen) complex was synthesized by reacting H_2(salophen) and $VOSO_4.5H_2O$ according to the previously reported protocol [61] and characterized by IR. The IR spectrum (Figure 3.3) displays a characteristic absorption band at 1600 cm^{-1} attributable to azomethine group (C=N) vibration. Azomethine group (C=N) vibration shift from 1610 cm^{-1} to 1600 cm^{-1} because C=N bond was weak (coordinate bond to vanadium). Moreover, the V=O stretching vibration frequency was detected around 978 cm^{-1} [67].

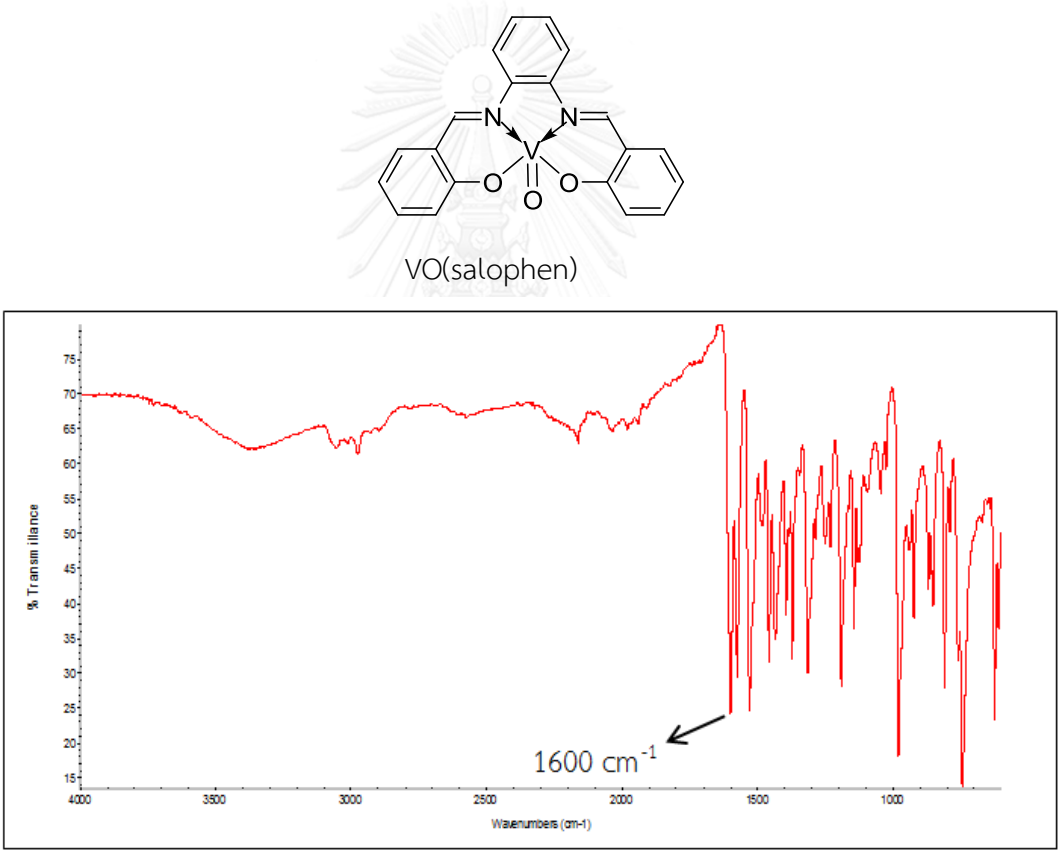
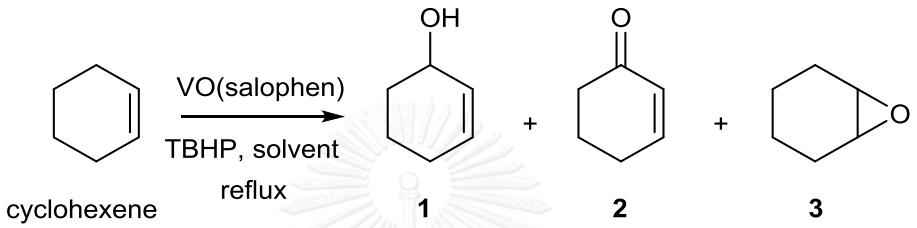


Figure 3.3 IR spectrum of VO(salophen) complex

3.3 Study on the optimum conditions for the oxidation of cyclohexene with TBHP catalyzed by VO(salophen).

Cyclohexene was selected as a model substrate. Various parameters including amount of catalyst, amount of oxidant, media, reaction time and type of oxidants were examined.



3.3.1 Effects of the amount of VO(salophen).

The amount of catalyst from 0 to 0.3 mmol was examined to observe its influence on the oxidation of cyclohexene. The results are presented in Table 3.1.

Table 3.1 The effects of the amount of VO(salophen) on cyclohexene oxidation.

Entry	Amount of VO(salophen) (mmol)	Product (mmol)			Selectivity enol/enone
		1	2	Σ	
1	0	0	trace	trace	-
2	0.05	1.375	0.130	1.505	10.6
3	0.10	1.587	0.147	1.734	10.8
4	0.30	1.729	0.156	1.885	11.1

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (vary), CH_3CN (10 mL), TBHP (4.5 mmol), reflux 6 h.

From Table 3.1, when VO(salophen) 0.30 mmol was used (entry 4), the reaction gave the highest yield of cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**) (~1.9 mmol). The similar yield of the desired products was observed when 0.10 mmol of catalyst was used (entry 3). The amount of catalyst of 0.10 mmol was the appropriate amount for the oxidation of cyclohexene under this particular condition with good selectivity of enol/enone, ~11 and high yield of product (~1.7 mmol). This present work was found to be unique and different from previous reports by Rayati and co-workers [52] and Boghaei and Mohebi [68]. Those two research groups reported that the oxidation of cyclohexene catalyzed by vanadyltetradentate Schiff base complexes led to the production of cyclohexene oxide (**3**) as a major product together with allylic oxidation products (**1**&**2**). It could be seen that this developed system was very selective yielding only the allylic oxidation products, mainly cyclohexan-2-en-1-ol (**1**).

3.3.2 Effects of solvents.

The solvent that could provide the homogenous reaction was required. The effects of solvent were studied and collected in Table 3.2 and Figure 3.4.

Table 3.2 The effects of solvent for the oxidation of cyclohexene catalyzed by VO(salophen).

Entry	Solvent	Product (mmol)				Selectivity enol+enone /epoxide
		1	2	3	Σ	
1	toluene	0.132	0.047	0.058	0.237	3.1
2	$C_2H_4Cl_2$	0.226	0.057	0.913	1.196	0.3
3	isooctane	0.061	0	0	0.061	-
4	$CHCl_3$	0	0.045	1.460	1.505	0.03
5	CH_3CN	2.530	0.405	0	2.935	-
6	CH_3OH	0.353	0	0.587	0.940	0.6
7	C_2H_5OH	0.276	0.262	0	0.538	-

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), solvent (10 mL), TBHP (9 mmol), reflux 6 h.

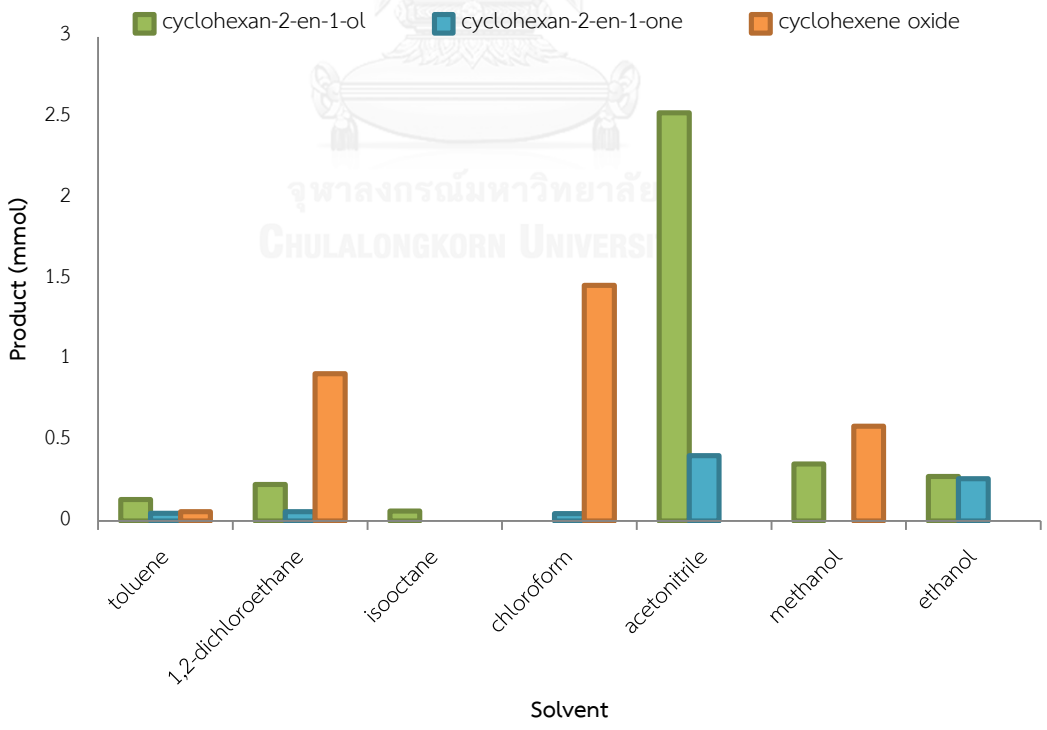


Figure 3.4 The effects of solvent on the oxidation of cyclohexene catalyzed by VO(salophen)

Because of less solubility of catalyst in toluene and isooctane, low yield of products was observed (entries 1-2). It should also be mentioned at this point that employing toluene, DCE and CH_3OH (entries 1, 2 and 6) also gave cyclohexene oxide (**3**), particularly using $CHCl_3$ provided cyclohexene oxide (**3**) as a major product (entry 4). Grivani and co-workers [6] reported that $CHCl_3$ gave good epoxidation yield.

When employing CH_3OH and C_2H_5OH, the oxidation reaction was found to produce a moderate amount of products. Using CH_3CN, a solvent of choice, provided the best result for both the total amount of the desired products (**1**&**2**) and the selectivity of the reaction towards allylic oxidation. No cyclohexene oxide (**3**) was detected. According to the literatures, Monfared and co-workers [53, 69] performed the reaction in CH_3CN with H_2O_2 catalyzed by oxovanadium complexes. It was observed that the catalytic activity of complex decreased in order of CH_3CN (relative dielectric constants) $\varepsilon/\varepsilon_0$ = 37.5>CH_3OH (32.7) >C_2H_5OH (26.6) > THF (7.3) > acetone (20.7) >$CHCl_3$ (4.9) >EtOAc (6.0) > CCl_4 (2.24) >DMF (36.7). Thus, this research revealed the same trend as previous observation to obtain the high yield of products in CH_3CN.

3.3.3 Effects of the amount of TBHP.

The variation of the amount of oxidant was examined. TBHP was the first chosen oxidant for the oxidation of cyclohexene. The results are presented in Table 3.3.

