ออกซิเดชันแบบเลือกจำเพาะของไฮโดรคาร์บอนอิ่มตัวเร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV)

นางสาวปวีณา พงษ์พิพัฒน์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาปิโตรเคมี
คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2559

SELECTIVE OXIDATION OF SATURATED HYDROCARBONS CATALYZED BY OXOVANADIUM(IV) COMPLEXES

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A Dissertation Submitted in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy Program in Petrochemistry
Faculty of Science
Chulalongkorn University
Academic Year 2016

Thesis Title SELECTIVE OXIDATION OF SATURATED HYDROCARBONS CATALYZED BY OXOVANADIUM(IV) COMPLEXES
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ปวีณา พงษ์พิพัฒน์ : ออกซิเดชันแบบเลือกจำเพาะของไฮโดรคาร์บอนอิ่มตัวเร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV) (SELECTIVE OXIDATION OF SATURATED HYDROCARBONS CATALYZED BY OXOVANADIUM(IV) COMPLEXES) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ดร.วรินทร ชวศิริ, 139 หน้า.

ได้พัฒนาออกซิเดชันแบบเลือกจำเพาะของไฮโดรคาร์บอนอิ่มตัวเร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV) โดยมีลิแกนด์สองชนิดคือ ชิฟเบสและกรดพิโคลินิก ได้นำสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV) ที่ได้รับการพิสูจน์เอกลักษณ์ด้วยวิธีที่เหมาะสมมาประยุกต์ภายใต้ระบบที่ใช้สารออกซิแดนท์ต่างกันสองระบบคือ ออกซิเจนและเปอร์ออกไซด์ ได้ศึกษาผลกระทบของสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV) เก้าชนิด ปริมาณและชนิดของซิงค์และกรดและตัวทำละลายต่อปฏิกิริยาออกซิเดชันที่เร่งปฏิกิริยาด้วยสารประกอบเชิงซ้อนออกโซวาเนเดียม(IV) ในระบบซิงค์-ไพริดีน-กรดแอซิติกภายใต้บรรยากาศออกซิเจน พบว่า VO(salophen) สามารถเร่งปฏิกิริยาได้ดีในเชิงปริมาณผลิตภัณฑ์ที่ต้องการและความเลือกจำเพาะ เมื่อใช้ตัวเร่งปฏิกิริยาร่วมกับ TBHP ที่อุณหภูมิรีฟลักซ์หรือใช้ร่วมกับ H_2O_2 ที่อุณหภูมิห้องในแอซิโทไนไทรล์ ทำให้เกิดปฏิกิริยาออกซิเดชันอย่างเลือกจำเพาะ ระบบของตัวเร่งปฏิกิริยาทั้งสามระบบแสดงลักษณะเฉพาะในการเกิดคีโทนเป็นผลิตภัณฑ์หลักและเกิดแอลกอฮอล์เล็กน้อย การใช้ $VO(pic)_2$ ในระบบ TBHP สามารถเกิดปฏิกิริยาได้เร็วกว่าเมื่อใช้ VO(salophen) และยังให้คีโทนเป็นผลิตภัณฑ์หลักในปริมาณที่น่าพอใจ นอกจากนี้การเติมเฮกซะโบรโมแอซีโทนหรือ HBA ลงไปในระบบสามารถให้แอลคิลโบรไมด์ได้อย่างมีประสิทธิภาพแทนที่ผลิตภัณฑ์จากปฏิกิริยาออกซิเดชัน จากการศึกษาการเลือกจำเพาะทางเคมีพบว่ากลไกการเกิดปฏิกิริยาในสองระบบแตกต่างกัน ในระบบซิงค์-ไพริดีน-กรดแอซิติก-ออกซิเจนนั้นกลไกไม่ได้เกิดผ่านกระบวนการฟรีแรดิคัล ในขณะที่ระบบเปอร์ออกไซด์ ปฏิกิริยาออกซิเดชันเกิดผ่านกระบวนการฟรีแรดิคัล

สาขาวิชา ปิโตรเคมี ลายมือชื่อนิสิต ....

ปีการศึกษา 2559 ลายมือชื่อ อ.ที่ปรึกษาหลัก ....

5472833023 : MAJOR PETROCHEMISTRY

KEYWORDS: SELECTIVE OXIDATION / OXIDATION OF SATURATED HYDROCARBONS / OXOVANADIUM(IV) COMPLEXES

PAWEENA PONGPIPATT: SELECTIVE OXIDATION OF SATURATED HYDROCARBONS CATALYZED BY OXOVANADIUM(IV) COMPLEXES. ADVISOR: ASST. PROF. WARINTHORN CHAVASIRI, Ph.D., 139 pp.

The development of the selective oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) complexes was disclosed. Two types of ligands including Schiff's base and picolinic acid could be prepared. The well-characterized oxovanadium(IV) complexes were applied under two diverse oxidizing agents: O_2 and peroxide. The oxidation catalyzed by oxovanadium(IV) Schiff's base complexes in zinc-pyridine-acetic acid system under O_2 was thoroughly investigated for the effects of nine Schiff's base complexes, amount and type of zinc, acid and solvent. VO(salophen) exhibited good activity in terms of yield of desired product(s) and selectivity. Utilizing this catalyst in combination with TBHP at reflux or H_2O_2 at room temperature in CH_3CN could promote the selective oxidation reaction. These three catalytic systems revealed the unique characteristics for ketone formation as a major product together with small amount of accompanying alcohol. Employing $VO(pic)_2$ in TBHP system, saturated hydrocarbons were oxidized faster than using VO(salophen) and still provided ketone as predominant product in good yield. The addition of hexabromoacetone (HBA) converted the activation process to furnish alkyl bromide efficiently instead of oxidized products. Chemoselectivity study implied the clues that reaction mechanisms of two systems were different. Non-radical pathway was operated in zinc-pyridine-acetic acid-O_2 system while for peroxide system, the oxidation proceeded *via* radical process.

Field of Study: Petrochemistry Student's Signature ....

Academic Year: 2016 Advisor's Signature ....

ACKNOWLEDGEMENTS

The author would like to express her deep gratitude to her thesis advisor, Assistant Professor Dr. Warinthorn Chavasiri for his valuable instruction, very kind assistance, generous guidance and encouragement throughout the course of this research. Appreciation is also expressed to the Faculty of Science, Chulalongkorn University and the Graduate School for financial support. The special thanks are extended to Natural Products Research Unit for the support of chemical and laboratory facilities.

The greatest thanks are also extended to Professor Dr. Pattarapan Prasassarakich, Assistant Professor Dr. Varawut Tangpasuthadol, Dr. Numpon Insin and Dr. Uthumporn Kankeaw serving as chairman and members of her thesis committee, respectively, for their valuable comments, suggestion, correction and help as thesis examiners.

Finally, a deep affectionate gratitude is acknowledged to her parents and family members for their understanding, encouragement and support throughout the course of education. Especially, thanks to her friends and laboratory members for their love, understanding, friendship and encouragement. Without them, the author would never have been able to achieve this goal.

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LIST OF ABBREVIATIONS

CH_3CN	acetonitrile
atm	atmosphere
cm^{-1}	unit of wavenumber
conc.	concentrated
$CHCl_3$	chloroform
$CDCl_3$	chloroform-D
J	coupling constant (NMR)
δ	chemical shift
°C	degree of Celsius
CH_2Cl_2	dichloromethane
d	doublet (NMR)
dd	doublet of doublets (NMR)
DMSO	dimethylsulfoxide
dt	doublet of triplets (NMR)
equiv.	equivalent (s)

LIST OF ABBREVIATIONS

EtOAc	ethyl acetate
EtOH	ethanol
g	gram (s)
Hz	hertz
h	hour (s)
haen	bis(2-hydroxyacetophenone)-*N,N'*-ethylenediimine
hnen	bis(2-hydroxy-1-naphthaldehyde)-*N,N'*-ethylenediimine
hnopen	bis(2-hydroxy-1-naphthaldehyde)-*N,N'*-*o*-phenylenediimine
H_2O_2	hydrogen peroxide
IR	infrared
m	multiplet (NMR)
m.p.	melting point
MeOH	methanol
µg	microgram (s)
µM	micromolar (s)

LIST OF ABBREVIATIONS

mg	milligram (s)
mm	millimeter (s)
min	minute (s)
mL	milliliter (s)
mmol	millimole (s)
MHz	megahertz
NMR	nuclear magnetic resonance
oven	bis(*o*-vanillin)-*N,N'*-ethylenediimine
%	percent
pH	potential of Hydrogen ion
ppm	part per million
q	quartet (NMR)
qui	quintet (NMR)
R_f	retention factor
rt	room temperature

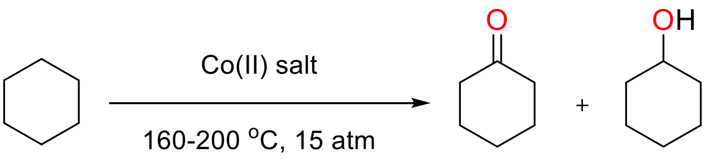
LIST OF ABBREVIATIONS

Na_2SO_4	sodium sulfate
s	singlet (NMR)
salen	bis(salicylaldehyde)-*N,N'*-ethylenediimine
saltn	bis(salicylaldehyde)-*N,N'*-trimethylenediimine
salophen	bis(salicylaldehyde)-*N,N'*-*o*-phenylenediimine
sap	*N*-salicylalidene-2-aminophenol
sac	*N*-salicylalidene-anthranilic acid
PPh_3	triphenylphosphine
t	triplet (NMR)
TBHP	*tert*-butyl hydroperoxide
TLC	thin layer chromatograph
UV	ultraviolet

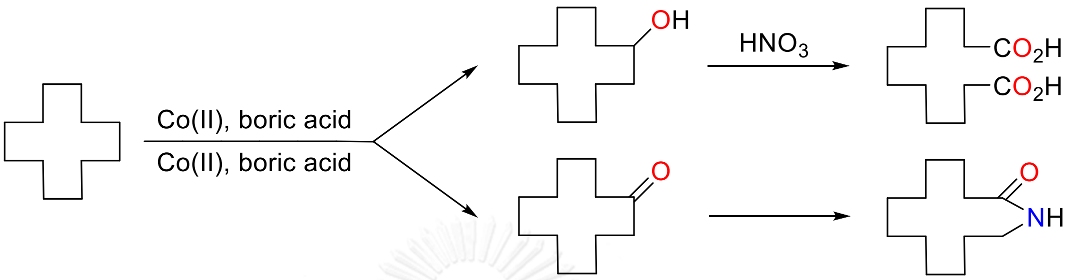
CHAPTER I

INTRODUCTION

Saturated hydrocarbons are widely used solely as an energy supplier or as a fuel source and generally are not expensive. The attempts to utilize this class of compounds by direct functionalization have been carried on for years. However, it has been realized that this is not a simple and easy task. This mainly rises from the inertness of their C-H bonds. Their bond dissociation energies (BDE) range from 85-91 kcal/mol for tertiary, to 90-95 kcal/mol for secondary and 97-104 kcal/mol for primary C-H bonds. [1] The breaking of these bonds thus usually requires high pressure, high temperature, basic or acidic conditions, or extremely strong and unselective reagents, *etc*. For example, cyclohexane is oxidized to cyclohexanone and cyclohexanol by using an soluble oxidation catalyst such as cobalt(II) salt (naphthenate or acetate) between 160 and 200 °C at 15 atm of air. Conversion is limited to about 4 %. [2]



Another major industrial application utilizing alkane is the synthesis of cyclododecanone and cyclododecanol from cyclododecane. These compounds are converted to dodecanedioic acid and lauryl lactam. These two products, with combined worldwide sale of 100 million pounds in 1990, are intermediates in the production of polyamides for several specialty applications.



In a process described by Chemische Werke Huls, cyclododecane containing a trace of cobalt(II) carboxylate was oxidized with air at 160-180 °C and 1-3 atm. The aqueous boric acid was concentrated and recycled to the oxidation reactor. Cyclododecanol and cyclododecanone (5:1) were formed in 80-82 % yield at 33 % conversion. [3]

Under these vigorous conditions, the chemical reaction is inevitably unselective and consequently many products are produced. Therefore, the direct oxidation of saturated hydrocarbons under mild conditions with high selectivity is an intellectually challenging and industrially important objective of current relevance.

Catalysis is the key to chemical transformations. Most industrial syntheses and nearly all biological reactions require catalysts. The catalysts can also influence the selectivity of chemical reactions. Similar to other organic transformations, the catalyst has an important role in an oxidation reaction. The selective activation of particular varieties of C-H bonds and the reduction of the activation energy of the oxidation process can be controlled after the desired substitution has been achieved. This research work will focus on oxovanadium(IV) complexes as catalyst for selective oxidation of saturated hydrocarbons.

1.1 Oxidative functionalization of saturated hydrocarbons

There are many systems which could selectively oxidize saturated hydrocarbons; for example, Fenton's system and biological system such as Cytochrome P-450 enzyme.

Fenton's system or Fenton reaction has been reported that ferrous ion strongly promotes the oxidation of saturated hydrocarbons by hydrogen peroxide (H_2O_2). The mechanism involved was thoroughly studied and was believed to concern with hydroxyl radical. [4]

Cytochromes P-450 are ubiquitous in nature, for example, liver of mammal, insects, yeast and some bacteria. [5] They have been reported to be able to transform saturated hydrocarbons such as cyclohexane to hydroxylated products and oxidative group transfer such as trichloroethylene at room temperature and atmospheric pressure or slightly above. Besides, these enzymes are found to catalyze a variety of oxidation such as *N*-oxidation, sulfoxidation and epoxidation under mild conditions. [6] Methane monooxygenase, propyl 4-hydroxylase, isopenicillin *N*-

synthase and γ-butyrobetaine hydroxylase are other groups of biological systems that could oxidize saturated hydrocarbons to ketones and alcohols. [7]

The development of new metal complex catalysts and single-pot methods for the oxidative functionalization of various organic substrates continues to be a challenging topic in areas of homogeneous catalysis, coordination, organic, bioinorganic, and green chemistry. The search for atom efficient, mild, and selective oxidation of saturated hydrocarbons, unsaturated hydrocarbons, arenes and alcohols is an object of particular significance. As naturally abundant carbon raw materials, saturated hydrocarbons are particularly attractive substrates for added value organic chemicals, but their high inertness generally constitutes a considerable limitation toward selective oxidative transformations under relatively mild conditions. However, the selection of an appropriate metal catalyst and a suitable oxidizing agent, along with thoroughly tuned reaction conditions, can open up an entry toward mild and efficient oxidative transformations of saturated hydrocarbons and other substrates.

Vanadium is known as biologically essential trace element [8], and is found in some haloperoxidases [9], nitrogenase [10], blood cells of tunicates [11], *etc*. Vanadium complexes are known to catalyze many synthetically useful organic reactions, and play very important role in living organisms. Oxovanadiums have been studied for application ranging from catalysis to oxidation reaction. The examples of oxovanadium complexes are shown in Figure 1.1. [12]

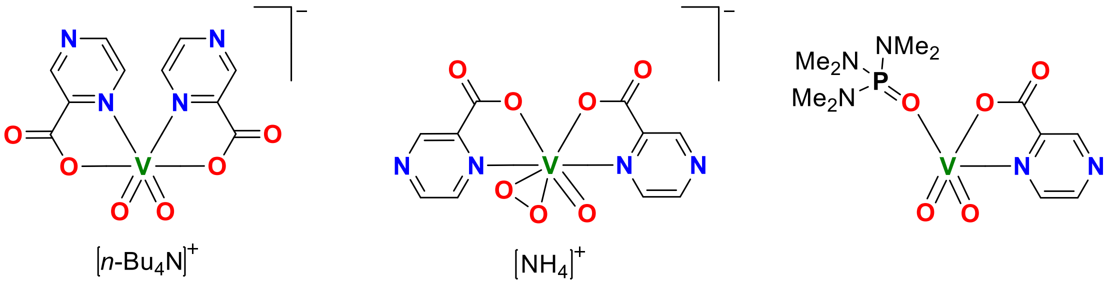


Figure 1.1 Structural formulae of oxovanadium complexes

1.2 Related literature of saturated hydrocarbon oxidation

From the intriguing abilities of biological systems, several chemical models have been later developed. Working towards the main aim to carry on the reaction at ambient temperature and atmospheric pressure is a very promising idea because one can reduce the capital cost which is the main objective in petrochemical industries. For example, Barton and colleagues in 1983 described that the oxidation of adamantane to 2-adamantanone, 1-adamantanol and 2-adamantanol could be achieved with unusual efficiency using O_2 and a system comprising H_2S and iron powder in pyridine containing acetic acid and a little water at room temperature and 1 atm of O_2. [13]

In 1994 Barton and Chavasiri presented the GoAgg^{V} oxidation system (pyridine-acetic acid with a catalytic amount of $Fe(NO_3)_3 \cdot 9H_2O$, *tert*-butyl hydroperoxide (TBHP) as an oxidant with the addition of extra ligand such as picolinic acid). This system was capable to oxidize cycloalkanes such as cyclohexane and cyclododecane providing the oxidized products, with the ketone being the major ones. The yield of the desired products and the ketone to alcohol ratio observed were greater than those in analogous systems using H_2O_2. [14]

In 1995, employing pyridine/acetic acid/H_2O_2 system, Anantaprayoon and Intarakamthornchai observed that cyclohexane could be selectively oxidized to ketone as major product and alcohol as minor at room temperature and atmospheric pressure. The system composing of iron(III) and 1,3-dicarbonyl ligand bearing donating group such as acetylacetone, benzoylacetone and dibenzoylmethane could also accelerate the rate of the oxidation of cyclohexane. [15]

In 1996 Nuntasri and Loayfakajohn showed that iron Schiff's base complexes, especially $(Fesalen)_2O$, exhibited the catalytic ability in pyridine/zinc-acetic acid system. Cyclohexane and cyclooctane could selectively be oxidized to mainly ketone at room temperature and atmospheric pressure. The efficiency of this oxidation system could be enhanced by the addition of ascorbic acid or by stepwise additions of zinc powder. [16]

In 1997 Barton and colleagues reported that saturated hydrocarbons and H_2S could be synergistically oxidized by O_2 to give efficiently ketones and the corresponding alcohols, employing catalysts based on Fe(II), picolinic acid and 4-*tert*-butylpyridine in CH_3CN at room temperature and nearly neutral pH. [17]

1.3 Vanadium complexes in organic synthesis

Vanadium is a biologically essential element. Its inclusion in enzymes such as bromoperoxidase [18, 19] and nitrogenase [20-24] reveals the importance of its redox chemistry. A number of model complex systems have been investigated in order to elucidate vanadium's redox mechanisms. [25-28] The metabolism, physiological role, and pharmacological effects of biologically active vanadium compounds have been evaluated since the last decade. [29-31]

Vanadium complexes, including organovanadium compounds, exist in a variety of configurations depending on their oxidation state and coordination number. [32] Vanadium can exist in oxidation states ranging from -3 to +5 and generally converts between states *via* one-electron redox processes. This versatility permits the development of organic reactions by controlling the vanadium compound's redox potential. This control can be obtained by cautiously selecting the substituents or ligands on the vanadium compound and solvent. In general, electron-withdrawing interactions with the vanadium exhibit positive potentials whereas electron-donating interactions lead to negative potentials.