Table 3.3 The effects of the amount of TBHP on cyclohexene oxidation catalyzed by VO(salophen).

Entry	Amount of TBHP (mmol)	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	0	0	0	0	-
2	4.5	1.587	0.147	1.734	10.8
3	9.0	2.530	0.405	2.935	6.3
4	13.5	2.633	0.696	3.329	3.8
5	18.0	2.419	1.734	4.154	1.4

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), TBHP (vary), reflux 6 h.

The amount of TBHP was varied from 0-18 mmol. From Table 3.3, it could be observed that when 4.5 mmol of TBHP was used, the yield of the desired product was high (~1.73 mmol) with excellent selectivity of enol/enone (~11) (entry 2). Using more TBHP, the product of cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**) were increased. On the contrary, Gonzrdin and co-workers [70] and Sehlotho and co-workers [33] reported the allylic oxidation of cyclohexene using iron complex and TBHP which produced allylic oxidation products (**1**&**2**) as a major product together with cyclohexene oxide (**3**).

3.3.4 Effects of reaction time.

The effect of the reaction time on the oxidation of cyclohexene was investigated. The results are shown in Table 3.4 and Figure 3.5.

Table 3.4 The effects of reaction time on cyclohexene oxidation catalyzed by VO(salophen).

Entry	Time (h)	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	1	0.800	0	0.800	-
2	4	1.551	0.138	1.689	11.2
3	6	1.587	0.147	1.734	10.8
4	18	1.645	0.178	1.823	9.2
5	24	1.924	0.196	2.120	9.8
6	48	1.942	0.254	2.196	7.6

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH3CN (10 mL), TBHP (4.5 mmol), reflux.

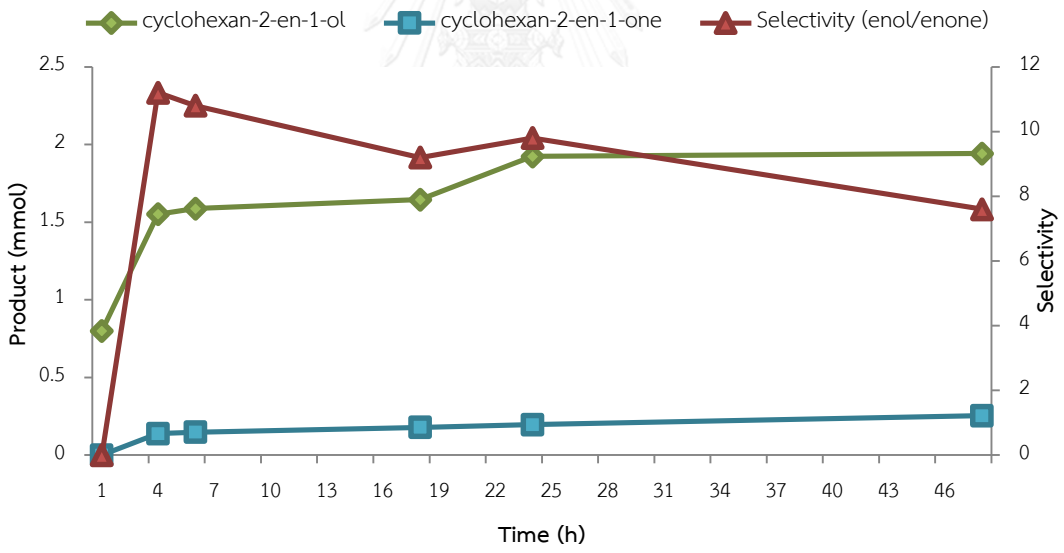


Figure 3.5 The effects of reaction time on the oxidation of cyclohexene catalyzed by VO(salophen)

Allylic oxidation and epoxidation are two basic competing processes for alkene functionalization both *in vivo* and *in vitro* [71]. Allylic oxidation is a process involving free radicals. The examination on the influence of VO(salophen) catalyst revealed that this reaction proceeded through allylic oxidation yielding cyclohexan-2-

en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**) and no epoxidation product was observed. From Table 3.4, when the reaction time increased to 24 h, the amount of cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**) was increased (entry 5). The highest selectivity ratio of cyclohexan-2-en-1-ol (**1**) to cyclohexan-2-en-1-one (**2**) was achieved at 4 h (entry 2). The outcome from this study revealed that the reaction time of 4 h (entry 2) was the most appropriate time for the oxidation of cyclohexene under optimum conditions.

3.4 Study on the optimum conditions for the oxidation of cyclohexene with H_2O_2 catalyzed by VO(salophen).

Various factors were also needed to evaluate in order to optimize the conditions for the oxidation of cyclohexene catalyzed by VO(salophen) using H_2O_2. Those parameters included amount of oxidant, reaction time, media, amount of catalyst and amount of substrate (cyclohexene).

3.4.1 Effect of the amount of H_2O_2.

The variation of the amount of H_2O_2 was investigated. The results are presented in Table 3.5.

Table 3.5 Effects of the amount of H_2O_2 on cyclohexene oxidation catalyzed by VO(salophen).

Entry	Amount of H_2O_2 (mmol)	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	0	0	0	0	-
2	2.0	0.800	0	0.800	-
3	4.5	1.981	0.458	2.439	4.3
4	9.0	1.491	1.217	2.708	1.2
5	13.5	1.483	1.466	2.949	1.0
6	18.0	1.727	1.973	3.700	0.9

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), 30% H_2O_2 (vary), RT, 6 h.

According to the literatures, Maurya and co-workers [72] reported the oxidation of cyclohexene catalyzed by oxovanadium(IV) and copper(II) exchanged zeolite-Y catalysts with H_2O_2 and revealed that the allylic oxidation product was detected as a major product.

In this work, the amount of oxidant (30% H_2O_2) was varied from 0-18 mmol. The most appropriate amount of H_2O_2 that provided the desired product of cyclohexan-2-en-1-ol (**1**) (~2 mmol) with good selectivity (enol/enone, ~4) was 4.5 mmol (entry 2). When the amount of H_2O_2 was increased, cyclohexan-2-en-1-one (**2**) was increased but cyclohexan-2-en-1-ol (**1**) was decreased. This was presumably derived from further oxidation of the latter. In entries 4-6, the observed selectivity (enol/enone) was decreased (1.2, 1.0 and 0.9, respectively). When the amount of H_2O_2 was increased, the activation process was increased. This system still showed a unique characteristic yielding cyclohexan-2-en-1-ol (**1**) as a major product.

3.4.2 Effect of reaction time.

The kinetic investigation on the oxidation of cyclohexene was conducted and the results are presented in Table 3.6 and Figure 3.6.

Table 3.6 Effects of reaction time on cyclohexene oxidation catalyzed by VO(salophen).

Entry	Time (h)	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	0.5	0.511	0.234	0.745	2.2
2	1	0.895	0.444	1.339	2.0
3	2	1.197	0.417	1.614	2.9
4	4	1.864	0.534	2.398	3.5
5	6	1.981	0.458	2.439	4.3
6	8	1.993	0.523	2.516	3.8
7	16	1.729	0.507	2.236	3.4

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), 30% H_2O_2 (4.5 mmol), RT.

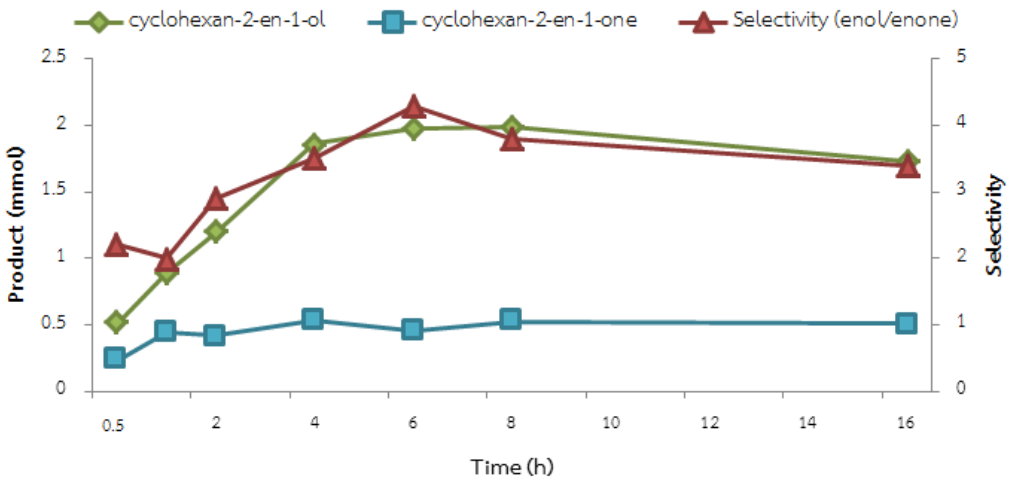


Figure 3.6 Effects of reaction time on cyclohexene oxidation catalyzed by VO(salophen)

The reaction time was varied from 0.5-16 h. When the reaction time was prolonged, the activation process was increased, *i.e.*, more allylic radicals were generated to produce more cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**).

The selectivity ratio of **1** to **2** was kept almost constant after 4 h (entry 4). The amount of products remained constant after 6 h (entry 5). Figure 3.6 reveals that approximately 4 h was the most appropriate time for allylic hydroxylation of cyclohexene under optimum conditions. When the reaction time was increased to 16 h (entry 7), the desired product deteriorated. The desired product may be further oxidized by H_2O_2 resulting in lower yield.

3.4.3 Effect of solvents.

The reaction media is one of essential parameters that needed to be scrutinized. The results are collected in Table 3.7 and Figure 3.7.

Table 3.7 Effects of solvent for oxidation of cyclohexene catalyzed by VO(salophen).

Entry	Solvent	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	neat	0.064	0	0.064	-
2	toluene	0.304	0.172	0.476	1.8
3	$C_2H_4Cl_2$	0.273	0.279	0.552	1.0
4	isooctane	0.256	0.134	0.390	1.9
5	$CHCl_3$	0.353	0.242	0.595	1.5
6	CH_3CN	1.864	0.534	2.398	3.5
7	CH_3OH	0.504	0.805	1.309	0.6
8	C_2H_5OH	0.566	0.714	1.280	0.8
9	pyridine: acetic acid (3:1)	0.250	0	0.25	-
10	DMF	0.159	0.352	0.511	0.4
11	THF	0.207	0.147	0.354	1.4

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), solvent (10 mL), 30% H_2O_2 (4.5 mmol), RT, 4 h.

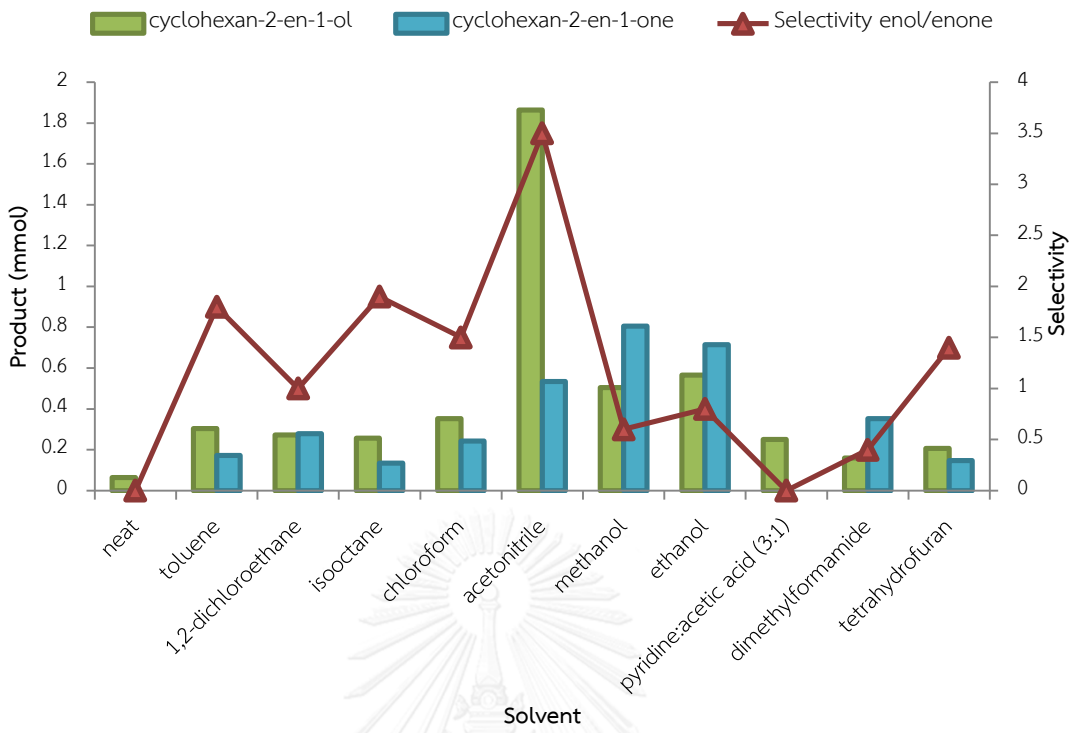


Figure 3.7 Effects of solvent on the oxidation of cyclohexene catalyzed by VO(salophen).

The use of polar protic solvents such as CH_3OH and C_2H_5OH (entries 7-8) resulted in moderate yield of product. The use of toluene, 1,2-dichloroethane ($C_2H_4Cl_2$), isooctane, and $CHCl_3$ (entries 2-5) provided low yield of product because of phase separation. It was found that the amount of cyclohexan-2-en-1-ol (**1**) was very low when the reaction media used was pyridine:acetic acid (3:1) (entry 9). In case of using DMF and THF (entries 10-11) small amount of products was attained, possibly because of the high coordinated ability of solvent [53]. These results clearly presented that CH_3CN was a solvent of choice providing the best result for both total amount of the desired products and the selectivity of the reaction towards allylic oxidation. No cyclohexene oxide (**3**) was detected.

3.4.4 Effect of the amount of catalyst.

The amount of VO(salophen) was varied to observe the outcome of the reaction. The results are presented in Table 3.8.

Table 3.8 Effects of the amount of VO(salophen) on cyclohexene oxidation.

Entry	Amount of VO(salophen) (mmol)	Product (mmol)			Selectivity enol/enone
		1	**2**	**∑**	
1	0	0.089	0	0.089	-
2	0.1	1.864	0.534	2.398	3.5
3	0.25	1.138	0.231	1.369	4.9
4	0.5	0.773	0.300	1.073	2.6

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (vary), CH_3CN (10 mL), 30% H_2O_2 (4.5 mmol), RT, 4 h.

The catalyst concentration seemed to be important for the activation process. Using VO(salophen) 0.1 mmol (entry 2), the reaction gave the highest yield of cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**). When the amount of VO(salophen) was further increased, the desired product was decreased. This might be because of too much catalyst probably causing side reactions competitively with the oxidation of cyclohexene. Thus, it was clear that the catalyst 0.1 mmol was appropriate for the oxidation of cyclohexene with good selectivity.

3.4.5 Effect of the amount of cyclohexene.

The oxidation reaction was carried out in the same manner as previously described with different amounts of cyclohexene. The results are presented in Table 3.9.

Table 3.9 Effects of the amount of cyclohexene on the oxidation catalyzed by VO(salophen).

Entry	Amount of cyclohexene (mmol)	Product (mmol)			Selectivity enol/enone
		1	2	∑	
1	5	0.235	0.202	0.437	1.2
2	10	0.547	0.396	0.943	1.4
3	25	1.864	0.534	2.398	3.5
4	50	2.235	0.511	2.746	4.4

Reaction conditions: cyclohexene (vary), VO(salophen) (0.10 mmol), CH_3CN (10 mL), 30% H_2O_2 (4.5 mmol), RT, 4 h.

The amount of cyclohexene was varied from 5-50 mmol. When the amount of cyclohexene was increased, the desired products (**1**&**2**) were increased. Using cyclohexene 25 mmol (entry 3), the oxidation reaction gave high yield of cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**) (~2.4 mmol). The results indicated that increasing of the amount of substrate did not affect on the outcome of the reaction.

3.5 Effects of type of oxidants.

Three types of oxidants were investigated namely 70%TBHP, 30%H_2O_2 and 2-ethyl butylraldehyde/O_2. The results are presented in Table 3.10.

Table 3.10 The effects of type of oxidants on cyclohexene oxidation catalyzed by VO(salophen).

Entry	Oxidant	Temp	Product (mmol)				Selectivity enol+enone/ epoxide
			1	2	3	∑	
1	TBHP	reflux	1.551	0.138	0	1.689	-
2	H_2O_2	RT	1.864	0.534	0	2.398	-
3	2-ethyl-butylraldehyde /O_2*	RT	0	0	0.585	0.585	-

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), oxidants (4.5 mmol), 4 h.

*cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), 2-ethylbutylraldehyde/O_2 (10 mmol), 24 h.

From Table 3.10, various oxidants including TBHP, H_2O_2 and 2-ethylbutyraldehyde/O_2 were investigated. The reactions were proceeded in very good yield (entry 2) employing H_2O_2 as an oxidant. TBHP and H_2O_2 (entries 1-2) gave cyclohexan-2-en-1-ol (**1**) as a major product and cyclohexan-2-en-1-one (**2**) as a minor one. Both of TBHP and H_2O_2 did not give cyclohexene oxide (**3**). Using 2-ethylbutylraldehyde/O_2 (entry 3) on the other hand produced solely cyclohexene oxide (**3**), however with very small amount of activation process. According to the literatures, Buranaprasertsuk and co-workers [73] used 2-ethylbutylraldehyde/O_2 for epoxidation of alkenes by cobalt(II) calix[4]pyrrole as a catalyst. This provided the epoxide in high yield. These results clearly showed that VO(salophen) was an unsuitable catalyst for the epoxidation of cyclohexene with 2-ethylbutylraldehyde/O_2.

3.6 Comparative study of the oxidizing agents on cyclohexene oxidation.

The effects of using TBHP and H_2O_2 were comparatively examined. The oxidation was carried out in CH_3CN and the results are presented in Figure 3.8.

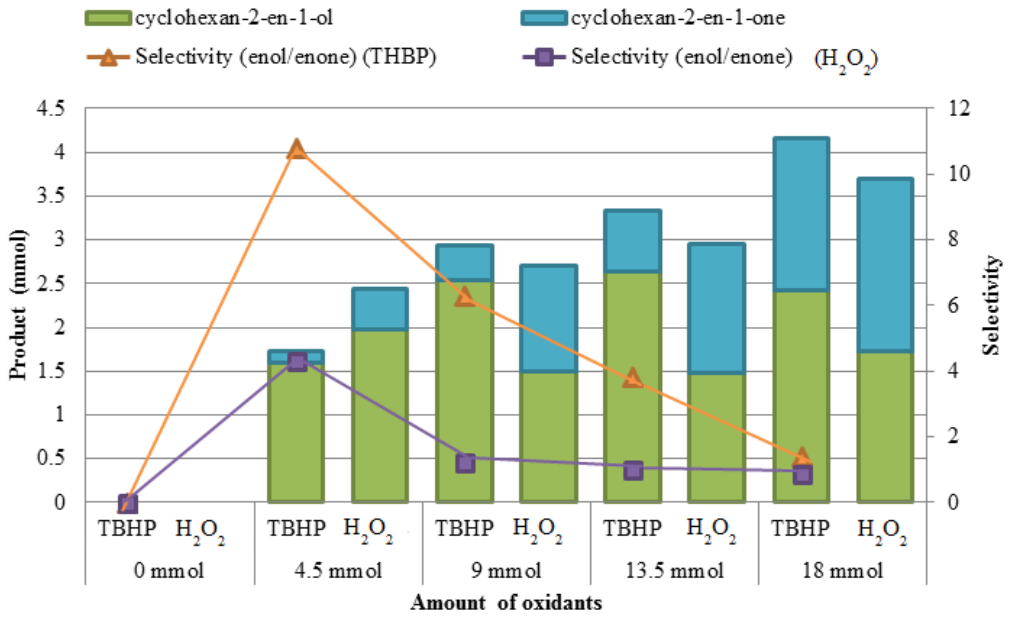


Figure 3.8 The effects of the amount of oxidant on cyclohexene oxidation catalyzed by VO(salophen).

Generally, under this developed system, the oxidation of cyclohexene catalyzed by VO(salophen) using TBHP or H_2O_2 produced a major product as cyclohexan-2-en-1-ol (**1**) together with a minor component as cyclohexan-2-en-1-one (**2**). From Figure 3.8, in the case of reaction selectivity (enol/enone), the reaction with TBHP provided higher enol/enone selectivity than that using H_2O_2. The reaction with H_2O_2 could proceed faster than that with TBHP, whereas in terms of the yield of desired products, the reaction with TBHP provided higher amount of allylic oxidation products (**1** & **2**) than that using H_2O_2. Nevertheless, using 18 mmol of TBHP or H_2O_2 gave the same enol/enone selectivity. An excess amount of oxidizing agent assisted further oxidation of cyclohexan-2-en-1-ol (**1**) to cyclohexan-2-en-1-one (**2**). It should be noted here that the oxidation using TBHP needed elevated temperature, while

that employing H_2O_2 could be possible to perform at RT. According to the literature, Barton and co-workers [74] reported that TBHP provided good yield of the desired products when the reaction was performed at 70°C.

3.7 Study on alkene oxidation catalyzed by VO(salophen).

To observe the scope of this developed oxidation, various alkenes including α-pinene, limonene, methyl oleate, 1-methylcyclohexene and 1-dodecene were chosen. The results are presented in Table 3.11.

Table 3.11 The oxidation of selected alkenes catalyzed by VO(salophen).