Vanadium compounds in high oxidation states can induce oxidative transformations. Pentavalent vanadium compounds (*e.g.*, $VOCl_3$, tetrahedral; VF_5, octahedral) are generally considered to be one-electron oxidants which utilize the V(V)-V(IV) couple. The redox potential of this couple increases with acidity, so the reactions are usually carried out in acidic aqueous media. A variety of oxidative synthetic reactions which utilize vanadium oxidants have been developed as demonstrated by the oxidative coupling of phenols.

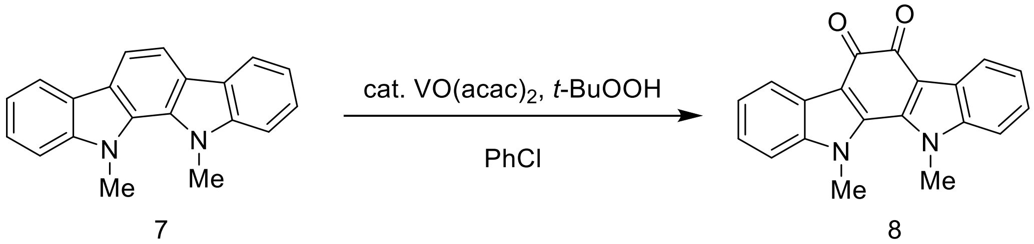
The scope of useful synthetic reactions can be broadened even further by exploiting the versatility of vanadium compound as an oxidant. The oxo functionality of oxovanadium compounds participates in a number of unique oxo-transfer reactions. Vanadium peroxides can cause either oxygenation or epoxidation, both of reactions have been widely studied. Vanadium compounds can also activate molecular oxygen for oxygenation reactions, which further increases vanadium's synthetic utility. Organovanadium compounds also possess the above mentioned, oxidation state-dependent redox properties. Although the synthetic utility of these organometallic reactions has not been thoroughly examined, they are expected to prove highly beneficial.

To provide efficient systems for organic synthesis, the redox potential of the vanadium complexes must be controlled in organic solvents. Furthermore, the redox cycles must be made to be reversible and catalytic. Thus far, only a few catalytic homogeneous systems have been reported and developed for industrial processes. This research focused on utilizing homogeneous vanadium compounds either stoichiometrically or catalytically in oxidation reaction.

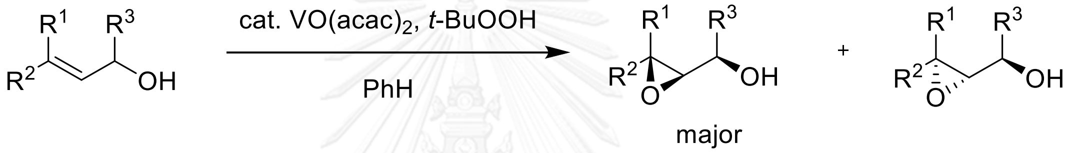
1.4 Vanadium complexes for oxidation reaction

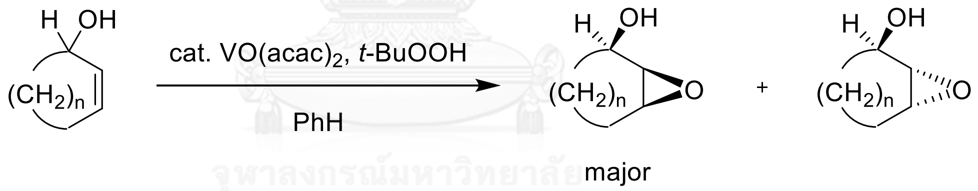
Oxovanadium peroxo complexes efficiently oxygenate organic compounds. For instance, upon treatment with $VO(O_2)(pic)LL'$ (pic = pyridine-2-carboxylate; L, L′= H_2O or MeOH), unsaturated hydrocarbons are non-stereoselectively oxidized to epoxides, allylic oxygenated products, and oxygenated cleavage products. [33] Likewise, benzene and toluene undergo hydroxylation at the ring carbons with a high NIH shift value. Saturated hydrocarbons are hydroxylated less readily and undergo a significant amount of epimerization and radical intermediate trapping with CCl_4. The oxovanadium(V) alkylperoxide, (dipic)-VO(OOR^1) (R^1 = *t*-Bu, CMe_2Ph), induces a similar oxidation in non-protic solvents. [34] These oxidation reactions probably proceed through vanadium-containing radical species. [35]

A polymer-supported Schiff base oxovanadium(V) complex related to $VO(O_2)(pic)LL'$ was effective for the catalytic hydroxylation of benzene with H_2O_2. [36] The indolecarbazole (7) was oxidized to the corresponding 9,10-dione (8) with TBHP in the presence of a catalytic amount of $VO(acac)_2$. [37]

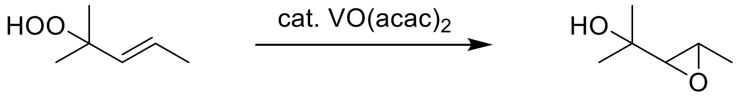


The VO(acac)$_2$-catalyzed epoxidation of allylic alcohols with alkyl hydroperoxide produced epoxy alcohols. [38] Unfunctionalized alkenes reacted more slowly, which allowed highly chemoselective monoepoxidation of olefinic alcohols like geraniol. Furthermore, VO(acac)$_2$, in combination with TBHP, diastereoselectively epoxidized allylic alcohols with selectivity complementary to that obtained by using *m*-CPBA. [39]



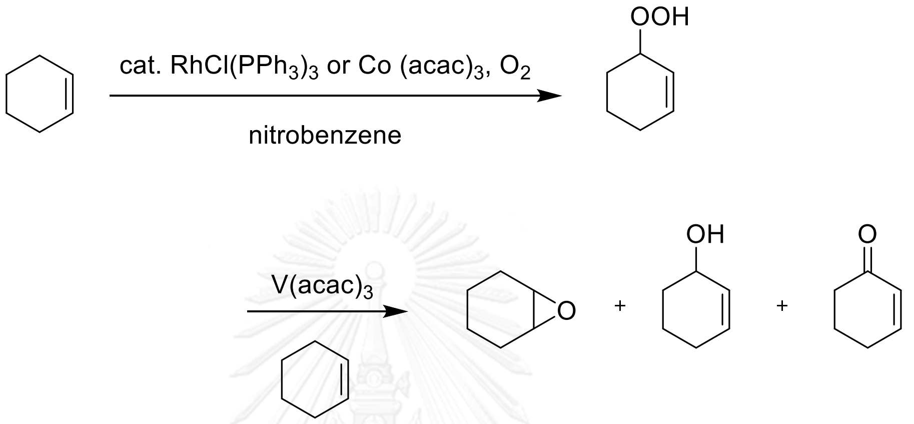


In this connection, catalytic, enantioselective epoxidation of allylic alcohols could be readily performed by the system consisting of titanium(IV) alkoxide and optically active tartarate ester. [40] VO(acac)$_2$-catalyzed oxygenations also extended to the transformation of allylic hydroperoxide (9) into epoxy alcohol (10). [41]



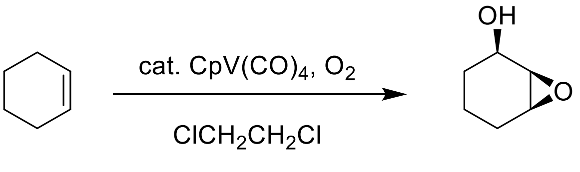
9 10

A bimetallic catalyst consisting of V(acac)$_3$ and RhCl(PPh$_3$)$_3$ or Co(acac)$_3$ induced the aerobic oxidation of cyclohexene to cyclohexene oxide, 2-cyclohexen-1-ol, and 2-cyclohexen-1-one, as shown below.

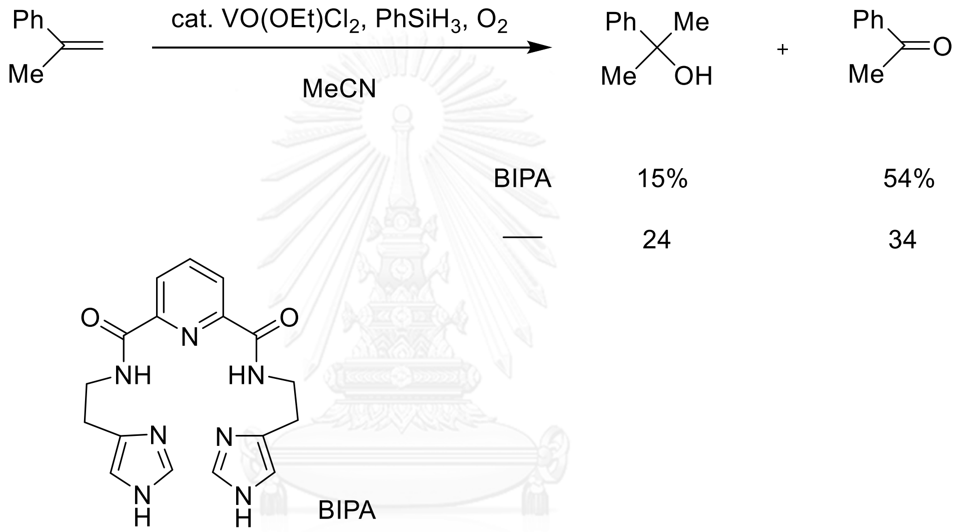


Allylic hydroperoxide was formed initially, which then served as oxidant for intermolecular epoxidation. [42] A combination of VO(acac)$_2$ or V(acac)$_3$ and rhodium(II) carboxylates also catalyzed the oxidation of cyclohexene to 1,2-epoxycyclohexen-3-ol. [43]

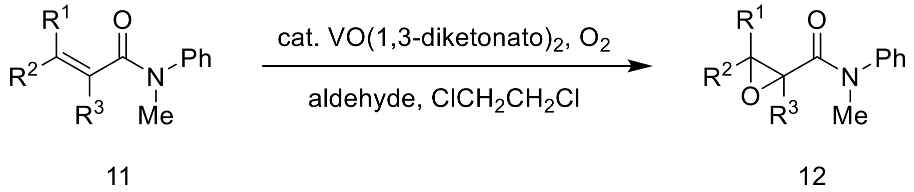
A V(acac)$_3$-AIBN system also aerobically oxidized cyclic olefins to produce epoxy alcohols. [44] Likewise, low-valent vanadium catalyst, CpV(CO)$_4$, induced stereoselective, aerobic epoxidation of cyclohexene to form *cis*-1,2-epoxycyclohexan-3-ol. [45]

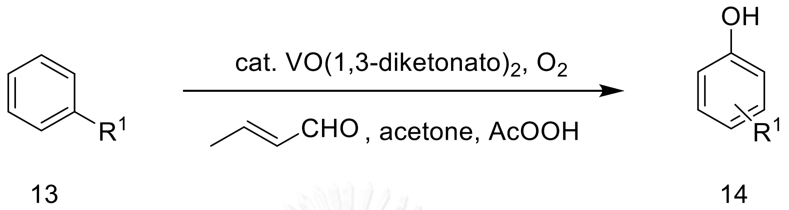


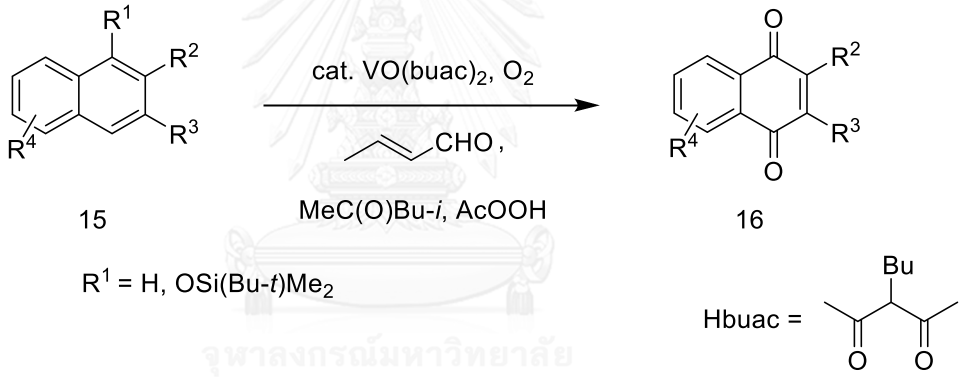
The $VO(OEt)Cl_2$-catalyzed reaction of styrenes with O_2 in the presence of a co-reductant such as $PhSiH_3$ resulted in both oxidation-reduction and oxidative bond cleavage of the styrene, as shown in Scheme below. [46] Coordination of *N*-heterocyclic multidentate ligand BIPA, the 2,6-pyridinedicarboxamide of histamine, increased the relative yield of the latter product. [46]



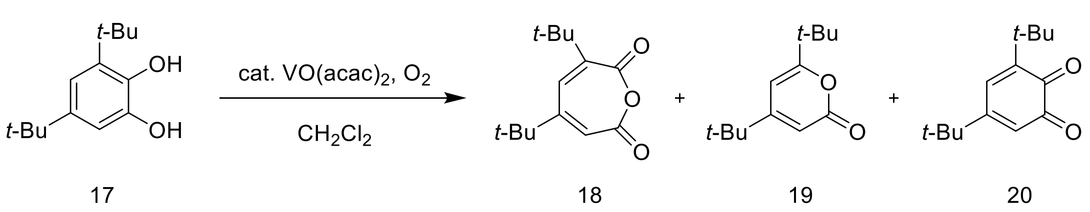
Oxovanadium(IV) complexes bearing 1,3-diketone ligands catalyzed the aerobic oxygenation of α,β- unsaturated carboxamides (11) in the presence of a co-reducing aldehyde to give 2,3-epoxycarboxamides (12). [47] This catalytic system also directly oxygenated benzene derivatives (13) to phenols (14). [48] Naphthalenes and naphthols (15) underwent further oxidation to 1,4-naphthoquinones (16). [49]



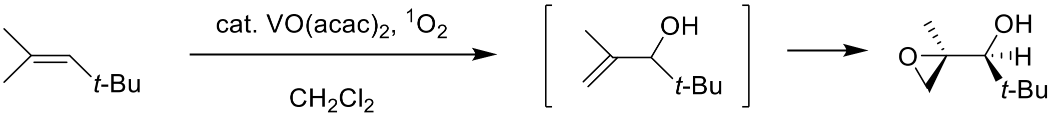




In the presence of catalytic amount of VO(acac)$_2$, 3,5-di-*tert*-butylpyrocatechol (17) was aerobically oxidized to muconic acid anhydride (18), 2-pyrone (19), and *o*-quinone (20). [50]



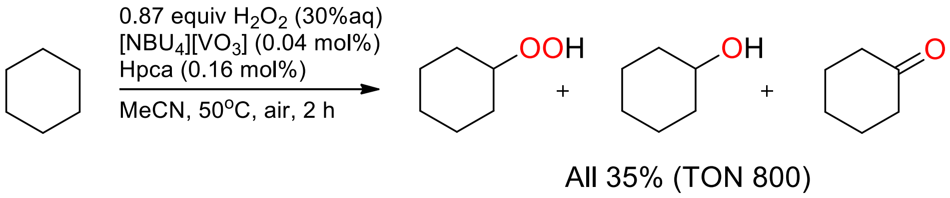
Finally, VO(acac)$_2$ catalyzed the photooxygenation of olefins to yield a one-pot diastereoselective synthesis of epoxy alcohols, as shown in below. [51]



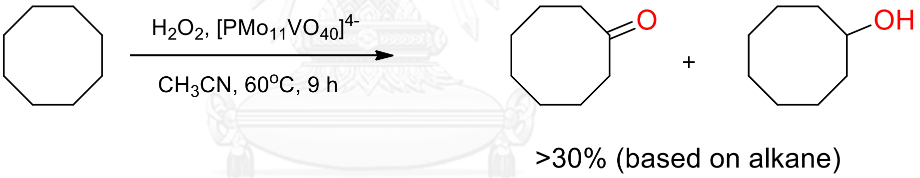
1.5 The oxidation of saturated hydrocarbons catalyzed by vanadium compounds

Vanadium oxo complexes were recognized catalysts, promoters, or stoichiometric oxidants for the oxidative transformation of diverse organic and inorganic substrates. In particular, a considerable number and variety of vanadium derivatives bearing N,O-ligands have been obtained and applied in different organic transformations.