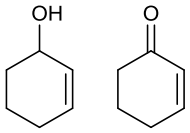
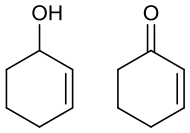
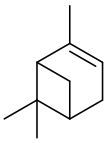
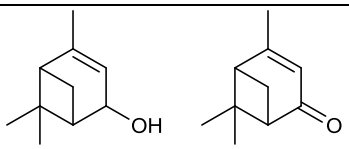
Entry	Alkene	Oxidant	% conversion	Product selectivity
1*		TBHP[a]	-	 (**1**, 92) (**2**, 8)
2*		H_2O_2[b]	-	 (**1**, 78) (**2**, 22)
3		TBHP[a]	53	 (**4**, 57) (**5**, 43)

Table 3.11 (continued)

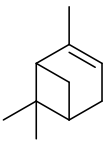
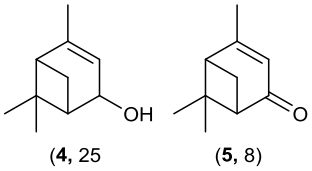
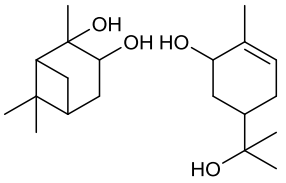
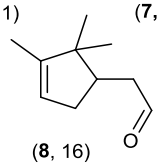
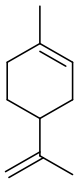
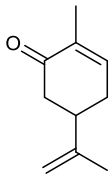
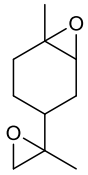
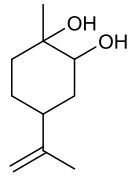
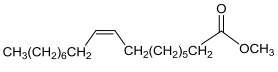
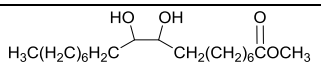
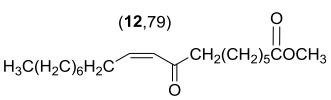
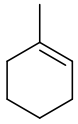
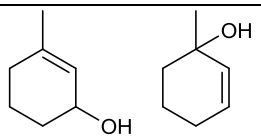
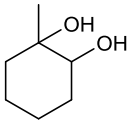
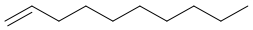
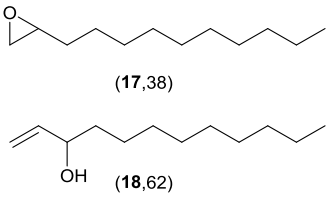
Entry	Alkene	Oxidant	% conversion	Product selectivity
4		H_2O_2[b]	68	 (**4,** 25) (**5,** 8)  (**6,** 11) (**7,** 40)  (**8**, 16)
5		TBHP[a]	-	no reaction
6		H_2O_2[b]	38	 (**9**, 18)  (**10**, 35)  (**11**, 47)
7		TBHP[a]	29	 (**12**,79)  (**13**,21)
8		H_2O_2[b]	-	no reaction

Table 3.11 (continued)

Entry	Alkene	Oxidant	% conversion	Product selectivity
9		TBHP[a]	81	 (**14**,54) (**15**,46)
10		H_2O_2[b]	73	 (**16**,100)
11		TBHP[a]	51	 (**17**,38) (**18**,62)
12		H_2O_2[b]	-	no reaction

Reaction conditions: alkene (5 mmol), VO(salophen) (0.1 mmol), CH_3CN (10 mL), oxidant (9 mmol), 4 h.

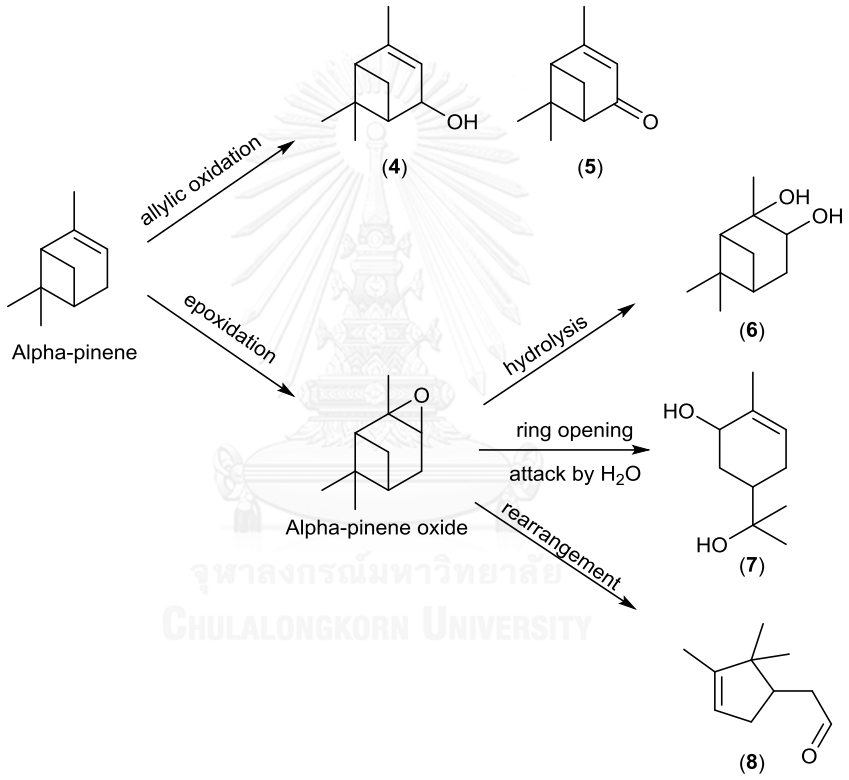
*cyclohexene (25 mmol), VO(salophen) (0.1 mmol), CH_3CN (10 mL), oxidant (4.5 mmol), 4 h.

[a] reflux, [b] RT

From Table 3.11, the oxidation of various alkenes with different functionalities catalyzed by VO(salophen) was thoroughly investigated. Cyclohexene (entries 1 and 2), an example of cycloalkene produced mainly cyclohexan-2-en-1-ol (**1**) with cyclohexan-2-en-1-one (**2**) as a minor product. The results obtained from this study revealed that both TBHP and H_2O_2 coupled with VO(salophen) were promising oxidation systems for allylic hydroxylation, not epoxidation.

α-Pinene (entries 3 and 4) was chosen as a representative of bicyclic compounds. Using TBHP (entry 3), only two products identified as verbenol (**4**) and

verbenone (**5**) (57 and 43% product selectivity, respectively) were detected. Unlike TBHP system, for the reaction employing H_2O_2 (entry 4), the formation of verbenol (**4**) (25% product selectivity) and verbenone (**5**) (8% product selectivity) (allylic oxidation products) together with epoxidation products as 1,2-pinanediol (**6**) (11% product selectivity), *trans*-sobrerol (**7**) (40% product selectivity) and campholenic aldehyde (**8**) (16% product selectivity) were observed. The possible pathway for product formation via both epoxidation and allylic oxidation are presented in Scheme 3.1.



Scheme 3.1 The oxidation of **α**-pinene by VO(salophen) using TBHP or H_2O_2

The formation of **α**-pinene oxide was attributed through the epoxidation while campholenic aldehyde (**8**) was formed by the rearrangement of **α**-pinene oxide. 1,2-Pinanediol (**6**) was derived from the hydrolysis and oxirane ring opening. *Trans*-obrerol (**7**) was derived from the ring opening, rearranges and attack by H_2O [75]. Verbenol (**4**) and verbenone (**5**) were generated by oxidation of allylic C–H bond.

Verbenone (**5**) was used for the preparation of taxol, which was introduced as a therapeutic agent [76]. Campholenic aldehyde (**8**) is an important intermediate to synthesize fragrances for perfumery industry [77]. All products and their distribution were determined by GC and GC-MS.

To verify the presence of certain products, verbenol (**4**) was attained from the reduction of verbenone (**5**) with $NaBH_4$ in EtOH [63]. The structure of verbenol (**4**) was characterized by ^1H NMR. The ^1H NMR spectrum of verbenol (**4**) is shown in Figure 3.9.

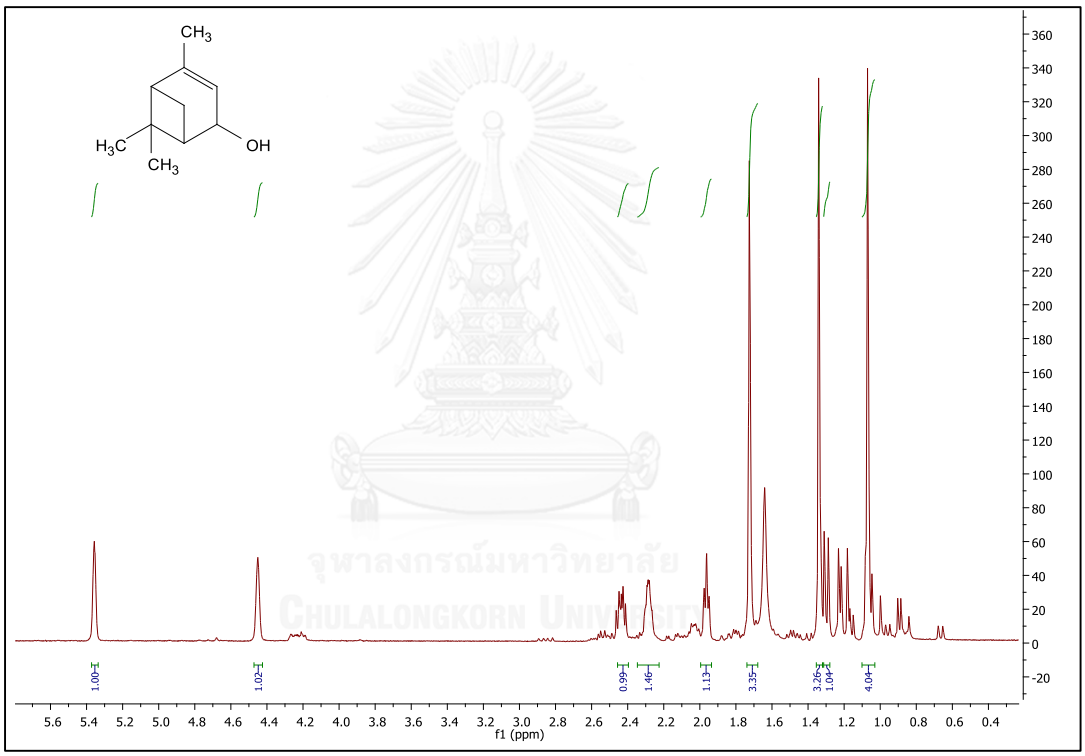
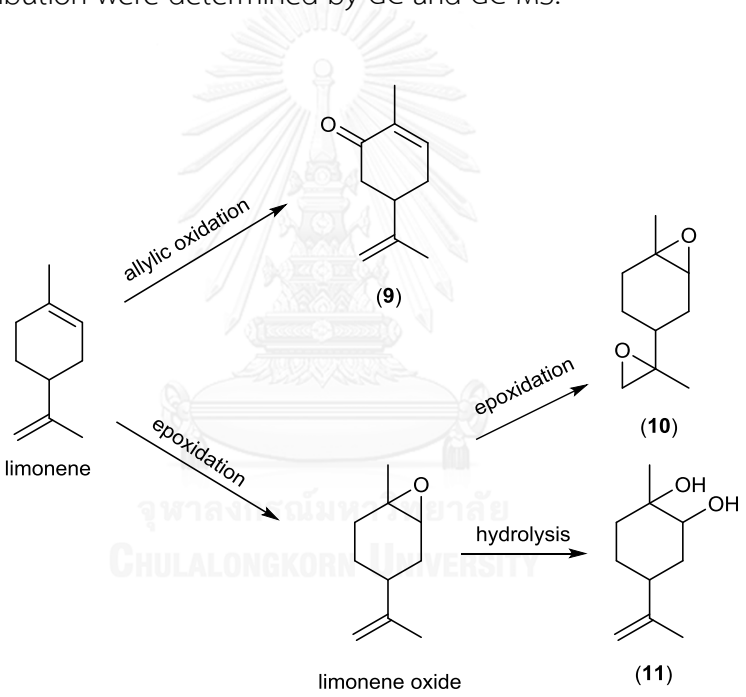


Figure 3.9 ^1H NMR spectrum of verbenol (**4**)

The ^1H NMR ($CDCl_3$) spectrum of verbenol (**4**) displays the vinyl proton at δ_H 5.37 (*s*, 1H), the methyl protons next to double bond at δ_H 1.36 (*s*, 3H), the hydroxyl proton at δ_H 4.45 (*s*, 1H), the proton on the carbon atom connecting hydroxyl group at δ_H 1.28 (*d*, *J* = 9.0 Hz, 1H), the methine protons of cyclobutane at δ_H 1.72 (*t*, *J* = 1.7 Hz, 1H) and 1.96 (*t*, *J* = 5.5 Hz, 1H), the methylene protons of cyclobutane at δ_H 2.28 (*m*, 1H) and 2.44 (*m*, 1H), and the methyl protons of cyclobutane at δ_H 1.10 (*s*, 6H).