In 1993, *c*-C_6H_{12} was oxidized by $[VO_3]^-$/Hpca/H_2O_2/O_2 system resulting in a mixture of cyclohexyl hydroperoxide (CyOOH, major primary product), cyclohexanol and cyclohexanone (final products), with the total product yield of 35% (based on *c*-C_6H_{12}) and TON of 800. The relative amounts of all three products depended significantly on the reaction parameters, such as time, temperature, concentrations of the $[VO_3]^-$ catalyst, Hpca co-catalyst, and H_2O_2. [52]

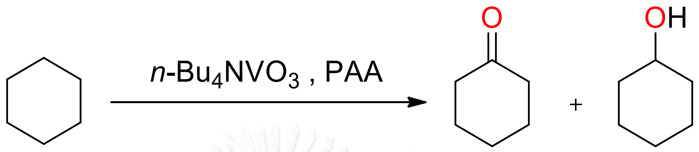


In 2001, alkane oxidation with H_2O_2 catalyzed homogeneously by vanadium-containing polyphosphomolybdates was investigated by Fink and co-workers. Various alkanes (cyclooctane, *n*-octane, adamantane, ethane) could be efficiently oxidized by H_2O_2 in CH_3CN using $[PMo_{11}VO_{40}]^{4-}$ and $[PMo_6V_5O_{39}]^{12-}$. The oxidation of saturated hydrocarbons gave rise to the corresponding alkyl hydroperoxides as the main products, which slowly decomposed in the course of the reaction to produce the corresponding ketones (aldehydes) and alcohols. The oxidation of cyclooctane at 60 °C in CH_3CN gave within 9 h oxygenates with turnover numbers >1000 and yields >30% based on the substrate. [53]



In 2003 Shul'pin and co-workers showed that $[VO_3]^-$/Hpca system also exhibited moderate activity in the aerobic oxidation of alkanes under mild conditions, but required the presence of reducing agents such as ascorbic acid or zinc. The oxidation of cyclohexane by air, in CH_3CN at 30 °C, catalyzed by $[VO_3]^-$ in the presence of Hpca, pyridine, acetic acid, and zinc metal furnished cyclohexanol, cyclohexanone and only negligible amounts of cyclohexyl hydroperoxide (total TON 78), as determined after the reduction with PPh_3 and subsequent GC analysis. In this oxidation, Hpca most likely acted as a mediator of proton and electron transfer. [54]

Furthermore, in 2004 Shul'pin and co-workers demonstrated that cyclohexane was oxidized to cyclohexanone and cyclohexanol by using an oxidation soluble catalyst such as *n*-Bu_4NVO_3 with peroxyacetic acid (PAA) in acetonitrile or acetic acid at 60 °C. [55]



In 2004 Fink and co-workers synthesized a series of mono- and oligonuclear vanadium(V) and vanadium(IV) complexes containing various chelating *N,O*-, N_3-, and O_2- ligands (Figure 1.2). All synthesized compounds were highly efficient oxidation catalysts for the reaction of cyclohexane with air and H_2O_2 in the presence of four equivalents of pyrazine-2-carboxylic acid (pcaH) per vanadium. [56]

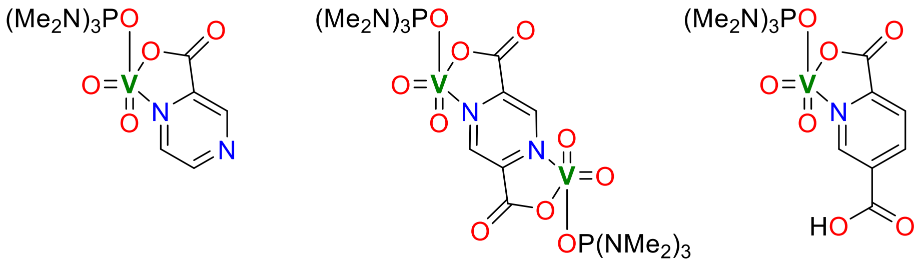


Figure 1.2 Mono- and dinuclear vanadium(V) complexes containing N,O-chelating ligands

In 2011 Si and co-workers prepared oxovanadium(V) complexes containing Schiff's base ligands. The complexes were used for C–H bond activation of the representative hydrocarbons including toluene, ethyl benzene and cyclohexane where H_2O_2 acts as oxidant. After 10 h cyclohexane was totally oxidized to cyclohexanol and cyclohexanone with high TON, while toluene was selectively oxidized to benzaldehyde (43%) after the period of 20 h without any side products. In case of ethyl benzene, the C–H bonds of benzylic carbon were easily oxidized to form acetophenone (58%) as major product. [57]

From literature reviews, various methods have been developed for saturated hydrocarbon oxidation. In recent years, further research has resulted in interesting catalytic systems based on the combination of various V, Fe, Mn, Re, and Cu complexes. A few reports involving the selective oxidation of saturated hydrocarbons utilizing oxovanadium(IV) complexes. Due to its inexpensiveness, availability and ease of preparation, this research is therefore focused on the development of oxovanadium(IV) complexes and system for the selective oxidation of saturated hydrocarbons.

1.6 Scope of study

This research is focused on the development of oxovanadium(IV) complexes and system for the selective oxidation of saturated hydrocarbons. Various types of ligands including Schiff's base, picolinic acid and its related compounds will be prepared and characterized. Oxovanadium(IV) complexes will be synthesized using the prepared ligands. The well characterized oxovanadium(IV) complexes will be explored for their catalytic activities towards the selective oxidation of saturated hydrocarbons under two diverse oxidizing agents: molecular O_2 and peroxide. The reaction conditions of selective oxidation will be optimized by evaluating the yield and selectivity of the desired product(s). The effect of additives in this developed system will also be investigated which would provide some clues for the chemoselectivity of the studied system. Moreover, their reaction mechanisms will be explored.

1.7 The goal of this research

The purpose of this research can be summarized as follows:

1. To synthesize Schiff's base and other ligands
2. To synthesize Schiff's base oxovanadium(IV) complexes and picolinate oxovanadium(IV) complexes
3. To study the optimum conditions for saturated hydrocarbons oxidation by using Schiff's base oxovanadium(IV) and picolinate oxovanadium(IV) complexes in O_2 and peroxide systems
4. To compare the efficiency and selectivity for saturated hydrocarbons oxidation by using Schiff's base oxovanadium(IV) and picolinate oxovanadium(IV) complexes in O_2 and peroxide systems

CHAPTER II

EXPERIMENTAL

2.1 Instruments and equipment

Melting points were determined on a Fisher-Johns melting point apparatus or Electrothermal digital melting point apparatus model IA9100 and are uncorrected.

Column chromatography was carried out on silica gel (Merck's silica gel 60 G Art 7734 (70-230 mesh)). Thin-layer chromatography (TLC) was performed on aluminum sheets pre-coated with silica gel (Merck's, Kieselgel 60 PF254).

The FT-IR spectra were recorded on a Fourier Transform Infrared Spectrophotometer on Nicolet model Impact 410: solid samples were mixed with to potassium bromide to form pellets and liquid samples were incorporated to sodium chloride cells.

The ^{1}H- and ^{13}C-NMR spectra were obtained in deuterated chloroform ($CDCl_3$) or deuterated dimethylsulfoxide (DMSO-d_6) on Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR spectrometer which operated at 400 MHz for ^{1}H and 100 MHz for ^{13}C nuclei and a Bruker Advance 400 NMR spectrometer (^{1}H 400 MHz; ^{13}C 100 MHz). The chemical shifts (δ) are assigned by comparison with residue solvent protons.

Gas chromatographic analysis was carried out on a Varian Gas Chromatography instrument equipped with a flame ionization detector (FID) with N_2

as a carrier gas. The column used for chromatography was a capillary column type of BP-1 and BP-21 (30 m long × 0.25 mm outer diameter × 0.25 μm film thickness) from SGE.

2.2 Chemicals

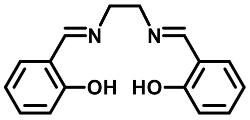
The reagents for synthesizing ligands and oxovanadium(IV) complexes were purchased from Fluka, Sigma-Aldrich and Merck chemical companies. All solvents used in this research were purified prior to use by standard methodology except for reagents and solvents which were reagent grades.

2.3 Syntheses

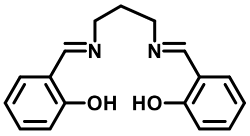
2.3.1 Syntheses and characterization of Schiff's base oxovanadium(IV) complexes

2.3.1.1 Syntheses of Schiff's base ligands

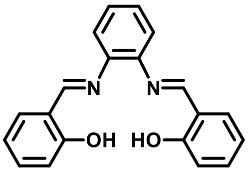
General procedure [58, 59]: An interested aldehyde or ketone (1 or 2 mol-equiv) was slowly added to a solution of aromatic amine (1 mol-equiv) in MeOH. The solution was stirred at room temperature until precipitate occurred. The precipitate was filtered off and recrystallized by an appropriate solvent. Nine synthesized Schiff's base ligands namely salen (1), saltn (2), salophen (3), haen (4), oven (5), hnen (6), hnopen (7), sap (8) and sac (9) are depicted as shown below. (Figure 2.1)



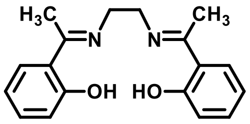
salen (1)



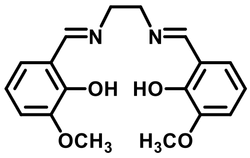
saltn (2)



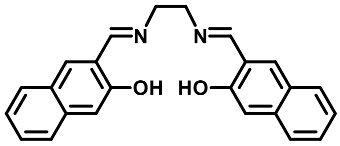
salophen (3)



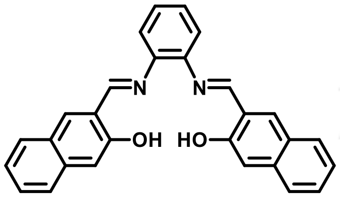
haen (4)



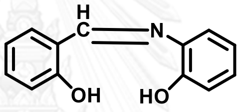
oven (5)



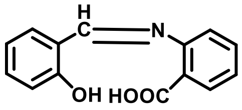
hnen (6)



hnopen (7)



sap (8)



sac (9)

Figure 2.1 Structures of Schiff's base ligands

2.3.1.2 Syntheses of Schiff's base oxovanadium(IV) complexes

General procedure [58, 60]: To an aqueous ethanolic solution of Schiff's base ligand (1 mol-equiv) and $VOSO_4 \cdot 5H_2O$ (1 mol-equiv), a solution of $CH_3COONa \cdot 3H_2O$ was added. A crystalline solid formed immediately. The mixture was further refluxed for approximately 3 h and then cooled overnight. The solid was washed with H_2O, EtOH and Et_2O and dried *in vacuo*.

2.3.1.3 Characterization of Schiff's base oxovanadium(IV) complexes

Schiff's base ligands:

Bis(salicylaldehyde)-N,N′-ethylenediimine (salen) [61] **(1)**: Bright yellow plate crystal (97%), m.p. 125-126 °C (95% EtOH), R_f 0.40 (dichloromethane). IR (KBr, cm^{-1}) 3500, 3050-3010, 2950-2870, 1640, 1600, 1450, 1280 and 1170; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.84 (4H, s), 6.83 (2H, dt, J = 7.48, 1.22 Hz), 6.93 (2H, d, J = 8.24 Hz), 7.18 (2H, dd, J = 7.63, 1.83 Hz), 7.26 (2H, dt, J = 7.78, 1.53 Hz), 8.29 (2H, s) and 13.20 (2H, s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 59.5 (2C), 116.8 (2C), 118.5 (2 x 2C), 131.4 (2C), 132.2 (2C), 160.9 (2C) and 166.3 (2C).

Bis(salicylaldehyde)-N,N′-trimethylenediimine (saltn) [62] **(2)**: Yellow plate crystal (93%), m.p. 51-52°C (*n*-hexane), R_f 0.71 (EtOAc). IR (KBr, cm^{-1}) 3500, 3080-3020, 2950-2860, 1640, 1600, 1450, 1290 and 1160; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.05-2.10 (2H, q, J = 6.71 Hz), 3.66-3.69 (4H, dt, J = 6.72, 0.92 Hz), 6.85 (8H, m), 8.33 (2H, s) and 13.42 (2H, s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 31.6 (1C), 56.7 (2C), 116.8 (2 x 2C), 118.7 (2C), 131.2 (2C), 132.2 (2C), 118.5 (2C), 161.0 (2C) and 165.8 (2C).

Bis(salicylaldehyde)-N,N′-o-phenylenediimine (salophen) [63] **(3)**: Orange needle crystal (82%), m.p. 191-192 °C (acetone), R_f 0.53 (dichloromethane). IR (KBr, cm^{-1}) 3500, 3050, 2950-2870, 1630, 1560-1485, 1275 and 1190; ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.85 (2H, t, J = 7.32 Hz), 7.02 (2H, d, J = 13.24 Hz), 7.20 (4H, m), 7.31 (2H, m), 7.35 (2H, m) and 8.60 (2H, s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 117.5 (2C), 118.9 (2C), 119.1(2C), 119.6 (2C), 127.7 (2C), 132.3 (2C), 133.3 (2C), 142.4 (2C), 161.3 (2C) and 163.6 (2C).

Bis(2-hydroxyacetophenone)-N,N′-ethylenediimine (haen) [64] **(4)**: Yellow needle crystal (83%), m.p. 199-200 °C (95% EtOH), R_f 0.60 (dichloromethane). IR (KBr, cm^{-1}) 3590-3270, 3070, 2950-2870, 1620, 1600, 1450, 1250, and 1180; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.37 (6H, s), 3.97 (4H, s), 6.78 (2H, dt, *J* = 7.70, 1.28 Hz), 6.91 (2H, dd, *J* = 8.55, 1.28 Hz), 7.27 (2H, dt, *J* = 7.91, 1.28 Hz) and 7.52 (2H, dd, *J* = 7.91, 1.50 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 14.7 (2C), 50.2 (2C), 117.4 (2C), 118.5 (2C), 119.4 (2C), 128.1 (2C), 132.4 (2C), 163.1 (2C) and 172.7 (2C).

Bis(o-vanillin)-N,N′-ethylenediimine (oven) [65] **(5)**: Yellow needle crystal (80%), m.p. 163-165 °C (EtOH) (lit.37 m.p. 163-165 °C), R_f 0.50 (EtOH). IR (KBr, cm^{-1}) 3500, 3050, 2840-2990, 1630, 1465, 1255 and 1080; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.88 (6H, s), 3.94 (4H, s), 6.77 (2H, t, *J* = 7.63 Hz), 6.84 (2H, dd, *J* = 7.94, 1.53 Hz), 6.90 (2H, dd, *J* = 7.94, 1.52 Hz), 8.32 (2H, s), 13.55 (2H,s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 56.0 (2C), 59.4 (2C), 114.1 (2C), 118.0 (2C), 118.4 (2C), 123.1 (2C), 148.3 (2C), 151.4 (2C) and 166.6 (2C).

Bis(2-hydroxy-1-naphthaldehyde)-N,N′-ethylenediimine (hnen) [66] **(6)**: Lemon yellow solid (77%), m.p. 270-271 °C (acetone), R_f 0.64 (EtOH). IR (KBr, cm^{-1}) 3570-3300, 3050-3010, 2950-2900, 1640, 1600, 1450, 1250, and 1110.

Bis(2-hydroxy-1-naphthaldehyde)-N,N′-o-phenylenediimine (hnopen) [67] **(7)**: Yellow-orange solid (92%), m.p. 215-217 °C (EtOH), R_f 0.51 (EtOH). IR (KBr, cm^{-1}) 3550-

3300, 3070, 2950-2870, 1640-1630, 1600, 1450, 1260 and 1180; ^{1}HNMR (CDCl$_3$) δ (ppm): 7.05 (2H, d, *J* = 9.12 Hz), 7.32-7.57 (6H, m), 7.80 (2H, d, *J* = 6.69 Hz), 7.95 (4H, d, *J* = 9.17 Hz), 8.53 (2H, d, *J* = 8.38 Hz) and 9.68 (2H, s); ^{13}C-NMR (CDCl$_3$) δ (ppm): 109.2 (2 x 2C), 119.7 (2C), 120.6 (2C), 121.6 (2C), 123.6 (2C), 126.9 (2C), 127.4 (2C), 128.1 (2C), 129.0 (2C), 133.0 (2C), 136.8 (2C), 138.5 (2C) 157.3 (2C) and 168.6 (2C).

N-salicylalidene-2-aminophenol (sap) [68] **(8)**: Bright red needle crystal (90%), m.p. 186-188 °C (acetone), R$_f$ 0.44 (EtOH). IR (KBr, cm^{-1}) 3500, 3050, 1640, 1600-1460, 1280 and 1150; ^{1}H-NMR (CDCl$_3$) δ (ppm): 5.79 (1H, s), 6.95-7.09 (4H, m), 7.15 (1H, dd, *J* = 7.79, 1.53 Hz), 7.22 (1H, dt, *J* = 7.94, 1.53 Hz), 7.40-7.45 (2H, m), 8.69 (1H, s) and 12.25 (1H, s); ^{13}C-NMR (CDCl$_3$) δ (ppm): 115.9 (1C), 117.3 (1C), 118.3 (1C), 119.3 (1C), 119.6 (1C), 121.0 (1C), 128.8 (1C), 132.7 (1C), 133.7 (1C), 135.8 (1C), 149.9 (1C), 160.6 (1C) and 164.0 (1C).

N-salicylalidene-anthranilic acid (sac) [68] **(9)**: Orange solid (67%), m.p. 182-184 °C (EtOH), R$_f$ 0.70 (EtOH). IR (KBr, cm^{-1}) 3500, 3100-3050, 1620, 1600, 1450, 1580-1460 and 1120; ^{1}H-NMR (CDCl$_3$) δ (ppm): 1.50 (1H, s), 6.66 (1H, dd, *J* = 8.54, 0.91 Hz), 6.67 (1H, dd, *J* = 8.53, 1.22 Hz), 6.99 (1H, d, *J* = 8.85 Hz), 7.03 (1H, dd, *J* = 7.33, 0.92 Hz), 7.30 (1H, dt, *J* = 7.78, 1.52 Hz), 7.52 (1H, dt, *J* = 7.64, 1.83 Hz), 7.56 (1H, dd, *J* = 7.78, 1.53 Hz), 7.90 (1H, dd, *J* = 8.29, 1.83 Hz), 9.90 (1H, s) and 11.0 (1H, s); ^{13}C-NMR (CDCl$_3$) δ (ppm): 114.5 (1C), 116.3 (1C), 117.2 (1C), 119.0 (2C), 119.4 (1C), 131.1 (1C), 133.6 (1C), 136.4 (1C), 130.4 (1C), 151.5 (1C), 160.7 (1C), 169.6 (1C) and 191.8 (1C).

Schiff's base oxovanadium(IV) complexes:

Bis(salicylaldehyde)-N,N′-ethylenediimine-Vanadium(IV) [69] **(10)**: Dark green solid (52%), m.p. 168 °C, R_f 0.42 (30% dichloromethane in EtOH). IR (KBr, cm^{-1}): 3500, 3020, 2920, 1630 and 994.

Bis(salicylaldehyde)-N,N′-trimethylenediimine-Vanadium(IV) [70] **(11)**: Orange solid (76%), dec. about 244 °C, R_f 0.79 (30% dichloromethane in EtOH). IR (KBr, cm^{-1}): 3500, 3050, 2920, 1630, 970 and 860.

Bis(salicylaldehyde)-N,N′-o-phenylenediimine-Vanadium(IV) [60] **(12)**: Greenish solid (84%), dec. about 170 °C, R_f 0.79 (30% dichloromethane in EtOH). IR (KBr, cm^{-1}): 3500, 3010, 2890, 1620 and 988.

Bis(2-hydroxyacetophenone)-N,N′-ethylenediimine-Vanadium(IV) [70] **(13)**: Black solid (78%), dec. about 290 °C, R_f 0.80 (30% dichloromethane in EtOH). IR (KBr, cm^{-1}): 3500, 3020, 2900, 1605 and 972.

Bis(o-vanillin)-N,N′-ethylenediimine-Vanadium(IV) [58] **(14)**: Brown solid (88%), dec. about 239 °C, R_f 0.14 (acetone). IR (KBr, cm^{-1}): 3500, 3020, 2960, 1605 and 994.

Bis(2-hydroxy-1-naphthaldehyde)-N,N′-ethylenediimine-Vanadium(IV) [58] **(15)**: Green solid (98%), dec. about 289 °C, R_f 0.73 (acetone). IR (KBr, cm^{-1}): 3500, 3010, 2910, 1620 and 988.

Bis(2-hydroxy-1-naphthaldehyde)-N,N′-o-phenylenediimine-Vanadium(IV) [58] **(16)**: Yellow-brown solid (90%), dec. about 255 °C, R_f 0.83 (30% dichloromethane in EtOH). IR (KBr, cm^{-1}): 3500, 3030, 2940, 1610 and 983.

N-salicylalidene-2-aminophenol-Vanadium(IV) [58] **(17)**: Dark-brown solid (95%), dec. about 261 $^{\circ}$C, R_f 0.52 (acetone). IR (KBr, cm^{-1}): 3500, 3010, 2930, 1615 and 994.

N-salicylalidene-anthranilic acid-Vanadium(IV) [58] **(18)**: Black solid (20%), dec. about 298 $^{\circ}$C, R_f 0.50 (EtOH). IR (KBr, cm^{-1}): 3500, 3030, 2940, 1605 and 984.

2.4 Catalytic activity

Part 1 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in O_2 system

2.4.1 Oxidation of saturated hydrocarbons

General procedure for the oxidation of cycloalkanes [58, 71]: Catalyst (0.25 mmol), cycloalkane (5 or 20 mmol), zinc grit (20 mmol), and acetic acid (2.3 mL) and pyridine (28 mL) were placed in a round bottom flask. The mixture was stirred continuously for 24 h at room temperature and O_2 atmospheric pressure. After the reaction was proceeded for a designed period of time, 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 solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of an appropriate internal standard (biphenyl).

2.4.2 Effect of Schiff's base oxovanadium(IV) complexes on reactivity of cyclododecane oxidation

Schiff's base oxovanadium(IV) complexes, **(10)-(18)** were employed as a catalyst in cycloalkane oxidation using reaction conditions described in the general procedure.

2.4.3 Effects of various parameters

Various factors affecting the oxidation reaction of cycloalkanes involved the amount of catalysts, zinc, carboxylic acids and solvents were thoroughly examined.

Optimum conditions study for cycloalkane oxidation

2.4.3.1 Effect of the amount of catalysts

The oxidation reaction of cycloalkane was carried out according to the general procedure, but the amount of VO(salophen) was varied to 0.10, 0.25, 0.50, 0.75 and 1.00 mmol.

2.4.3.2 Effect of solvents

The oxidation of cycloalkane was carried out according to the general procedure, but the varied solvents (pyridine, 2-picoline, 3-picoline, 4-picoline, acetone and CH_3CN) and a solvent mixture (pyridine and varied solvents; 1: 1 v/v) were experimented.

2.4.3.3 Effect of zinc

The oxidation of cycloalkane was carried out as that described in the general procedure, but zinc powder was used instead of zinc grit.

2.4.3.4 Effect of carboxylic acids

The oxidation of cycloalkane was carried out according to the general procedure, but the varied carboxylic acids (formic acid, butyric acid, pivalic acid, chloroacetic acid, dichloroacetic acid, 2-chloropropionic acid and 2-picolinic acid) were employed to replace acetic acid. The effect of the amount of acetic acid was further studied by deviating to 0, 0.5, 1.0, 1.5, 2.0, 2.3, 2.5, 3.0 and 5.0 mL.

2.5 Kinetic study

The general oxidation procedure of cyclododecane catalyzed by utilizing VO(salophen) was carried out. At different reaction time proceeded (2, 4, 6, 8, 16, 20, 24 and 48 h), an aliquot from the reaction mixture was taken, worked up and analyzed by GC.

2.6 Chemoselectivity study

Following the general oxidation procedure, absolute EtOH, isopropanol, ethylene glycol, hydroquinone and derivatives, triethylamine, aniline, *N,N′*-dimethylaniline, *N,N′*-dimethylacetamide, anisole, methyl benzoate, ascorbic acid and triphenylphosphine were separately added as a co-substrate to the oxidation reaction of cyclododecane.

2.7 Catalytic activity of other substrates

Saturated hydrocarbons: adamantane and ethyl benzene were oxidized under optimized conditions. Reaction conditions were the same as those described in the general procedure.

2.8 Comparative study on relative reactivity of cycloalkane in oxidation reactions

Two competitive cycloalkanes: cyclohexane and either cyclopentane, cyclooctane or cyclododecane, respectively, were oxidized employing the general oxidation procedure.

2.9 Competitive studies on the oxidation of cycloalkane and alcohol

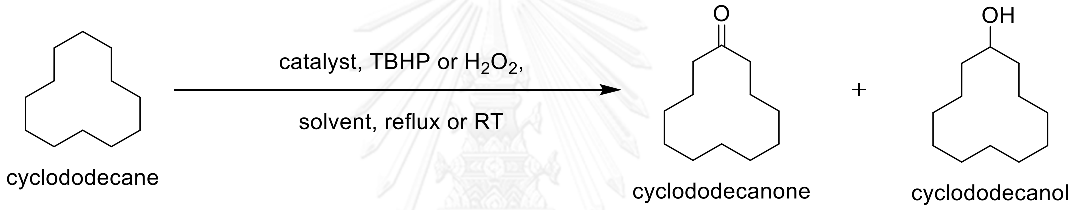
The oxidation reaction was carried out in the same fashion as general procedure, but cyclohexane and cyclododecanol or cyclododecane and cyclohexanol were used as substrate.

Part 2 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in peroxide system

2.10 Catalytic activity

2.10.1 Oxidation of saturated hydrocarbons

General procedure for the oxidation of cycloalkanes: Catalyst, cyclododecane, oxidizing agent (TBHP or H_2O_2) and solvent were placed in a round bottom flask. The mixture was refluxed continuously for 24 h.



After the reaction was proceeded for a designed period of time, 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 solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of biphenyl that used as an internal standard.

2.10.2 Effects of various parameters

Various factors affecting the oxidation reaction of cycloalkanes involved the amount of catalysts, oxidizing agents and solvents were thoroughly examined.

Optimum conditions study for cycloalkane oxidation

2.10.2.1 Effect of the amount of catalysts

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the amount of VO(salophen) was varied to 0, 0.025, 0.05 and 0.10 mmol.

2.10.2.2 Effect of solvents

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the varied solvents ($CHCl_3$, isooctane, toluene and CH_3CN) were experimented.

2.10.2.3 Effect of oxidizing agents

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the varied oxidizing agents (TBHP or H_2O_2) were studied. The effects of the amount of oxidizing agents were further explored by deviating to 0, 10, 15 and 20 mmol.

2.11 Kinetic study

The general oxidation procedure of cyclohexane catalyzed by VO(salophen) was carried out. At different reaction time proceeded (0.5, 1, 2, 4, 6, 8, 16, 20 and 24 h), an aliquot from the reaction mixture was taken, worked up and analyzed by GC.

2.12 Chemoselectivity study

Following the general oxidation procedure, absolute EtOH, isopropanol, hydroquinone and derivatives, ascorbic acid and triphenylphosphine were separately added as a co-substrate to the oxidation reaction of cyclododecane.

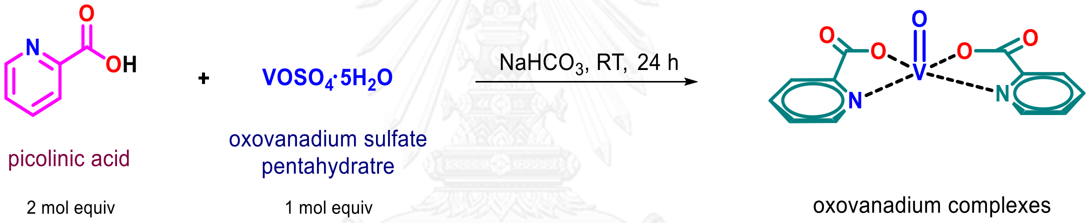
2.13 Catalytic activity of other substrates

Saturated hydrocarbons: adamantane and ethyl benzene were oxidized under optimized conditions. Reaction conditions were the same as those described in the general procedure.

Part 3 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in peroxide system

2.14 Synthesis of oxovanadium(IV) complexes

To an aqueous solution of $VOSO_4{\cdot}5H_2O$ and picolinic acid was added 10% $NaHCO_3$. The mixture was stirred for 24 h at room temperature, then the precipitate was collected by filtration and air-dried to give oxovanadium(IV) picolinate complex ($VO(pic)_2$) **(19)** as light blue solid (81% based on Hpic). IR (Figure 2.2, KBr, cm^{-1}): 3500-2800, 1640, 1570 and 960. [72]



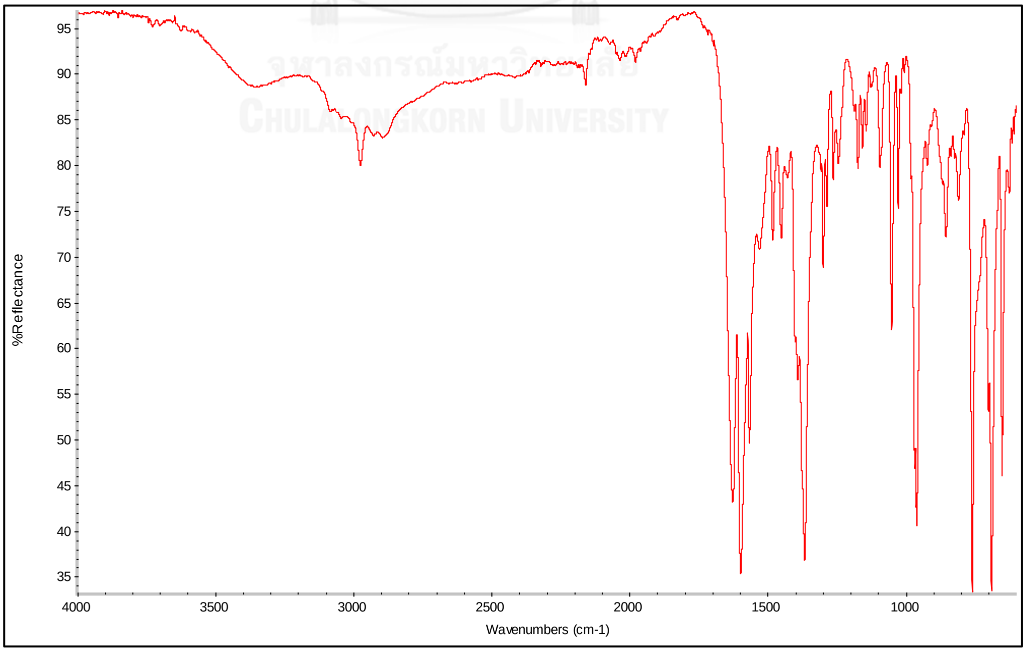


Figure 2.2 IR spectrum of $VO(pic)_2$

2.15 Catalytic oxidation of cyclododecane

2.15.1 Oxidation of saturated hydrocarbons

Catalyst, cyclododecane, TBHP and solvent were placed in a round bottom flask. The mixture was refluxed continuously for desired time. After the reaction was proceeded for a designed period of time, 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 solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of biphenyl that used as an internal standard.

2.15.2 Effects of various parameters

Various factors affecting the oxidation reaction of cycloalkanes involved the amount of catalysts, oxidizing agents and solvents were thoroughly determined.

Optimum conditions study for cycloalkane oxidation

2.15.2.1 Effect of the amount of catalysts

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the amount of $VO(pic)_2$ was varied to 0, 0.05 and 0.10 mmol.

2.15.2.2 Effect of solvents

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the varied solvents ($CHCl_3$, isooctane, CH_2Cl_2, 1,2-DCE, MeOH, acetone, CCl_4, CH_3CN and THF) were experimented.

2.15.2.3 Effect of oxidizing agents

The oxidation reaction of cyclododecane was carried out according to the general procedure, but the varied amount of oxidizing agents (TBHP) was studied. The effect of the amount of oxidizing agent was explored by deviating to 0, 5, 10 and 20 mmol.

2.16 Kinetic study

The general oxidation procedure of cyclododecane catalyzed by $VO(pic)_2$ was carried out. At different reaction time proceeded (2, 4, 8, 16, 20 and 24 h), an aliquot from the reaction mixture was taken, worked up and analyzed by GC.

2.17 Catalytic activity of other substrates

Saturated hydrocarbons: cyclooctane, adamantane, ethyl benzene, propyl benzene, xanthene, tetralin, diphenylmethane and acenaphthene were oxidized under optimized conditions. Reaction conditions were the same as those described in the general procedure.

2.18 Competitive oxidations

Competitive oxidations were carried out with the following pairs of cyclododecane with another alkane: absolute EtOH, isopropanol, hydroquinone, triphenylphosphine, ascorbic acid, aniline, methyl salicylate, triethylamine, anisole and ethylene glycol. In a round bottom flask was added to 10 mL acetonitrile solution containing a pair of substrates (1 mmol each). Reaction conditions were the same as those described in the general procedure. The extracted organic layer was analyzed by GC with the addition of an exact amount of an internal standard, biphenyl.

Part 4 Bromination of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in peroxide system

2.19 Catalytic bromination of cyclododecane

2.19.1 Bromination of saturated hydrocarbons

Catalyst, cyclododecane, brominating agent, TBHP and solvent were placed in a round bottom flask. The mixture was refluxed continuously for desired time. After the reaction was proceeded for a designed period of time, 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 solution of $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of biphenyl that used as an internal standard.

2.19.2 Effects of various parameters

Various factors affecting the bromination reaction of cycloalkanes involved the amount of catalysts, oxidizing agents and solvents were thoroughly examined.

Optimum conditions study for cycloalkane bromination

2.19.2.1 Effect of the amount of catalysts

The bromination reaction of cyclododecane was carried out according to the general procedure, but the amount of $VO(pic)_2$ was varied to 0, 0.05 and 0.10 mmol.

2.19.2.2 Effect of solvents

The bromination reaction of cyclododecane was carried out according to the general procedure, but the varied solvents ($CHCl_3$, isooctane, CH_2Cl_2, 1,2-DCE, MeOH, acetone, CCl_4 and CH_3CN) were experimented.

2.19.2.3 Effect of oxidizing agents

The bromination reaction of cyclododecane was carried out according to the general procedure, but the varied amount of TBHP was studied. The effect of the amount of oxidizing agent was explored by deviating to 0, 3, 5, 10, 15 and 20 mmol.

2.19.2.4 Effect of brominating agents

The bromination reaction of cyclododecane was carried out according to the general procedure, but the varied brominating agents ($BrCCl_3$, $Br_3CCOCBr_3$, Br_2, CBr_4 and NBS) were experimented. The effect of the amount of brominating agent was further studied by deviating to 0, 1.0, 3.0 and 5.0 equiv to substrate.

2.20 Kinetic study

The general bromination procedure of cyclododecane utilizing $VO(pic)_2$ as catalyst was carried out. At different reaction time proceeded (0.5, 1, 2, 4, 6, 8 and 24 h), an aliquot from the reaction mixture was taken, worked up and analyzed by GC.

2.21 Catalytic activity of other substrates

Saturated hydrocarbons: adamantane, dodecane, ethyl benzene, acetophenone, 2,4-dimethylpentane and isooctane were oxidized under optimized conditions. Reaction conditions were the same as those described in the general procedure.

2.22 Chemoselectivity of alkyl bromide synthesis

Chemoselectivity of this bromination reaction was carried out under general procedure but substrate was changed to cyclododecanol. Reaction conditions were the same as those described in the general procedure. The extracted organic layer was analyzed by GC with the addition of an exact amount of an internal standard, biphenyl.