Limonene (entries 5 and 6) was monocyclic monoterpene. Under this examined conditions, limonene was not oxidized by TBHP system (entry 5). On the other hand using H_2O_2 (entry 6), the oxidation of limonene gave main three products: carvone (**9**), limonene dioxide (**10**) and limonene glycol (**11**) (18, 35 and 47% product selectivity, respectively). In Scheme 3.2, carvone (**9**) was believed to produce from allylic oxidation whereas limonene dioxide (**10**) and limonene glycol (**11**) were derived from the epoxidation process. To illustrate this, the epoxidation of limonene yielded limonene oxide while limonene dioxide (**10**) was formed by epoxidation and limonene glycol (**11**) was reformed by hydrolysis and opening of ring. All products and their distribution were determined by GC and GC-MS.



Scheme 3.2 The oxidation of limonene by VO(salophen) using H_2O_2

The allylic oxidation of limonene typically produced carveol and carvone (**9**). Therefore, to ascertain for the presence of the target product, carveol was synthesized from the reduction of carvone (**9**) with $NaBH_4$ and $CeCl_3.7H_2O$ in MeOH [64]. The structure of carveol was characterized by ^1H NMR. The ^1H NMR spectrum of carveol is shown in Figure 3.10.

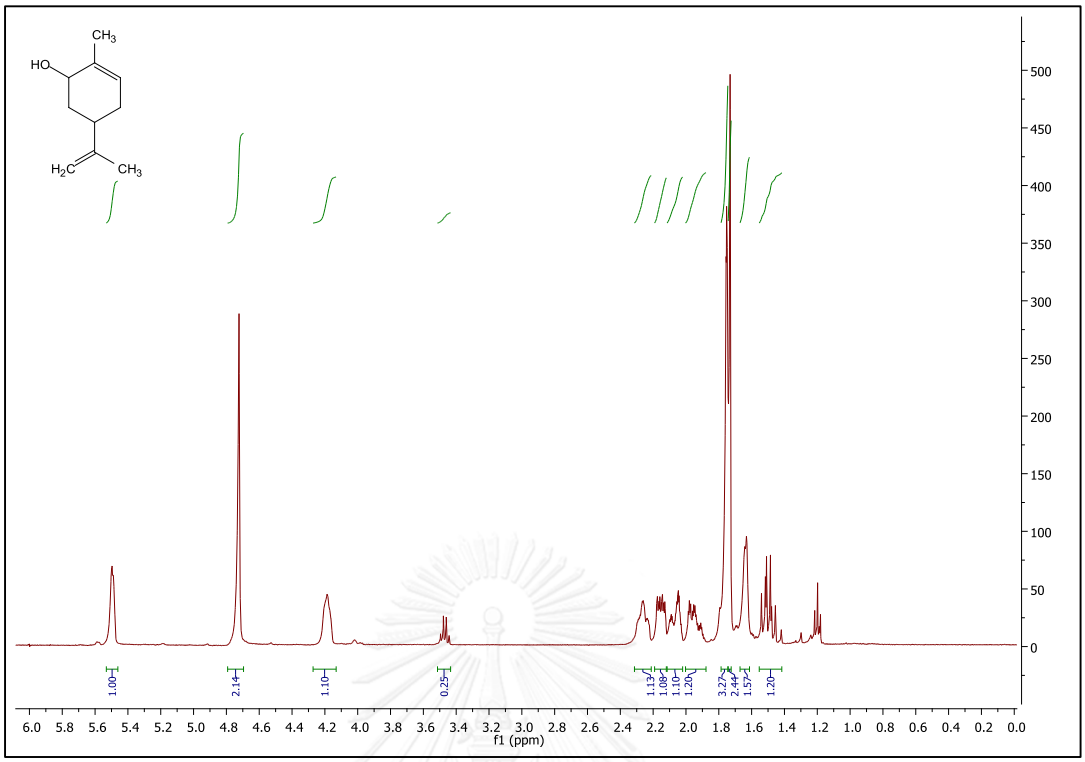


Figure 3.10 ^{1}H NMR spectrum of carveol

The ^{1}H NMR ($CDCl_3$) spectrum of carveol displays the vinyl proton at δ_H 5.50 (*s*, 1H), the vinyl protons of propylene at δ_H 4.72 (*s*, 2H), the methyl protons at δ_H 1.74 (*s*, 3H), the hydroxyl proton at δ_H 1.63 (*s*, 1H), the proton on the carbon atom connecting hydroxyl group at δ_H 4.19 (*s*, 1H), the methine protons at δ_H 1.92–2.30 (*m*, 4H), the methyl protons of propylene at δ_H 1.72 (*s*, 3H) and the methine protons neighboring to the propylene group at δ_H 1.46-1.54 (*td*, *J* =12.1, 9.7 Hz, 1H).

Methyl oleate was selected as another substrate to examine the scope of this reaction. Thus this target substrate was synthesized from the esterification of oleic acid in MeOH with H_2SO_4 [65]. The structure of methyl oleate was characterized by ^{1}H NMR. The ^{1}H NMR spectrum of methyl oleate is shown in Figure 3.11.

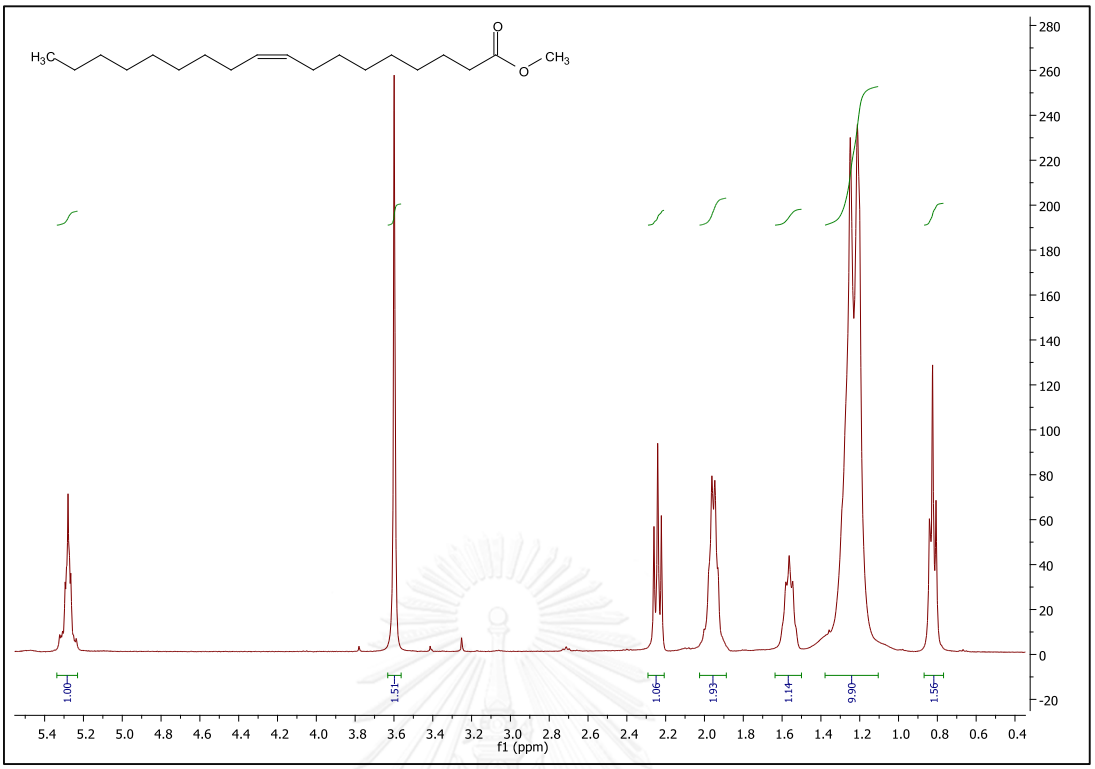
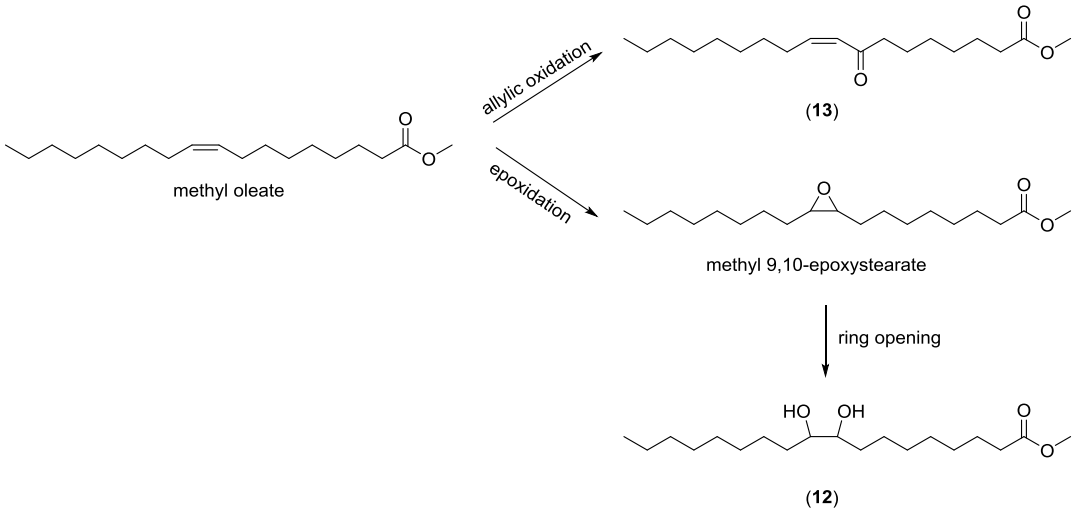


Figure 3.11 ^{1}H NMR spectrum of methyl oleate

The ^{1}H NMR ($CDCl_3$) spectrum of methyl oleate displays the vinyl proton at δ_H 5.28 (*m*, 2H), the ester methyl protons located next to the carbonyl carbon at δ_H 3.60 (*s*, 3H), the methyl protons at δ_H 0.82 (*t, J* =7.1 Hz, 3H), the protons neighboring to the carbonyl carbon at δ_H 2.24 (*t*, *J* =7.7 Hz, 2H), the proton connecting vinyl group at δ_H 1.96 (*m*, 4H) and the methylene protons at δ_H 1.23 (*m*, 20H) and 1.56 (*t*, *J* =7.1 Hz, 2H).