2.23 Competitive brominations

Competitive brominations were carried out with the following pairs of cyclododecane with another alkane or alcohol. In a round bottom flask was added to 10 mL acetonitrile solution containing a pair of substrates (1 mmol each). Reaction conditions were the same as those described in the general procedure. The extracted organic layer was analyzed by GC with the addition of an exact amount of an internal standard, biphenyl.

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CHAPTER III

RESULTS AND DISCUSSION

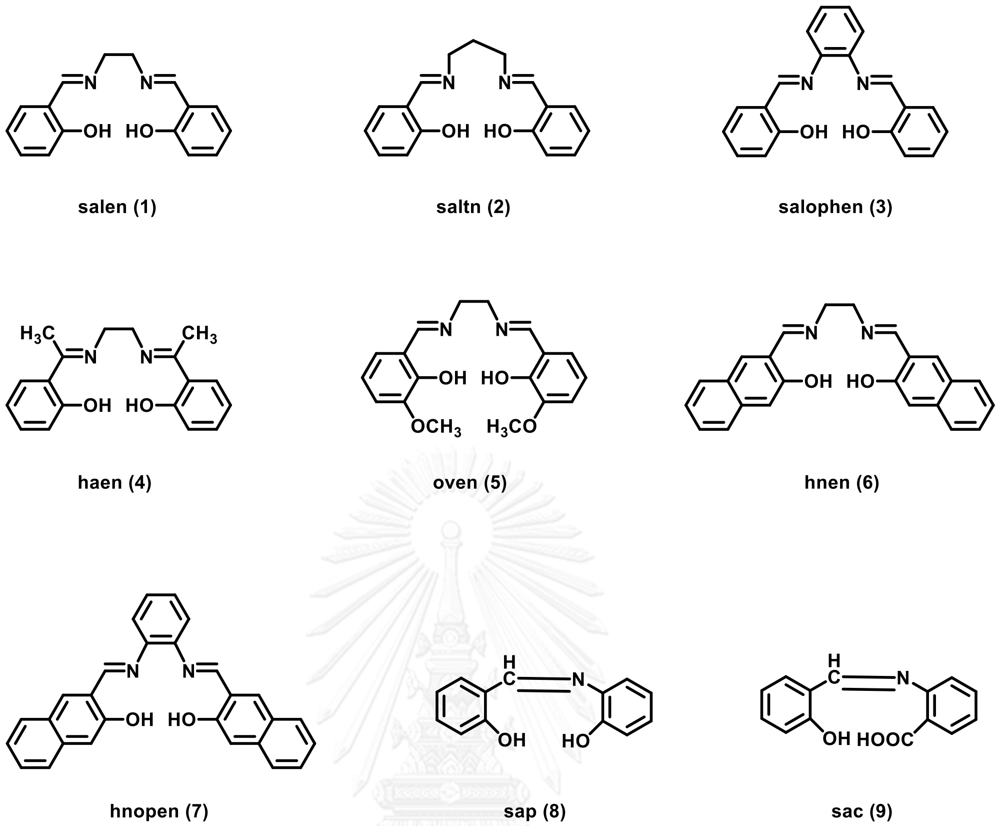
The purposes of this research were to synthesize Schiff's base and picolinate oxovanadium(IV) complexes as catalysts for saturated hydrocarbons oxidation in O_2 and peroxide systems. The comparison of the efficiency and selectivity for saturated hydrocarbons oxidation in both systems was also carried out. This chapter was separated into four parts. The first part mentions about using oxovanadium(IV) Schiff's base complexes in O_2 system for the oxidation of saturated hydrocarbons. The second part was the oxidation reaction catalyzed by oxovanadium(IV) Schiff's base complexes using peroxides. Saturated hydrocarbons oxidation catalyzed by oxovanadium(IV) picolinate complexes in peroxide system was cited in part three. The last part covered the bromination of saturated hydrocarbons using the optimized conditions from part three to successfully obtain alkyl bromide.

Part 1 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes using O_2

3.1 Syntheses and characterization of Schiff's base oxovanadium(IV) complexes

3.1.1 Effect of Schiff's base ligands

Cyclododecane was chosen because it could give good mass balance with respect to the hydrocarbon and its oxidation products, cyclododecanone and cyclododecanol. The oxidation of cyclododecane was examined to observe both the rate of the reaction (observed at 2 h) and the amount of the desired products obtained (observed at 24 h). Nine Schiff's base ligands (**1**-**9**, Figure 3.1) were complexed with oxovanadium(IV) to gain Schiff's base oxovanadium(IV) complexes **(10-18)**, respectively. The effects of various Schiff's base oxovanadium(IV) complexes on cyclododecane oxidation are presented in Table 3.1 and Figure 3.2.



salen (1)
saltn (2)
salophen (3)
haen (4)
oven (5)
hnen (6)
hnopen (7)
sap (8)
sac (9)

Figure 3.1 Structures of Schiff's base ligands used in this study

Table 3.1 Effect of Schiff's base ligands on cyclododecane oxidation

Oxovanadium (IV) complexes	**Product (% yield)**					
	2 h		**24 h**			
	(none)	**(nol)**	**(none)**	**(nol)**	**(none)+(nol)**	**MB**
(10)	6.0	trace	10.7	trace	10.7	100
(11)	5.7	trace	11.4	trace	11.4	100
(12)	8.3	trace	11.1	trace	11.1	99
(13)	trace	trace	9.9	trace	9.9	101
(14)	4.5	trace	8.4	trace	8.4	98
(15)	4.9	trace	8.6	trace	8.6	101
(16)	8.2	trace	11.6	trace	11.6	98
(17)	7.5	trace	9.8	trace	9.8	101
(18)	8.3	trace	12.4	trace	12.4	99

Reaction conditions: cyclododecane (5 mmol), oxovanadium(IV) complex (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31g) at RT
(none) cyclododecanone **(nol)** cyclododecanol

It was observed that nine complexes **(10- 18)** could be utilized as catalysts for the oxidation of cyclododecane. Cyclododecanone was formed with significant amount observed at 2 h using every oxovanadium(IV) complex, except for **(13)**. Considering the reaction selectivity, Schiff's base oxovanadium(IV) complexes provided good selectivity. The amount of cyclododecanone occurred as a major product while the amount of cyclododecanol occurred in trace amount both at 2 and 24 h.

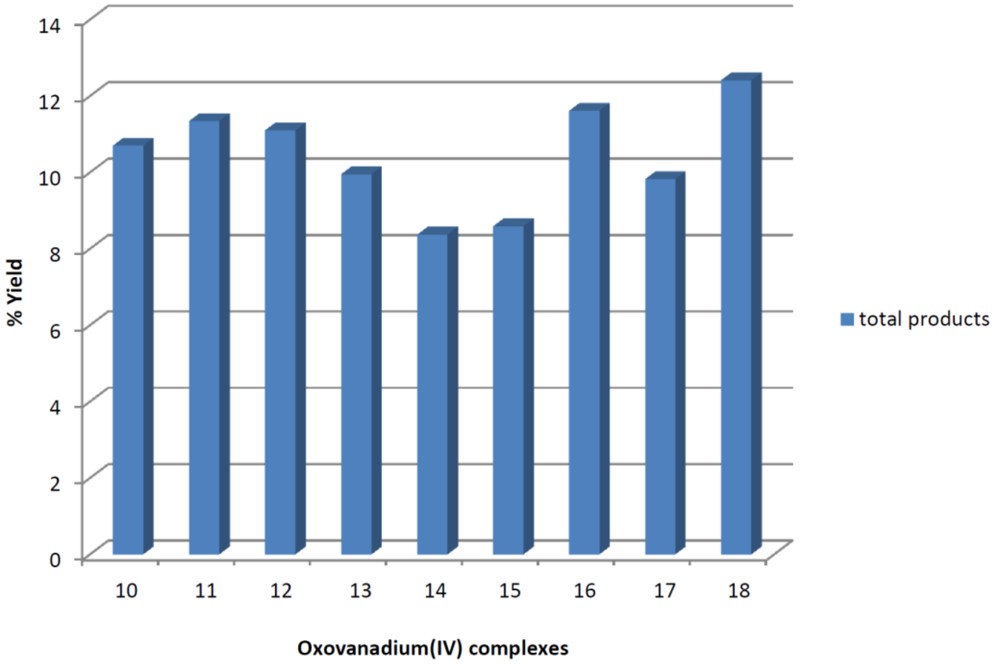
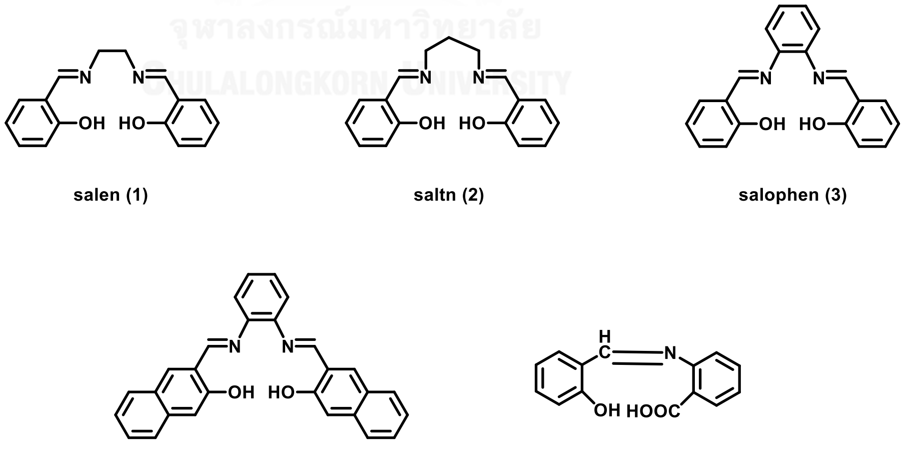


Figure 3.2 Comparative study on the oxidation of cyclododecane catalyzed by various oxovanadium(IV) complexes

Considering the structures of all Schiff's base ligands, each Schiff's base ligand gave different yields. The electron-donating ligands could stabilize vanadium center. As can be seen in Figure 3.1 that ligands **(4)**, **(5)** and **(6)** containing electron-withdrawing groups resulted in lessened amount of product. Comparing ligands **(8)** and **(9)**, ligand **(8)** exhibited electron-withdrawing interactions with the vanadium, these interactions caused decreasing of yield of product. Therefore, ligands that provided good results were **(1)**, **(2)**, **(3)**, **(7)** and **(9)** (Figure 3.3). Using these five Schiff's base oxovanadium(IV) complexes (**(10)**, **(11)**, **(12)**, **(16)** and **(18)**), it was observed that the complexes exhibited as an efficient catalyst for oxidation of saturated hydrocarbons. Comparing with other literatures that were metal catalyzed oxidation of saturated hydrocarbons, some reactions gave hydroxylation product. Mimoun and co-worker using vanadium(V) peroxo complexes in cycloalkane oxidation, reaction proceeded under 20 °C and alcohol was obtained as a major product. [33] Saussine and co-worker reported hydroxylation of hydrocarbons catalyzed by cobalt(III) alkylperoxy complexes. Alcohol was selectively produced in this system. [73] Oxidation of saturated hydrocarbons catalyzed by titanium silicalite was studied by Clerici, alkane was rapidly hydroxylated to give an alcohol. [74] Moreover, Tetard investigated the alkane hydroxylation reactions catalyzed by binuclear manganese and iron complexes. Ketone and alcohol were produced in equivalent amount. [75] Therefore, the complexes in this research were effective catalysts for selective oxidation of alkane to ketone.



salen (1) **saltn (2)** **salophen (3)**

hnopen (7) **sac (9)**

Figure 3.3 Structures of the five effective Schiff's base ligands

3.2 Optimum conditions for cyclododecane oxidation

3.2.1 Effect of the amount of catalysts

The amount of catalyst was one of crucial parameters that needed to be evaluated. Bis(salicylaldehyde)-*N,N′*-*o*-phenylenediimine-vanadium(IV) (VO(salophen) **(12)** was selected to study in this section due to high amount of catalyst that could be synthesized and provided good results of cyclododecane oxidation. The results are presented in Figure 3.4.

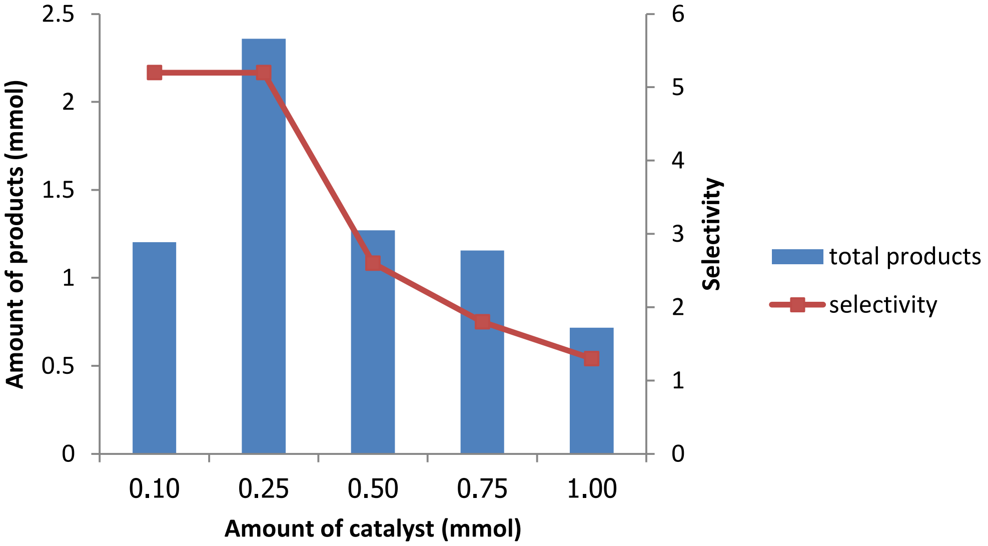


Figure 3.4 Effect of the amount of catalyst (VO(salophen)) on cyclohexane oxidation at 24 h

In the absence of (VO(salophen)), no oxidation occurred. The total yield was depended on the amount of catalyst used. The sample was taken at 2 and 24 h interval. The first taken time (2 h) was performed to observe how fast the oxidation occurred, while at 24 h was taken to examine the total amount of the desired products obtained and the selectivity of the reaction. Using VO(salophen) 0.25 mmol gave the highest yield of the target product (2.2 mmol) and the highest selectivity of ketone to alcohol ratio (5.3). When the amount of catalyst was less or more than 0.25 mmol, the reaction rate was decreased. The reason was probably because the excess of catalyst used may cause side oxidation reactions occur competitively. Therefore, the amount of catalyst has an important role to the amount of products occurred. For selectivity of ketone formation, it could be observed that ketone was selectively produced in 5 to 1 ratio with the highest yield of products at 0.25 mmol catalyst used. Increasing amount of catalyst resulted in reducing of selectivity.

3.2.2 Effect of solvents

In this study, the solvent that could provide the homogenous reaction was required. From the experiments described above, pyridine was the first solvent chosen because it could dissolve both oxovanadium(IV) complex and model substrate. Other solvents were also selected to determine if they could replace pyridine. The effects of selected solvents are displayed in Figure 3.5.

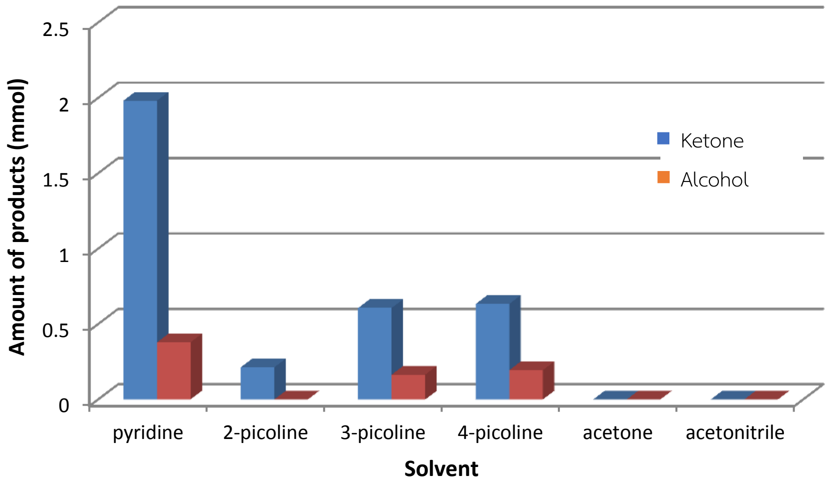


Figure 3.5 Effect of solvents on the oxidation reaction

2-, 3- and 4-Picolines, acetone, and CH_3CN were examined whether they could replace pyridine. From the results, it was found that the amount of desired products (cyclododecanone and cyclododecanol) was significantly decreased when the reaction media was not pyridine. In case of 2-, 3- and 4-picolines, there were stronger bases than pyridine. The stronger base could affect to proper pH of reaction media, therefore, the yield of products were reduced. When employing acetone, the oxidation reaction produced trace amount of the desired products. In the case of using CH_3CN, the oxidation of cyclododecane did not occur. Undesired reactions may occur instead. A possible reaction may be the decomposition of species containing real oxidizing power. [76] This solvent effect clearly showed the necessity of pyridine under these studied oxidation reactions. Taking to the consideration from selectivity, using pyridine still gave the highest selectivity of ketone to alcohol production.

Another aspect that should be explored was co-solvent. If the amount of pyridine used was lessened and replaced with co-solvent, it will affect on the amount of desired product or not. In this case, other solvents were selected to determine whether they can be mixed with pyridine in reaction media. The effects of co-solvent are shown in Figure 3.6.

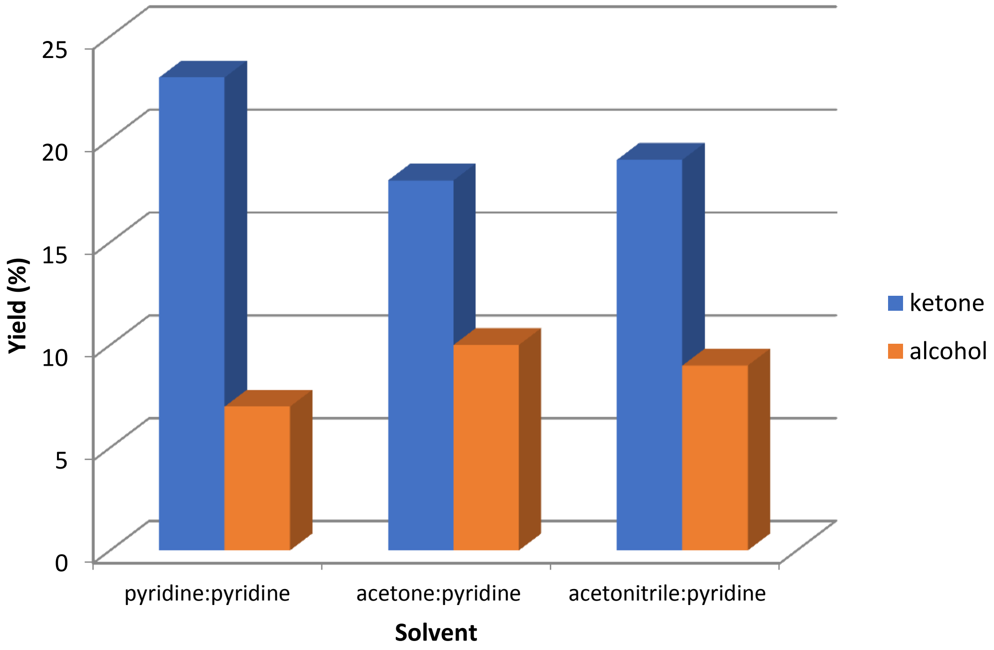


Figure 3.6 Effects of co-solvent

Using acetone or CH_3CN with pyridine in 1:1 ratio V/V, %yield of desired products were decreased. Moreover, selectivity also decreased in both mixed reaction media. Thus, the most proper solvent for this reaction was pyridine only.

3.2.3 Effect of zinc

The system comprising of zinc and O_2 is commonly known to produce superoxide which was believed to be the real oxidizing agent in this oxidation reaction. [76] The form of zinc used was another influent factor to be considered. The results are exhibited in Figure 3.7.

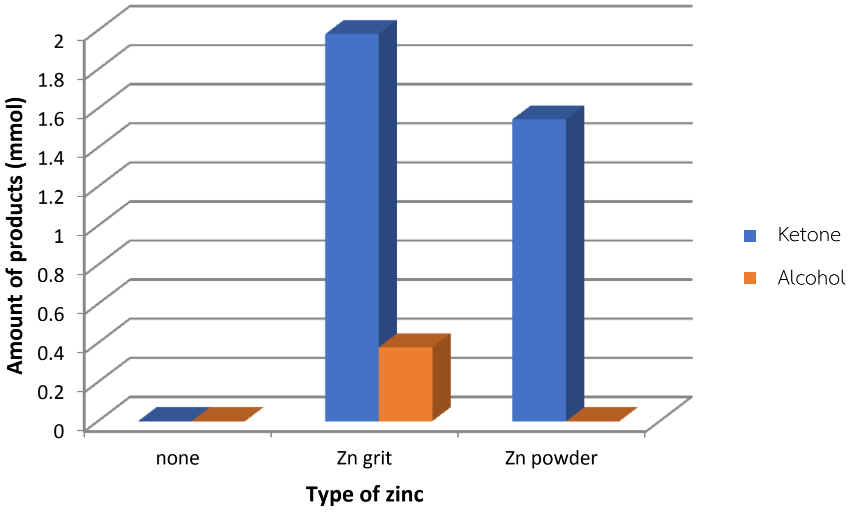


Figure 3.7 Effect of zinc in the oxidation reaction

It was showed that no products obtained in the absence of zinc in cyclohexane oxidation. Two types of zinc were used in this system. Zinc powder has particle size less than 45 µm and zinc grit has particle size between 45 µm to 3 mm. By using zinc grit, the amount of cyclohexane at 2 h did not show any difference compared with using zinc powder. Nevertheless, the yield at 24 h when using zinc powder was less than when zinc grit was used. Therefore, zinc grit was an important component. It should be noted that zinc powder had surface active area more than zinc grit but this oxidation reaction catalyzed by oxovanadium(IV) complexes seemed not to be affected. Another reason that zinc grit gave higher yield than zinc powder because of high surface, zinc powder could be dissolved in solution easily than zinc grit, therefore, time for zinc in system as reducing agent was lessen. Consequently, the amount of products was generated decreasingly.

The amount of zinc used was another factor that should be studied besides the surface area of zinc. The assumption is the more zinc used, the more desired products obtained. Because real oxidant superoxide was produced from zinc and O_2 so a large amount of zinc could produce a large amount of oxidant. The superoxide generated should affect to the yield of corresponding ketone and alcohol. The effects of amount of zinc used are revealed in Table 3.2.

Table 3.2 Effect of amount of zinc on cyclododecane oxidation

Entry	**Amount of zinc (mmol)**	**GC yield (%)**			
		(cane)	**(none)**	**(nol)**	**MB**
1	0	99	0	0	99
2	10	83	12	3	98
3	20	70	22	7	99
4	30	78	15	4	97

(cane) cyclododecane **(none)** cyclododecanone **(nol)** cyclododecanol

From the results in Table 3.3, a large amount of zinc could produce a large amount of oxidant and affected to %yield of corresponding ketone and alcohol. Zinc that dissolved completely at the end of reaction would reduce O_2 to produce superoxide efficiently. The maximum yield of desired products was achieved when employing 20 mmol of zinc in reaction system. When using excess amount of zinc (30 mmol), both ketone and alcohol were produced in lessen amount. This might be due to the excess of zinc could not be dissolved all in reaction and not necessary to this oxidation system.

3.2.4 Effect of the amount and type of carboxylic acids

Carboxylic acid was another parameter in this oxidation reaction. Preliminary studies disclosed that acetic acid profoundly affected on cyclohexane oxidation. Cyclohexanone and cyclohexanol did not occur in the absence of acetic acid. The variation of amount of acetic acid was also investigated. The most appropriate amount of acetic acid was 2.3 mL. The more or less amount of acetic acid gave comparable or poor results. Furthermore, the amount of proper acid had an effect to the amount of product observed. Owing to the dissolved time period of zinc by acid, its effect gave the different amount of products. The results are presented in Figure 3.8.

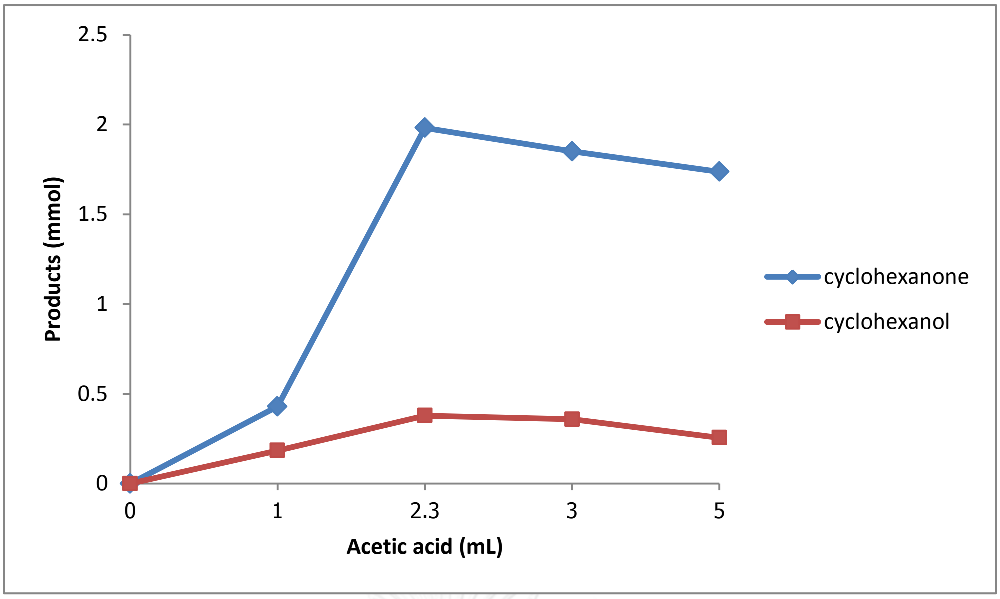


Figure 3.8 Effect of the amount of acetic acid on cyclohexane oxidation

From Figure 3.8, the amount of desired products started to decrease when 3.0 mL of acetic acid was used. Then, for the oxidation of cyclododecane, the amount of acetic acid used was varied in 0, 0.5, 1.0, 1.5, 2.0, 2.3, 2.5 and 3.0 mL. The effects of the amount of acetic acid on cyclododecane oxidation are displayed in Figure 3.9.

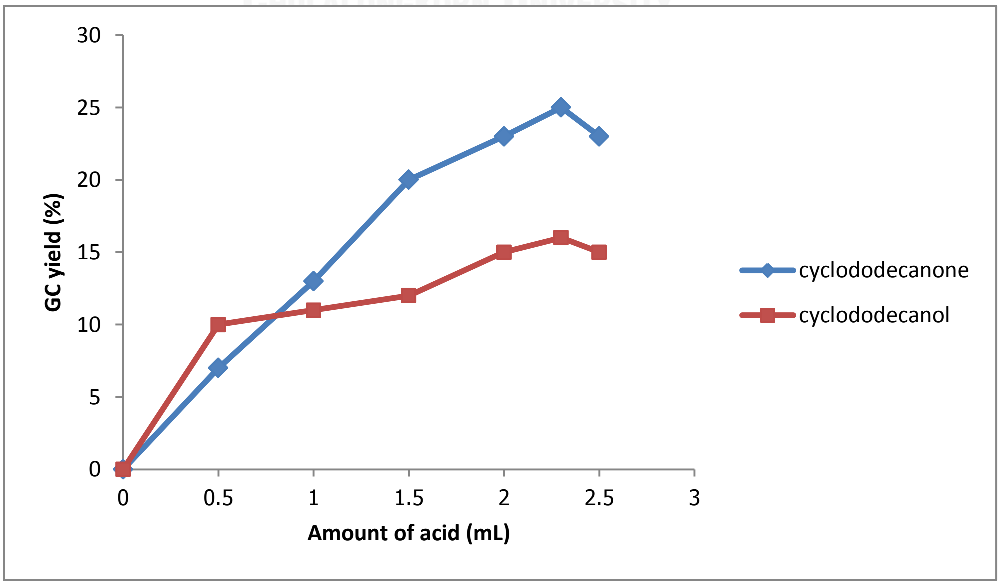


Figure 3.9 Effect of the amount of acetic acid on cyclododecane oxidation reaction

As shown in Figure 3.9, the observed result was the same trend as the effect of the amount of acetic acid on cyclohexane oxidation reaction. 2.3 mL of acetic acid used in this oxidation system gave the highest yield of cyclododecanone and cyclododecanol. For further study, 2.3 mL of acetic acid was used as proper amount of acid.

Considering from the amount of products achieved the search for other proper carboxylic acids were tried whether they can take the place of acetic acid in this oxidation system. It was clearly seen that acetic acid was still a suitable carboxylic acid among various carboxylic acids studied considered from the highest yield and selectivity (both ketone and alcohol) at 24 h. The effects of carboxylic acids are presented in Figure 3.10.

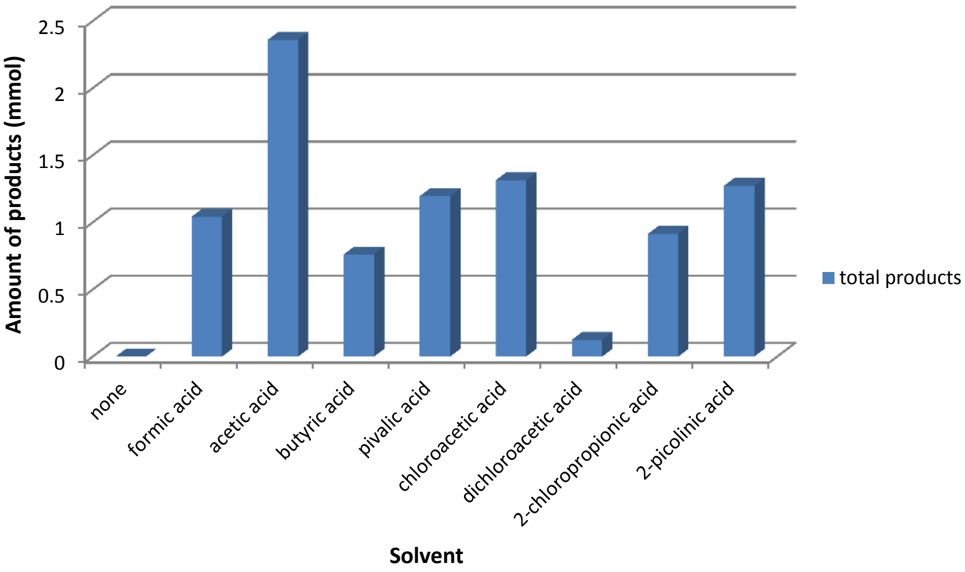


Figure 3.10 Effect of carboxylic acid on the oxidation reaction

From the results in previous study indicated that acetic acid was an important factor in this oxidation system. Other carboxylic acids were used instead but resulted in lessen amount of products. The stronger acid (comparing with acetic acid) such as chloroacetic acid, dichloroacetic acid, 2-chloropropionic acid and formic acid could accelerate zinc to dissolve easily in reaction mixture into homogeneous phase. As described before that if the dissolving time of zinc was shortened it would decrease the amount of desired products. In case of weaker acid (comparing with acetic acid), it could not dissolve zinc well resulted in small amount of products generated. In conclusion, acetic acid was the best one for this oxidation system.

3.3 Kinetic study on the oxidation of cyclododecane

Various catalytic systems attempt to improve the reactions to proceed at room temperature and atmospheric pressure. Nevertheless, the rates of these reactions are generally slow. [77] Therefore, the catalytic systems that consume less time to complete the reaction should be needed. The rate of cyclododecane oxidation catalyzed by VO(salophen) was studied and the results are displayed in Figure 3.11.

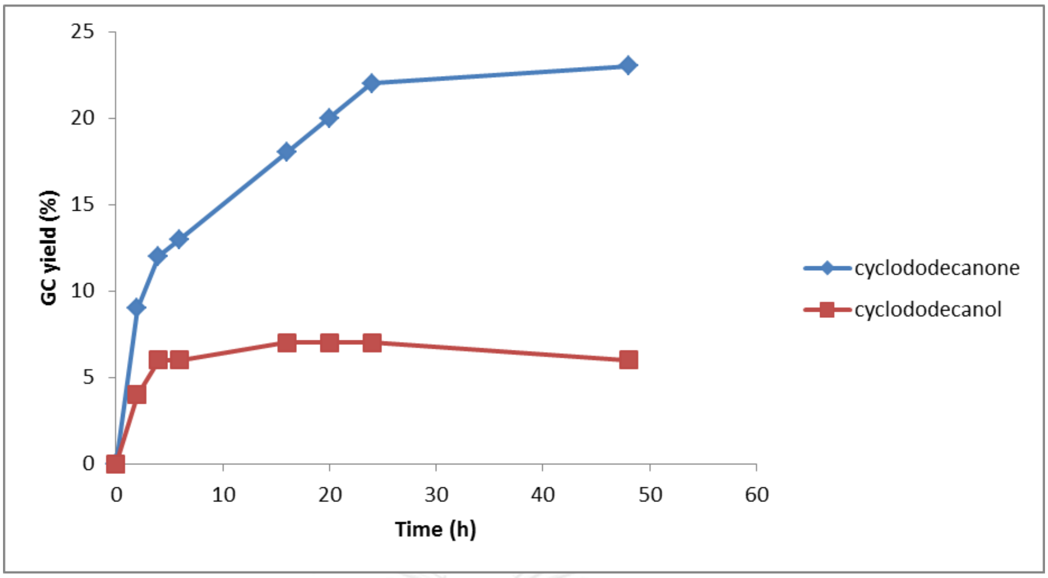


Figure 3.11 Kinetic study on cyclododecane oxidation catalyzed by VO(salophen)

From Figure 3.11, it was found that ketone was selectively obtained as a main product and occurred rapidly within 4 h. After that, cyclododecanone still increased within a period of time and started to be constant from 24 h until 48 h. In case of cyclododecanol, the yield was increased during the first period and became constant after 16 h. The half-life for ketone formation was 125 min. It can thus be concluded that this oxidation system consumed less time to gain the high yield of desired products and selectivity and the reaction was completed within 24 h. Comparing with a process described by Chemische Werke Huls, the oxidation of cyclododecane in the presence of trace of cobalt(II) carboxylate resulted in alcohol and ketone 5 to 1 ratio. [3] Other researches using Fe(III)-catalyzed functionalization of cyclododecane revealed that cyclododecanone and cyclododecanol were formed in different rates.

When using $FeCl_3 \cdot 6H_2O$, the half-life of ketone formation was 170 min. [78] Another literature revealed the cyclododecanone formation with half-life of 180 min catalyzed by $FeCl_2 \cdot 4H_20$. [79] If the half-life of ketone formation was less, it showed that the rate of reaction was faster than others. Therefore, this optimized system could enhance the rate of reaction comparing with previous literatures. The appropriate complex catalysts may assist the oxidation reaction to take place with satisfied rates and in some case may elevate the selectivity of reactions as required.

3.4 Chemoselectivity study on the oxidation of cyclododecane

Another feature that needs to be evaluated is chemoselectivity. The addition of an additive to the system would imply some clues for the studied system. The results are summarized in Table 3.3 and Figure 3.12.