The oxidation of methyl oleate using TBHP (entry 7) gave methyl 9,10-dihydroxy stearate (**12**) as a major product and methyl 8-oxooctadec-9-enoate (**13**) (79 and 21% product selectivity, respectively). Methyl 8-oxooctadec-9-enoate (**13**) was produced from allylic oxidation. Methyl 9,10-dihydroxy stearate (**12**) was produced from epoxidation followed by ring opening. Under TBHP system, the attained products were derived *via* both allylic oxidation and epoxidation as presented in Scheme 3.3. All products and their distribution were determined by GC. Nonetheless, it was found that methyl oleate could not be oxidized in H_2O_2 system (entry 8).



Scheme 3.3 The oxidation of methyl oleate by VO(salophen) using TBHP

To verify the presence of the products, the separation of the reaction crude was conducted as follows. The whole reaction mixture was extracted according to the general procedure and all solvents were removed. The crude product was purified by silica gel column using a mixture of hexane-EtOAc as an eluent. The equivalent fractions monitored by TLC were combined and the solvents were completely evaporated. The structure of methyl 9,10-dihydroxy stearate (**12**) was characterized by ^{1}H NMR. The ^{1}H NMR spectrum of methyl 9,10-dihydroxy stearate (**12**) is shown in Figure 3.12.

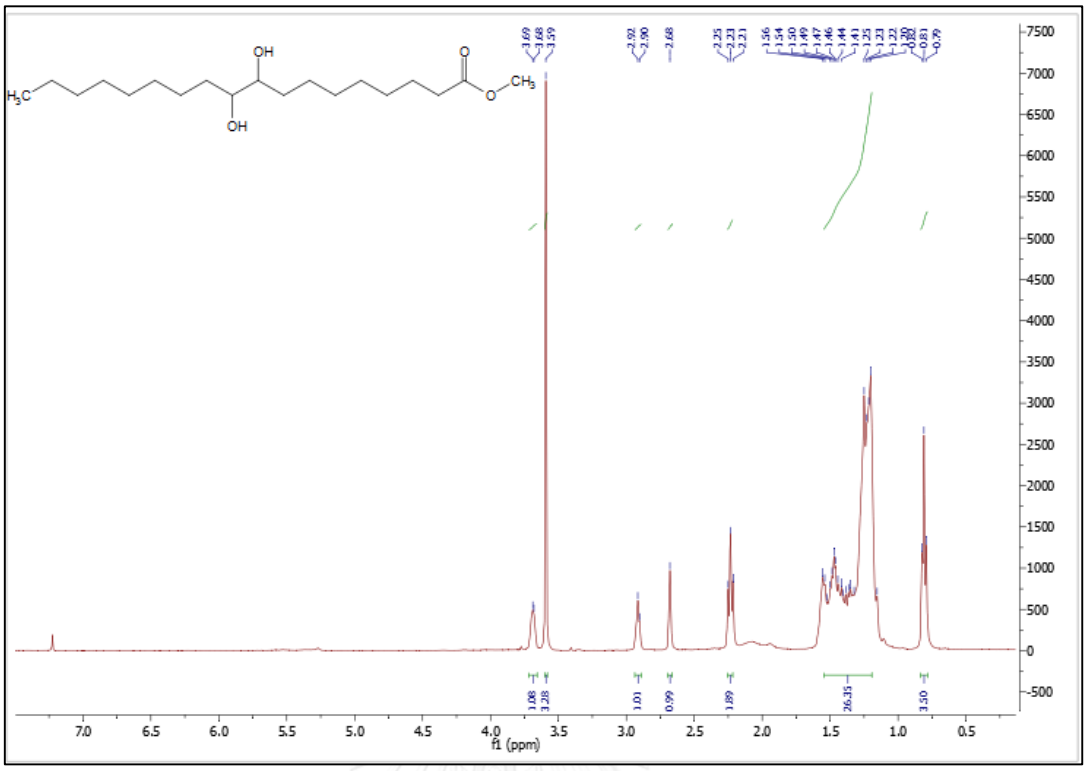


Figure 3.12 ^{1}H NMR spectrum of methyl 9,10-dihydroxy stearate (**12**)

The ^{1}H NMR ($CDCl_3$) spectrum of methyl 9,10-dihydroxy stearate(**12**) displays the ester methyl protons located next to the carbonyl carbon at δ_H 3.59 (*s*, 3H), the methyl protons at δ_H 0.81 (*t, J* = 6.2 Hz, 3H), the protons next to the carbonyl carbon at δ_H 2.23 (*t*, *J* = 6.7 Hz, 2H), the methylene protons at δ_H 1.20-1.56 (*m*, 26H), the proton on the carbon atom connecting to hydroxyl group at δ_H 3.68 (*m*, 1H) and at 2.92 (*m*, 1H) and the hydroxyl groups δ_H 2.68 (*s*, 2H).

The structure of methyl 8-oxooctadec-9-enoate (**13**) was characterized by ^{1}H NMR. The ^{1}H NMR spectrum of methyl 8-oxooctadec-9-enoate (**13**) is shown in Figure 3.13.

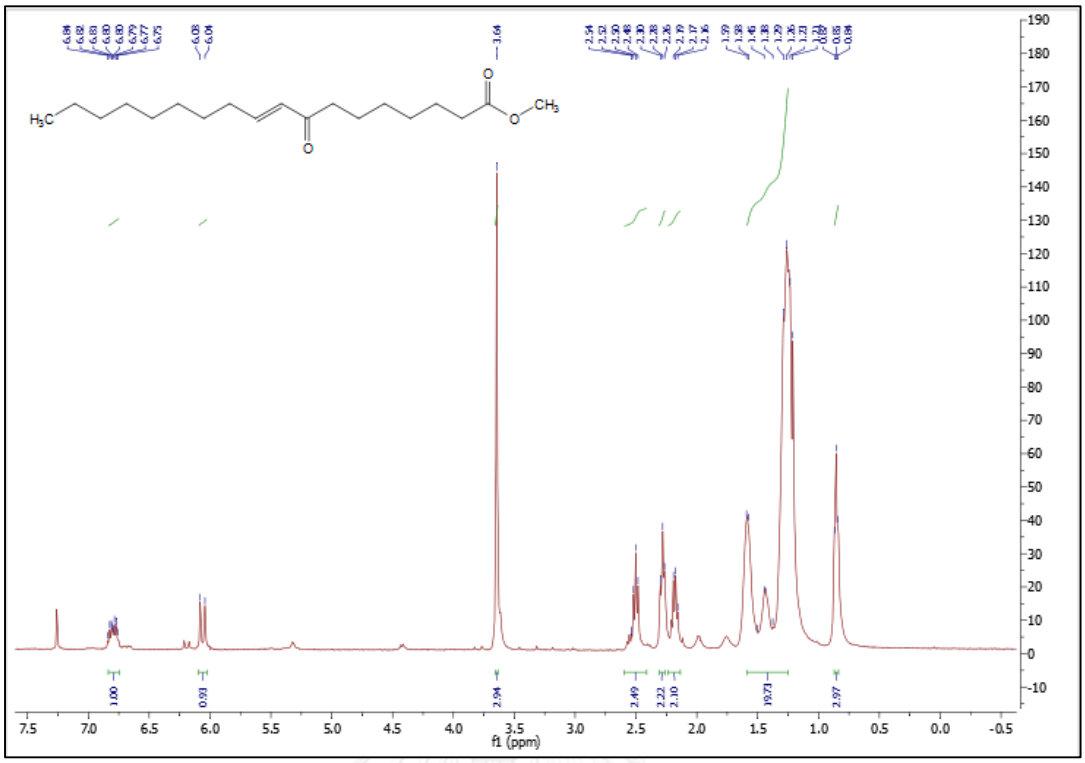


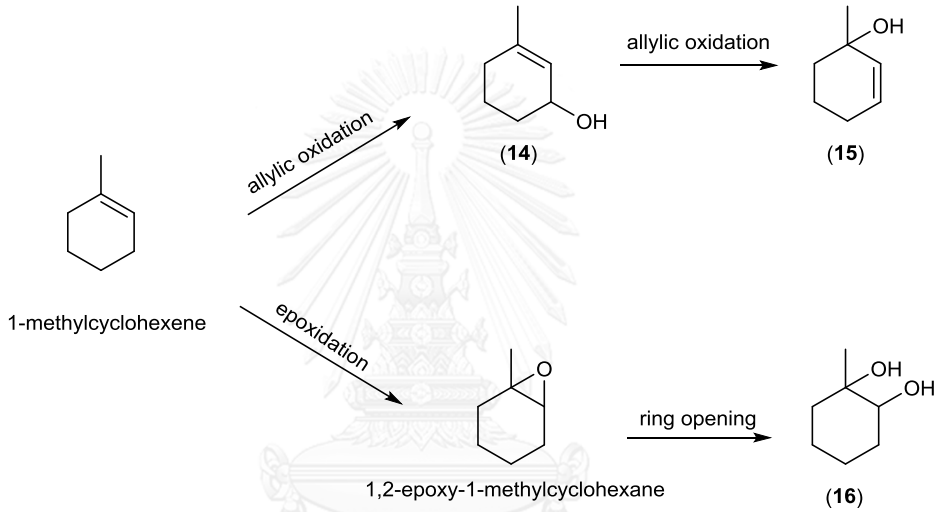
Figure 3.13 ^{1}H NMR spectrum of methyl 8-oxooctadec-9-enoate (**13**)

The ^{1}H NMR ($CDCl_3$) spectrum of methyl 8-oxooctadec-9-enoate (**13**) displays the ester methyl protons located next to the carbonyl carbon at δ_H 3.64 (*s*, 3H), the methyl protons at δ_H 0.85 (*t, J* =5.2 Hz, 3H), the protons neighboring carbonyl carbon at δ_H 2.28 (*t*, *J* =7.2 Hz, 2H), the methylene protons at δ_H 1.26-1.59 (*m*, 20H), the proton on the carbon atom neighboring carbonyl carbon at δ_H 2.51 (*t*, *J* = 7.4 Hz, 2H) and at 2.18 (*t*, *J* = 7.1 Hz, 2H), the vinyl proton connecting to carbonyl carbon at δ_H 6.04-6.21 (*d*, *J* = 15.4 Hz, 1H) and the vinyl proton δ_H 6.71-6.85 (*m*, 1H).

Using 1-methylcyclohexene (entries 9 and 10) as a substrate, the oxidation using TBHP (entry 9) gave 3-methyl-2-cyclohexen-1-ol (**14**) (54% product selectivity) and 1-methyl-2-cyclohexen-1-ol (**15**) (46% product selectivity). This indicated that the main reaction proceeded through allylic oxidation. 1-Methyl-2-cyclohexen-1-ol (**15**) was further transformed from allylic oxidation of 3-methyl-2-cyclohexen-1-ol (**14**) [78]. In 2013, Roiban and co-workers [78] showed that the oxidation of 3-methyl-2-cyclohexen-1-ol (**14**) afforded 1-methyl-2-cyclohexen-1-ol (**15**). According to the literature, Bilis and co-workers [79] presented that the oxidation of 1-

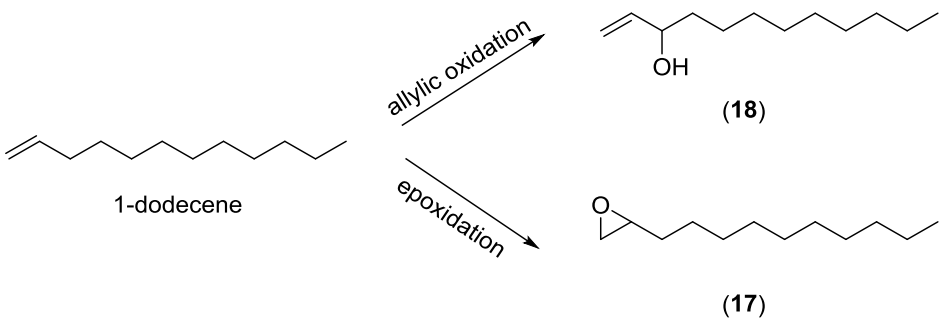
methylcyclohexene with homogeneous and heterogeneous non-heme iron (III) catalysts using H_2O_2 produced *cis*-epoxide, 1-methyl-2-cyclohexen-1-ol (**15**), 3-methyl-2-cyclohexen-1-ol (**14**) and 3-methyl-2-cyclohexen-1-one.

Nonetheless, the reaction with H_2O_2 (entry 10) yielded 1-methyl-1,2-cyclohexanediol (**16**) (100% product selectivity). This product should derive from the epoxide ring opening of 1-methylcyclohexene oxide. All products and their distribution were determined by GC and GC-MS.



Scheme 3.4 The oxidation of 1-methylcyclohexene by VO(salophen) using TBHP or H_2O_2.

1-Dodecene (entries 11 and 12) was an instance of aliphatic terminal alkene. The reaction with TBHP (entry 11) gave 1-dodecene oxide (**17**) (38% product selectivity) and dodec-1-en-3-ol (**18**) (62% product selectivity) as major products. In Scheme 3.5, these products were attained from both processes (epoxidation and allylic oxidation). However, using H_2O_2 (entry 12), this substrate was not oxidized. All products and their distribution were determined by GC.



Scheme 3.5 The oxidation of 1-dodecene by VO(salophen) using TBHP.

To confirm the presence of the obtained product, the reaction mixture was extracted according to the general procedure and all solvents were removed. The crude product was purified by silica gel column eluting by a mixture of hexane-EtOAc. Each fraction was monitored by TLC, and equivalent fractions were combined. The separation led to the isolation of dodec-1-en-3-ol (**18**) which was confirmed its identity by ^{1}H NMR. The ^{1}H NMR spectrum of dodec-1-en-3-ol (**18**) is shown in Figure 3.14.

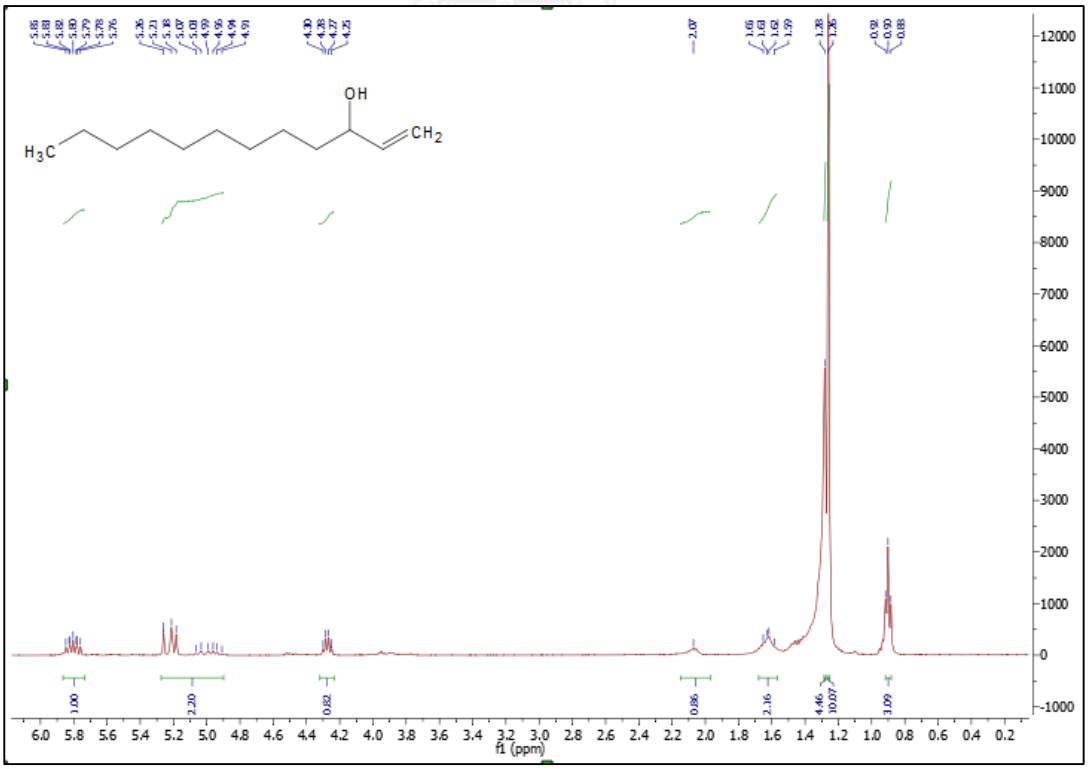


Figure 3.14 ^{1}H NMR spectrum of dodec-1-en-3-ol (**18**)

The ^{1}H NMR ($CDCl_3$) spectrum of dodec-1-en-3-ol (**18**) displays the vinyl protons at δ_H 4.94-5.26 (*m*, 2H), the vinyl proton neighboring to a hydroxyl group at δ_H 5.76-5.85 (*m*, H), the proton on the carbon atom connecting to a hydroxyl group at δ_H 4.26 (*m*, 1H), the methyl protons at δ_H 0.90 (*t, J* = 6.6 Hz, 3H), the methylene protons neighboring to a hydroxyl group at δ_H 1.60 (*t*, *J* = 7.7 Hz, 2H), the hydroxyl group at δ_H 2.04 (*s*, 1H) and the methylene protons at δ_H 1.26 (*s*, 10H) and 1.28 (*s*, 4H).

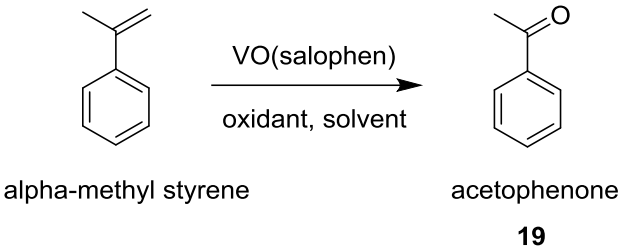
The oxidation of various selected alkenes catalyzed by this developed VO(salophen) catalyst system including α-pinene, limonene, methyl oleate, 1-methylcyclohexene and 1-dodecene provided allylic oxidation products and epoxidized products in moderate yield with excellent selectivity. In TBHP system, aliphatic alkenes (methyl oleate and 1-dodecene) produced both allylic oxidation and epoxidation products. 1-Dodecene formed higher selectivity of allylic oxidation product more than epoxidation product, while methyl oleate produced higher selectivity for epoxidation products than allylic oxidation product. α-Pinene, limonene and 1-methylcyclohexene proceeded only allylic oxidation products.

In H_2O_2 system, long chain alkenes (methyl oleate and 1-dodecene) were not oxidized under the conditions investigated, presumably longer reaction time was needed. α-Pinene and limonene produced both allylic oxidation and epoxidation products. Both alkenes gave preferential selectivity over epoxidation. The product of epoxide was further undergone ring opening to yield final products. For 1-methylcyclohexene, only epoxidation was observed.

3.8 Study on the optimum conditions for oxidative cleavage of α-methyl styrene.

To extend the investigation of this developed oxidation system, the oxidative cleavage of α-methylstyrene to acetophenone was conducted. The reaction was

optimized by varying type of oxidant, the amount of oxidant, solvent and amount of **α**-methylstyrene.



3.8.1 Effect of type of oxidants.

Two selected oxidants namely H_2O_2 and TBHP were tested for this oxidative cleavage reaction. The effects of oxidants on the oxidative cleavage of **α**-methylstyrene are presented in Table 3.12.

Table 3.12 The effect of oxidants on the oxidative cleavage of **α**-methylstyrene catalyzed by VO(salophen).

Entry	Oxidant	Temp.	%yield		Mass balance (MB)
			α-methylstyrene recovery (%)	**19**	
1	H_2O_2	RT	22.58	26.07	48.65
2	TBHP	reflux	0	21.69	21.69

Reaction conditions: **α**-methylstyrene (5 mmol), VO(salophen) (0.1 mmol), CH_3CN (10 mL), oxidant (9 mmol), 4 h.

The reaction with H_2O_2 or TBHP (entries 1-2) produced acetophenone (**19**) and undesired product, presumably polymeric material. Polymer derived from **α**-methylstyrene was formed free radical polymerization. The reaction using H_2O_2 gave higher yield of acetophenone (**19**) than TBHP. According to the literatures, Lin and co-workers [80] reported that using cobalt(II) chloride catalyst, the oxidation of **α**-methylstyrene in *tert*-butyl alcohol under O_2 atmosphere at 75ºC for 20 h, two

reaction pathways: oxidative cleavage of the C=C bond to the corresponding carbonyl compound and alkene polymerization were competed.

3.8.2 Effect of the amount of H_2O_2.

The variation of the amount of H_2O_2 was studied for the oxidative cleavage reaction of **α**-methylstyrene. The results are displayed in Table 3.13.

Table 3.13 The effects of the amount of H_2O_2 on the oxidative cleavage of **α**-methylstyrene catalyzed by VO(salophen).

Entry	Amount of H_2O_2 (mmol)	%yield		Mass balance (MB)
		α-methylstyrene recovery (%)	**19**	
1	0	79.41	1.98	81.39
2	4.5	31.65	19.07	50.72
3	9	22.58	26.07	48.65
4	13.5	22.77	25.49	48.26
5	18	13.95	25.76	39.61

Reaction conditions: **α**-methylstyrene (5 mmol), VO(salophen) (0.1 mmol), CH_3CN (10 mL), H_2O_2 (vary), RT, 4 h

The amount of H_2O_2 was varied from 0-18 mmol. From Table 3.13, it could be observed that when 9 mmol of H_2O_2 was used, the highest yield of acetophenone (**19**) (~26%) was obtained (entry 3). Using more H_2O_2, the yield of acetophenone (**19**) did not differ, the recovery of **α**-methylstyrene was decreased whereas polymer was increased (entries 4-5).