Table 3.3 Chemoselectivity study on the oxidation of cyclododecane

Entry	**Additive**	**% yield at 24 h**			
		(none)	**(nol)**	**(none)+(nol)**	**(none)/ (nol)**
1	None	13	2	15	6.5
2	Absolute ethanol	12	3	15	4.0
3	Isopropanol	11	3	14	3.7
4	Ethylene glycol	10	2	12	5.0
5	Hydroquinone	6	8	14	0.8
6	2-Methylhydroquinone	5	9	14	0.6
7	2,3-Dimethylhydroquinone	5	11	16	0.4
8	*tert*-Butylhydroquinone	6	11	17	0.5
9	2,5-di-*tert*-Butylhydroquinone	5	13	18	0.4
10	Triethylamine	8	7	15	1.1
11	Aniline	4	7	11	0.6
12	*N,N′*-Dimethylaniline	3	0	3	-
13	*N,N′*-Dimethylacetamide	12	3	15	4.0
14	Anisole	12	3	15	4.0
15	Methyl benzoate	14	3	17	4.7
16	Ascorbic acid	13	9	22	1.4
17	Triphenylphosphine	8	14	22	0.6

Reaction conditions: cyclododecane (5 mmol), VO(salophen) (0.25 mmol), additive (5 mmol) pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

(none) cyclododecanone **(nol)** cyclododecanol

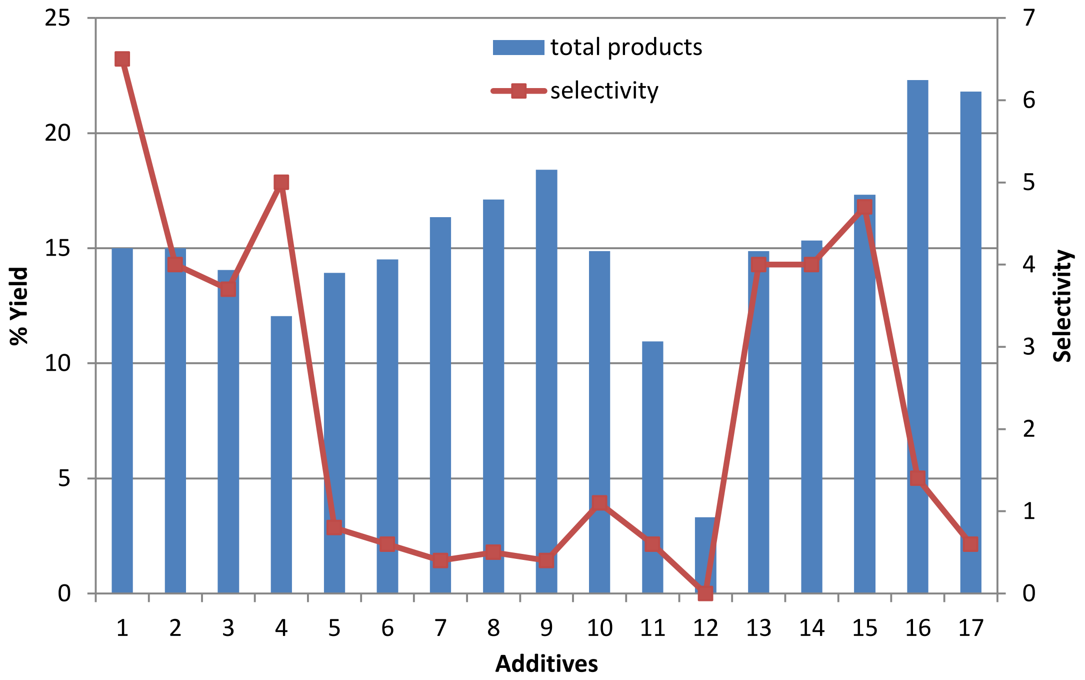


Figure 3.12 Chemoselectivity study

Sixteen compounds (entries 2-17) were used as an additive in cyclododecane oxidation reaction. It could be seen that oxidation process was still proceeded but in different extent of amount of oxidation product and selectivity. Besides entry 1 (none additive added) that gave highest selectivity, the (none)/(nol) ratio of some additives provided good selectivity of ketone formation especially the compounds that easily oxidizable. Conversely, the compounds that can act as reducing agent would increase amount of alcohol resulting in lower selectivity.

In the case of absolute ethanol, isopropanol and ethylene glycol (entries 2-4) which were known as easily oxidizable compounds, the activation process of cycloalkane still occurred to produce the corresponding ketone and alcohol comparing with the optimized oxidation system (entry 1). Total yield was slightly decreased when ethylene glycol was added. This investigation implied that the high valent intermediate generated should prevail the C-H bond oxididation of saturated hydrocarbons. Therefore, the proposed high valent oxovanadium intermediate was formed and selectively oxidized saturated hydrocarbon to their corresponding ketone and alcohol.

Another group of additives was hydroquinone and its derivatives. Those compounds were known to be easily transformed to quinones by various metal-catalyzed oxidation systems. [80] The addition of various substituted hydroquinones (entries 5-9) provided another interesting result. The oxidation of saturated hydrocarbon still occurred with increasing amount of alcohol. Therefore, it was clearly supported that the high valent oxovanadium intermediate should be responsible for the oxidation of saturated hydrocarbons over these additives. Nonetheless, the amounts of alcohol and total products were significantly increased especially in the presence of hydroquinones bearing electron donating groups. The increasing amount of cyclododecanol from this series of experiment also implied the presence of the second intermediate. To illustrate this, the second intermediate should be a species that could be reduced to alcohol in the presence of reducing agent. This possible species would believe to be hydroperoxide which was used to verify its occurrence in Gif-type oxidation system. [81]

In entries 10-11, the effects of amines such as trimethylamine and aniline were studied, the oxidation of cyclododecane was proceeded with higher amount of alcohol obtained. However, the addition of *N,N′*-dimethylaniline (entry 12) seriously affected on the oxidation process. The oxidation process of cyclododecane was lessened and produced cyclododecanone only 3% while none of cyclododecanol was detected. The oxidation reaction in the presence of acetamide group such as *N,N′*-dimethylacetamide in entry 13 could produce ketone more or less the same as normal oxidation in entry 1.

In addition, a test of a possible electron transfer mechanism, anisole and methyl benzoate (entries 14-15) were used. These compounds had slightly affected on the oxidation process. The oxidation of cycloalkane was still predominated, especially; in the presence of methyl benzoate the reaction still gave ketone in high yield.

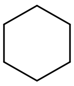
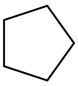
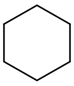
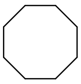
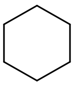
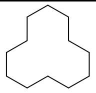
The next interesting additive was ascorbic acid, a well-known biochemical reductant. In the presence of this compound, the ketone to alcohol selectivity was decreased. This investigation clearly revealed that the addition of ascorbic acid had markedly affected to the oxidation process. The increasing amount of alcohol was derived from the transformation of hydroperoxide to alcohol by ascorbic acid. Another good reducing agent in this chemoselectivity study was triphenylphosphine (PPh_3). The yield of alcohol significantly increased while amount of ketone decreased when PPh_3 added. This results revealed that PPh_3 was selectively reduced the intermediate in reaction process resulted in alcohol formation.

From Table 3.3, the outcome from chemoselectivity study provided important clues for mechanistic study. The addition of various easily oxidizable compounds implied the presence of high valent oxovanadium species that responsible selectively for the activation of C-H of saturated hydrocarbons predominantly to the other functional groups. The results from the addition of reducing agents strongly supported the concept for the presence of second intermediate in the activation process, possibly alkyl hydroperoxide. As a conclusion, at least two distinct intermediates should be appearing along the pathway of the transformation from saturated hydrocarbons to ketones or alcohols.

3.5 Comparative study on relative reactivity of cycloalkane in oxidation reactions

Two competitive cycloalkanes; cyclohexane and either cyclopentane, cyclooctane or cyclododecane, respectively, were oxidized employing the general oxidation procedure. Relative reactivities of cycloalkanes are concluded in Table 3.4.

Table 3.4 Comparison of reactivity order per hydrogen for a series of cycloalkanes

R^1H	R^2H	Products (mmol)				Relative reactivity (R^2H/R^1H)
		2 h		24 h		
		R^1=O	R^2=O	R^1=O	R^2=O	
		0.9	0.8	1.4	0.9	0.76
		0.3	0.2	0.7	0.5	0.69
		0.3	0.5	0.7	1.1	1.62

Reaction conditions: substrates (5 mmol each), VO(salophen) (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

In 1963 and 1974, Huyser and Traynham reported that the relative reactivity of cyclopentane/cyclohexane was normally more than 1.0 when the reaction pathway occurred *via* radical reaction. [82, 83] Conversely, if that of cyclopentane/cyclohexane was less than 1.0, the reaction was proceeded by non-radical reaction. To justify whether the mechanism of the oxidation of cycloalkanes occurred *via* radical pathway, the comparison of relative reactivity order per hydrogen towards a series of cyclic saturated hydrocarbons was systematically studied. From Table 3.4, the relative reactivity of cyclopentane/cyclohexane was less than 1.0. Generally, cyclopentyl radical could occur faster than cyclohexyl radical to reduce ring strain, consequently, the relative reactivity was more than 1.0. In addition, if the reaction pathway occurred *via* radical reaction, the order of reactivity of the cycloalkanes toward hydrogen abstraction is cyclooctyl > cycloheptyl > cyclopentyl > cyclohexyl. Therefore, this oxidation reaction should proceed *via* non-radical pathway. Moreover, the relative reactivity was almost complied with the comparison relative reactivity in the oxidation of cycloalkanes catalyzed by iron catalyst (Gif-type system). [84] This study indicated that the proposed mechanism of this reaction occurred *via* non-radical reaction. [7]

3.6 Competitive studies on the oxidation of cycloalkane and alcohol

The oxidation reaction was carried out under the general procedure, but cyclohexane and cyclododecanol or cyclododecane and cyclohexanol were used as competitive substrates. The competitive studies on the oxidation between cyclohexane **(1)** and cyclododecanol **(6)** and *vice versa* between cyclododecane **(4)** and cyclohexanol **(3)** were examined and displayed in Table 3.5.

Table 3.5 Competitive studies on the oxidation of cycloalkane and alcohol

Substrates	Products (mmol)							
	2 h				24 h			
	(2)	**(3)**	**(5)**	**(6)**	**(2)**	**(3)**	**(5)**	**(6)**
(1)+(6)	trace	trace	1.2	5.4	3.6	1.9	1.3	5.6
(4)+(3)	0.5	1.8	0.2	0.07	0.7	1.7	0.5	0.2

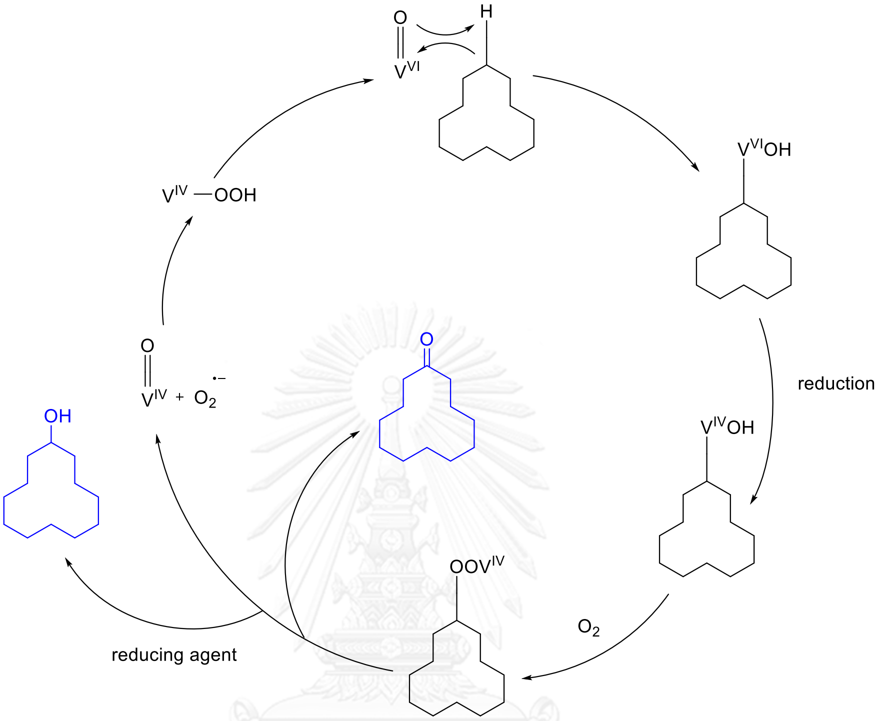
Reaction conditions: substrates (10 mmol each), VO(salophen) (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

(2) cyclohexanone **(3)** cyclohexanol **(5)** cyclododecanone **(6)** cyclododecanol

To confirm the assumption that the oxidized product derived from saturated hydrocarbon, competitive experiment was observed. Selected substrates were alkane and alcohol with different in number of carbon atoms. The competitive studies on the oxidation between cyclohexane-cyclododecanol and cyclododecane-cyclohexanol were explored. In general, alcohol can be oxidized to ketone easier than alkane since C-O bond is weaker than C-H bond. However, the results indicated that cycloalkanes (cyclohexane and cyclododecane) were still oxidized in this reaction system. Reaction between cyclododecane and cyclohexanol still gave oxidation products from cyclododecane. Similarly, the reaction between cyclododecanol and cyclohexane could give cyclohexanone and cyclohexanol. Therefore, it can be concluded that the corresponding ketone and alcohol could occur from alkane substrate in this optimized system. These results revealed that the oxidation reaction catalyzed by oxovanadium(IV) Schiff's base complexes was selectively functionalized to alkane. The competitive study confirmed that high valent V^{VI}=O intermediate was accountable for the transformation from alkane to ketone.

3.7 Mechanistic study

The clues for mechanistic pathway derived from chemoselectivity study, the comparative study on relation reactivity of cycloalkanes in the oxidation reaction demonstrated that this saturated hydrocarbon oxidation proceeded *via* non-radical pathway. The mechanism was proposed as that of Gif-type systems in Scheme 3.1. [7]



Scheme 3.1 Proposed mechanistic pathway for oxovanadium(IV)-catalyzed cycloalkane oxidation

Firstly, zinc surface was activated by acetic acid resulted in Zn(0) that could reduce O_2 in atmosphere to produce superoxide which was believed to be the real oxidizing agent. Then, superoxide reacted with catalyst and high valent oxovanadium V^{VI}=O intermediate was formed. The high valent species were coordinated with cycloalkane substrate and finally alkyl hydroperoxide was generated. After that, ketone and alcohol were yielded as oxidation products.

Conclusion of the developed system

The oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in zinc-pyridine-acetic acid system under O_2 atmospheric pressure was optimized in this part. Ketone was selectively achieved as a main product. The proposed mechanism was proceeded *via* non-radical reaction. High valent oxovanadium $V^{VI}=O$ intermediate was selectively responded for C-H oxidation of alkane to ketone or alcohol more than other functional groups.

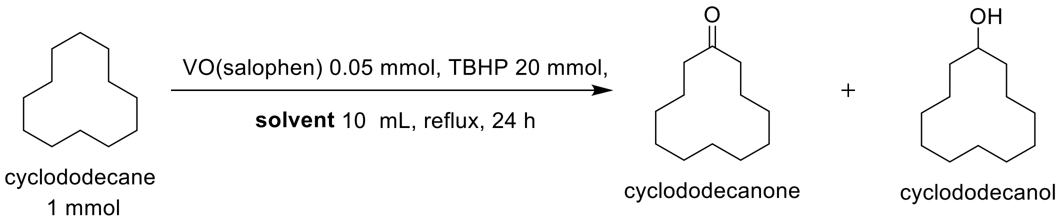
Part 2 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in peroxide system

H_2O_2 and TBHP have been well-known to be employed in metal catalyzed process as an efficient oxidizing agent. [85] In previous literature, saturated hydrocarbons can be selectively converted into the corresponding ketones or alcohols in the absence of solvent using a combination of TBHP and catalytic amount of Fe(III) and Cu(II) complexes. [86] In this part, H_2O_2 and TBHP were used instead of zinc/O_2 system. VO(salophen) was used as catalyst at atmospheric pressure around 80°C in selected solvent system.

3.8 Optimum condition for cyclododecane oxidation

3.8.1 Effect of solvent

In this peroxide system, the solvent that could provide homogenous reaction was required. Another solvent was seeked to employ instead of pyridine. Selected solvents used in this study were referred from the results in part 1 and other literatures reviews. The other factors were controlled and the effects of solvent are presented in Figure 3.13.