3.8.3 Effect of solvents.

The effect of solvent was another important factor in the oxidative cleavage reaction of **α**-methylstyrene. Several solvents were examined and the results are shown in Table 3.14.

Table 3.14 The effects of solvents on the oxidative cleavage of **α**-methylstyrene catalyzed by VO(salophen).

Entry	Solvent	%yield		Mass balance (MB)
		α-methylstyrene recovery (%)	**19**	
1	neat	82.00	2.26	84.27
2	$C_2H_4Cl_2$	53.21	2.31	55.52
3	$CHCl_3$	90.37	3.07	93.44
4	CCl_4	72.80	2.00	74.80
5	isooctane	75.42	2.00	77.42
6	toluene	65.73	1.83	67.56
7	CH_3CN	22.58	26.07	48.65
8	CH_3OH	15.66	20.6	36.26
9	C_2H_5OH	33.95	16.92	50.87

Reaction conditions: **α**-methylstyrene (5 mmol), VO(salophen) (0.1 mmol), solvent (10 mL), H_2O_2 (9 mmol), RT, 4 h

Reactions in CH_3CN, CH_3OH and C_2H_5OH gave acetophenone (**19**) in good yield (entries 7-9) while $C_2H_4Cl_2$, $CHCl_3$, CCl_4, isooctane and toluene (entries 2-6) presented acetophenone (**19**) in low yield. Thus, CH_3CN is the solvent of choice for further study.

3.8.4 Effect of the amount of substrate.

The effect of the amount of **α**-methylstyrene was explored and the results are presented in Table 3.15.

Table 3.15 The effects of the amount of **α**-methylstyrene on the oxidative cleavage catalyzed by VO(salophen).

Entry	Amount of **α**-methylstyrene (mmol)	%yield		Mass balance (MB)
		α-methylstyrene recovery (%)	**19**	
1	1	46.13	24.93	71.06
2	5	22.58	26.07	48.65
3	10	36.21	19.32	55.53
4	25	55.89	5.03	60.92

Reaction conditions: **α**-methylstyrene (vary), VO(salophen) (0.1 mmol), CH_3CN (10 mL), H_2O_2 (9 mmol), RT, 4 h.

From Table 3.15, the use of **α**-methylstyrene 5 mmol and H_2O_2 9 mmol (entry 2) gave high yield of acetophenone (**19**) (26% yield). In addition, the reactions with increasing amount of **α**-methylstyrene 10 and 25 mmol (entries 3-4) gave low yield of acetophenone (**19**) (19 and 5% yield, respectively).

The optimized conditions for the oxidative cleavage of **α**-methylstyrene could be summarized as follows: the mixture of **α**-methylstyrene (5 mmol), H_2O_2 (9 mmol) and VO(salophen) (0.1 mmol) was stirred in CH_3CN (10 ml) at RT 4 h. According to the literatures, Wang and co-workers [81] reported the transformation of **α**-methylstyrene to acetophenone (**19**) with AIBN in CH_3NO_2 at 60 ºC for 12 h and O_2. Although high yield was reported, a major drawback of this method was a long reaction time required.

3.9 Comparative study of selectivity on cyclohexene oxidation

In this section, oxovanadium complexes were selected as a catalyst for in cyclohexene oxidation. The selectivity of three different products (allylic oxidation and epoxidation) in the oxidation of cyclohexene compared to previous reports [52, 53] in which either a mixture of products could be selectively obtained.

Table 3.16 Comparison of catalytic activities for the selective preparation of cyclohexan-2-en-1-ol (**1**), cyclohexan-2-en-1-one (**2**) and cyclohexene oxide (**3**), respectively, using different catalysts.

Reference	Catalyst	Type of oxidant	Temp. (°C)	Product selectivity		
				1	2	3
Our work	VO(salophen)	TBHP	reflux	92	8	0
Our work	VO(salophen)	H_2O_2	RT	78	22	0
[52]*	VOL^3 (H_2L^3 = 2-hydroxyacetophenone instead of 2-hydroxy-1-naphtaldehyde	TBHP	reflux	6.1	32.3	61.5
[53]**	$VO(OMe)L^2$ (H_2L_2 = (*E*)-3-hydroxy-N´-(2-hydroxybenzylidene)-2-naphthohydrazide)	H_2O_2	60	59.8	8.7	31.5

Reaction conditions: cyclohexene (25 mmol), VO(salophen) (0.10 mmol), CH_3CN (10 mL), oxidant (4.5 mmol), 4 h.

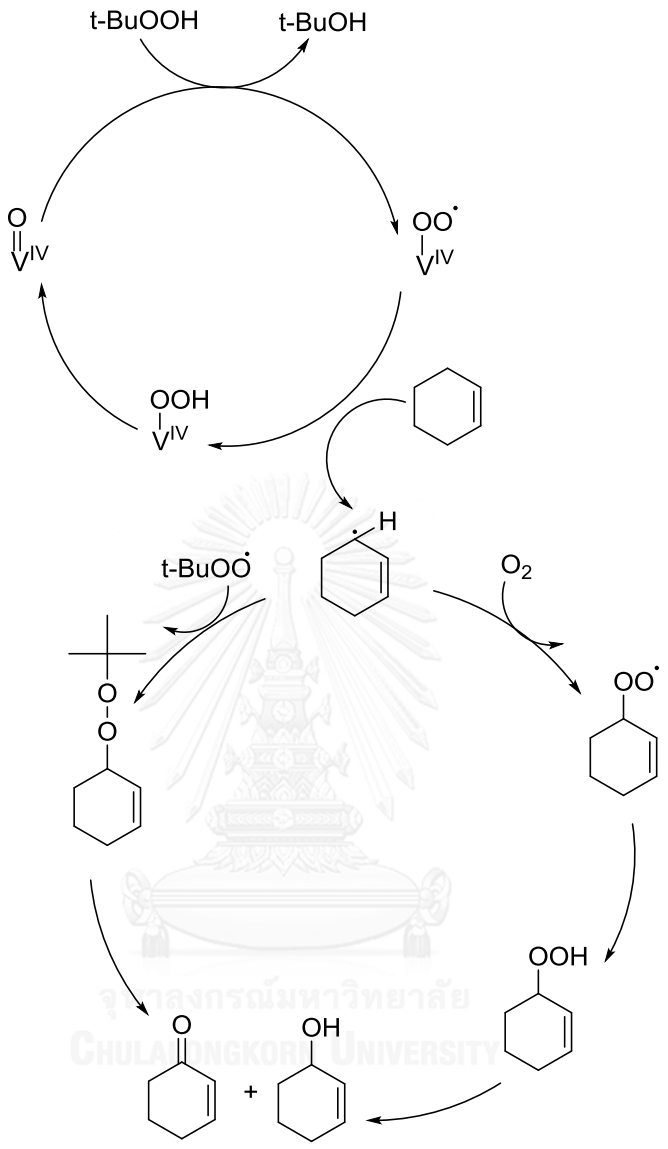
***** cyclohexene (9.8 mmol), catalyst (0.10 mmol), CH_3CN (10 mL), oxidant (9.8 mmol), 6 h.

****** cyclohexene (1 mmol), catalyst (2.5 μmol), CH_3CN (3 mL), oxidant (2 mmol), 4 h.

Comparing selectivity of products with previously reported, as presented in Table 3.16. The oxidation of cyclohexene with oxovanadium complexes with different Schiff base ligand gave allylic oxidation products and epoxidation product. It showed my researched must produce only allylic oxidation (cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**)). In previous report, both allylic oxidation and epoxidation were detected. Rayati and co-workers [52] showed selectivity of cyclohexene oxide (**3**) from epoxidation as major product. Monfared and co-workers [53] gave selectivity of cyclohexan-2-en-1-ol (**1**) from allylic oxidation as major product. However, in terms of selectivity, using VO(salophen) complex offerred higher selectivity of cyclohexan-2-en-1-ol (**1**) than previously reported and selectivity only allylic oxidation.

3.10 Proposed mechanism for the oxidation of cyclohexene catalyzed by VO(salophen) using TBHP

The reaction was believed to proceed via allylic proton abstraction by radical species from cleavage of TBHP catalyzed by VO(salophen) complex. The mechanism for allylic oxidation of cyclohexene catalyzed by VO(salophen) was proposed as shown in Scheme 3.6



Scheme 3.6 Proposed mechanism for allylic oxidation of cyclohexene catalyzed by VO(salophen)

From the proposed mechanism of allylic oxidation, cyclohexene was transformed to the desired products (cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**)). The pathway involving the abstraction at allylic position to yield allylic radical which could react with *t*-BuOO• to give an intermediate (peroxide) and finally it could decompose to cyclohexan-2-en-1-ol (**1**) and cyclohexan-2-en-1-one (**2**). However, allylic radical could react with O_2 to give hydroperoxyl radical intermediate

and convert to not stable cyclohexenyl hydroperoxide. The decomposition of cyclohexenyl hydroperoxide finally yielded allylic oxidation products.

CHAPTER IV

CONCLUSION

During the course of this research, the main focus of this research is to synthesize, characterize and utilize VO(salophen) as homogeneous catalyst for the oxidation of alkenes. The VO(salophen) complex was prepared by reacting the H_2(salophen) and $VOSO_4.5H_2O$. Its structure was characterized by IR.

The conditions for allylic oxidation of alkenes were optimized using cyclohexene as a chemical model. The allylic oxidation of cyclohexene using TBHP catalyzed by VO(salophen) uniquely produced cyclohexan-2-en-1-ol (**1**) as a major product and cyclohexan-2-en-1-one (**2**) as a minor. No epoxidized product could be detected. The most appropriate conditions were disclosed as cyclohexene 25 mmol, VO(salophen) 0.1 mmol, 70% TBHP 4.5 mmol in refluxing CH_3CN for 4 h. For the choice of using H_2O_2, the optimized conditions were cyclohexene 25 mmol, VO(salophen) 0.1 mmol, 30% H_2O_2 4.5 mmol in CH_3CN for 4 h at RT.

The scope and limitation of the oxidation by VO(salophen) and TBHP or H_2O_2 were studied on a variety of alkenes. The reaction could oxidize various organic substrates (**α**-pinene, limonene, methyl oleate, 1-methylcyclohexene and 1-dodecene) to their corresponding oxidized products with different yield extent. Thus, some conditions modification may need for individual substrate. The oxidative cleavage catalyzed by VO(salophen) for **α**-methylstyrene using H_2O_2 yielding acetophenone was also conducted. Nonetheless, the outcome was not much impressed since polymerization seemed to be a competitive process.

Suggestion for future work

Since the uniqueness of this developed system is the production of allylic alcohol, more substrates should be examined. Particularly those containing sensitive functional groups are still required for further investigation. In addition, further study on the enantiomeric hydroxylation of alkenes should be scrutinized. The chiral allylic

alcohols should be valuable product in chemical industries, not only for petrochemical industries, but also drug and agrochemical industries.

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