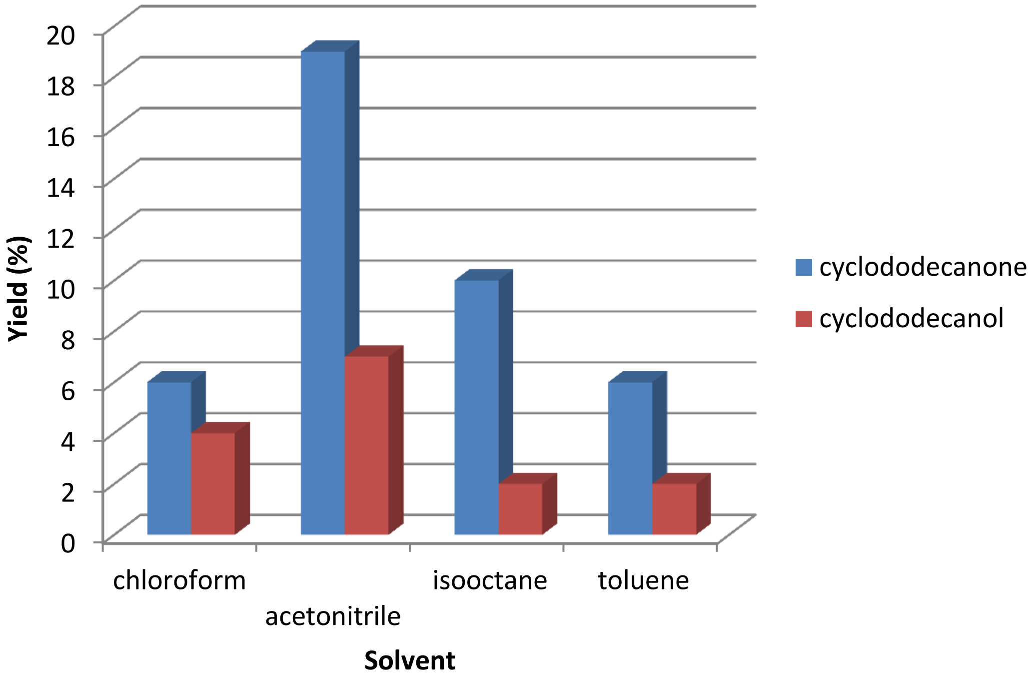


Figure 3.13 Effects of solvent

The yield of products was dependent on solvent. Four kinds of solvents were used as summarized in Figure 3.13. CH_3CN gave the best yield (18%) and selectivity of ketone to alcohol ratio (5.7) for cyclododecane oxidation. For H_2O_2 system, the results showed the same trend as TBHP system that CH_3CN was the best solvent of choice. Therefore, next study CH_3CN was selected as proper reaction media. Saussine *et al*. using cobalt(III) alkylperoxy complexes catalyzed the oxidation of hydrocarbons with TBHP and hydroxylated product was selectively occurred. [73] Another TBHP system reported that alkane oxidation reactions in CH_3CN catalyzed by binuclear manganese and iron complexes were produced oxygenated products unselectively. [75] Furthermore, alkane oxidation with H_2O_2 catalyzed homogeneously in CH_3CN by vanadium-containing polyphosphomolybdates was investigated by Fink. [87] The alcohol products were selectively generated in system.

3.8.2 Effect of the amount of catalysts

The amount of catalyst was another crucial parameter that needed to be evaluated. The results of the amount of catalyst of both TBHP and H_2O_2 system in cyclododecane oxidation are displayed in Figures 3.14 and 3.15, respectively.

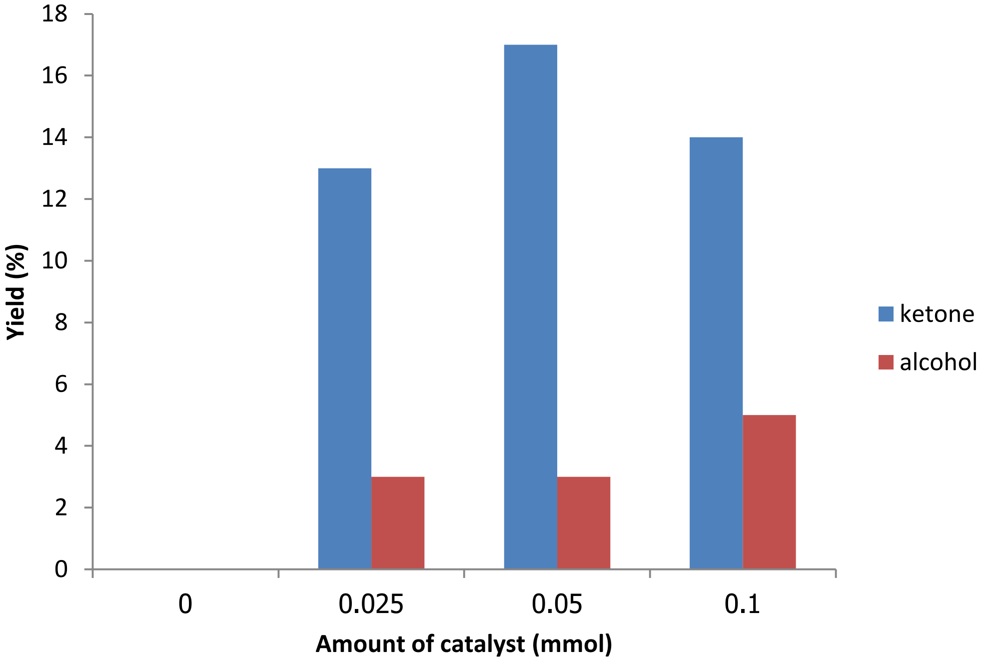


Figure 3.14 Effects of amount of catalyst in TBHP system

Using VO(salophen) 0.05 mmol gave the highest reaction yield (17%) and highest selectivity of ketone to alcohol ratio (5.6) compared with 0.025 and 0.1 mmol of catalyst. When the amount of catalyst was less or more than 0.05 mmol, the reaction rate decreased. With the excess or lack of VO(salophen), lower yield was obtained. Therefore, the amount of proper catalyst was important. The excess of catalyst used may cause side oxidation reactions occur competitively with cyclododecane oxidation.

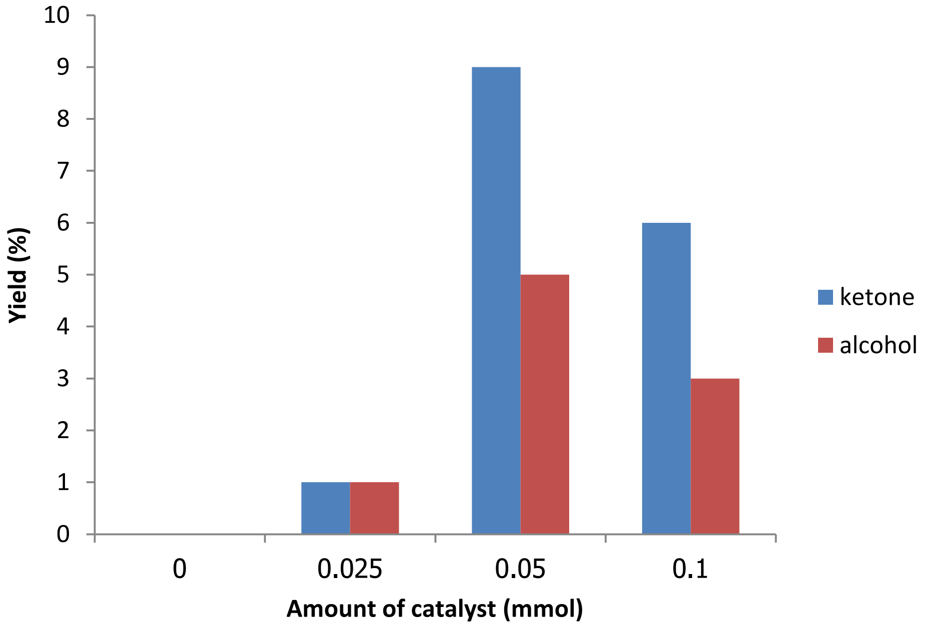


Figure 3.15 Effects of the amount of catalyst in H_2O_2 system

For H_2O_2 system, using VO(salophen) 0.05 mmol gave the highest reaction yield (9%) and highest selectivity of ketone to alcohol ratio (1.8) compared with 0.025 and 0.1 mmol catalyst used. The difference between these two commercial peroxides was when the amount of catalyst used in H_2O_2 system was zero or less than 0.05 mmol, the reaction occurred in decreasing rate. It could be seen in Figure

3.15 that small amount of products generated. The decreased rate showed in reducing yield of desired products in every varied amount of catalyst.

3.8.3 Effect of type and amount of oxidant

As clearly manifested in part 1 that Zinc had a crucial role as a producer of oxidant. Therefore type and amount of both TBHP and H_2O_2 were investigated to determine whether they affected on yield and selectivity. The resulted are accumulated in Table 3.6.

Table 3.6 Effects of type and amount of oxidant

Entry	Oxidant (mmol)	Temp (°C)	Amount of oxidant (mmol)	Yield (%)		Ratio of none/nol
				(none)	(nol)	
1	70% TBHP	reflux	10	7	10	0.70
2			15	15	4	3.75
3			20	16	3	5.33
4	30% H_2O_2	RT (35)	10	4	6	0.67
5			15	10	7	1.43
6			20	9	5	1.80

Reaction conditions: cyclododecane (1 mmol), catalyst (0.05 mmol), 70% TBHP or 30% H_2O_2, CH_3CN 10 mL, reflux 24 h

Using different oxidant could give different results of yield and selectivity. From Table 3.6, comparing the use of TBHP (entries 1-3) with H_2O_2 (entries 4-6), TBHP system gave higher yield (19%) of desired products and selectivity (5.3). Major product was ketone in both systems. The selectivity and product yield were better when the amount of oxidant in the system increased. Consideration reaction temperature, TBHP system was needed to heat up around $80^{\circ}C$ because at that temperature TBHP dissociated to active radical that should react with another compound afterward. If reaction heated up more than $80^{\circ}C$, the desired products were decreased. These might be due to thermal decomposition of TBHP. On the other hand, the oxidation reaction at room temperature was investigated in TBHP system and reaction could not proceed. In H_2O_2 system, the reaction could occur at room temperature. The same reason with TBHP that the reaction temperature should suitable for the oxidant used in system, H_2O_2 can dissociate to active radical at room temperature ($35^{\circ}C$), so this reaction proceeded easily at room temperature. Conversely, using high temperature could be resulted in thermal decomposition of H_2O_2 and less amount of products were achieved. The oxidation temperature was important and related to oxidant used in system as mentioned before by Monfared.[88] When the oxidation system was heated, there was a lower conversion due to the decomposition of H_2O_2.

3.9 Kinetic study: oxidation of cyclohexane

To understand the rate of the oxidation reaction of cycloalkane in peroxide system, cyclohexane was used. Cyclododecane could give an explanation about kinetic study but for peroxide system the rate of cyclododecane oxidation was slower than that as seen in Table 3.6, especially in H_2O_2 system. Therefore, cyclohexane was used to clarify the study on the rate of this oxidation system.

Kinetic studies of cyclohexane oxidation in TBHP system are presented in Figure 3.16. Rate of reaction was fast in first 2 h and continuously increased until 16 h and kept constant afterward. Although cyclohexanone was a major product but cyclohexanol increased in the same trend of ketone. Alcohol was produced in parallel with ketone in first 2 h and continuously increased until 16 h and then started to keep constant. Half-life for ketone and alcohol formation was 120 min.

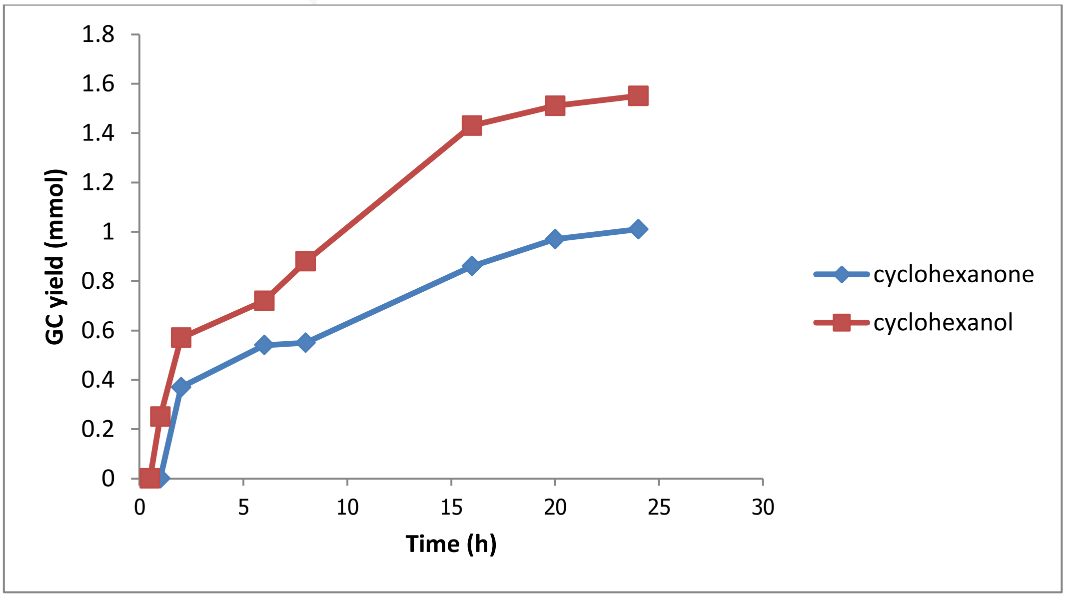


Figure 3.16 Kinetic study of cyclohexane oxidation in TBHP system

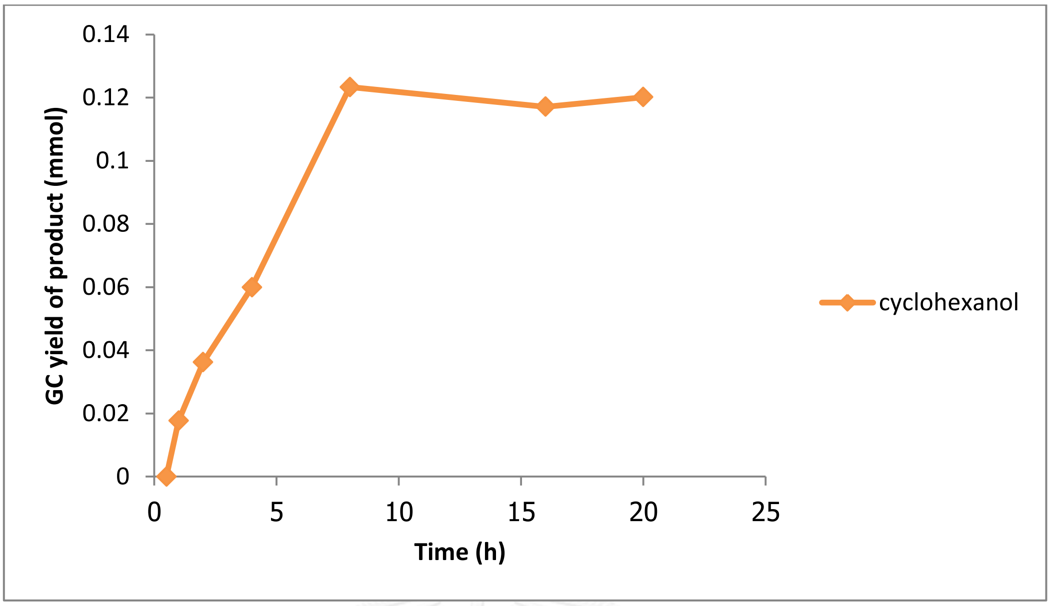


Figure 3.17 Kinetic study of cyclohexane oxidation in H_2O_2 system

For the kinetic study in H_2O_2 system in Figure 3.17, no cyclohexanone was observed. It was surprisingly that cyclohexanol was selective as a product of the oxidation reaction. Selectivity of this system was 100% and the yield was increased rapidly within 6 h. Half-life for alcohol formation was 240 min. Comparing with TBHP system, the rate of reaction was faster than that in H_2O_2 system. In first 2 h, the oxidation in TBHP system gave cyclohexanol 0.4 mmol while in H_2O_2 system yielded alcohol only 0.04 mmol. This study was supported the result of cyclododecane oxidation in section 3.8.3 that using TBHP was more effective than H_2O_2. In case of cyclohexane oxidation, the chosen oxidant gave different results completely. If a main objective was selectivity, H_2O_2 should be an appropriate oxidizing agent in peroxide system.

3.10 Comparison of three oxidation systems for saturated hydrocarbons

Another important topic that needs to be evaluated is the comparison of three systems of cyclododecane oxidation. The results are summarized in Table 3.7.

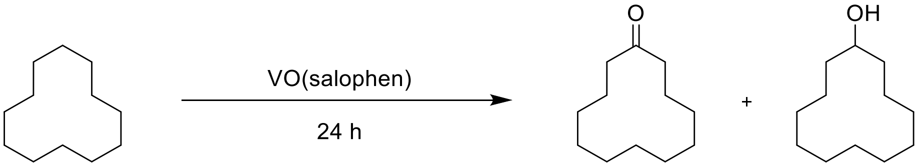


Table 3.7 Effects of oxidizing agent

Entry	Oxidizing agent (mmol)	Temp (°C)	Solvent	% Yield (none)	% Yield (nol)	Ratio of none/nol
1	70% TBHP (20)	Reflux	CH_3CN	17	3	5.67
2	30% H_2O_2 (20)	RT (35)	CH_3CN	10	6	1.67
3	zinc/acetic acid/O_2 (20)	RT (35)	Pyridine	22	7	3.14

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP, 30% H_2O_2 or zinc/acetic acid/O_2, CH_3CN 10 mL, 24 h

As assessed from Table 3.7, the amount of oxidizing agent was fixed as 20 mmol. From each optimized condition, the third entry (zinc/acetic acid/O_2 system) gave the best yield of desired products. Considering selectivity for ketone to alcohol ratio, the highest selectivity was achieved from TBHP system. For H_2O_2 system, both total yield of product and selectivity were the lowest. Comparing with another literature in 1993, cyclohexane was oxidized by $[VO_3]^-$/Hpca/H_2O_2/O_2 system resulting in a mixture of cyclohexyl hydroperoxide, cyclohexanol and cyclohexanone with the total product yield of 35%. [52] In 2001, alkane oxidation with H_2O_2 catalyzed homogeneously by vanadium-containing polyphosphomolybdates was investigated. Various alkanes could be oxidized by H_2O_2 in CH_3CN. The oxidation of cyclooctane at 60 °C in CH_3CN gave within 9 h oxygenates with low yields. [53] In 2003 Shul’pin and co-workers showed that $[VO_3]^-$/Hpca system also exhibited moderate activity in the aerobic oxidation of alkanes under mild conditions, but required the presence of reducing agents such as ascorbic acid or zinc. [54] Compared with previous literature, this developed oxidation system was effective for the selective oxidation of saturated hydrocarbons.

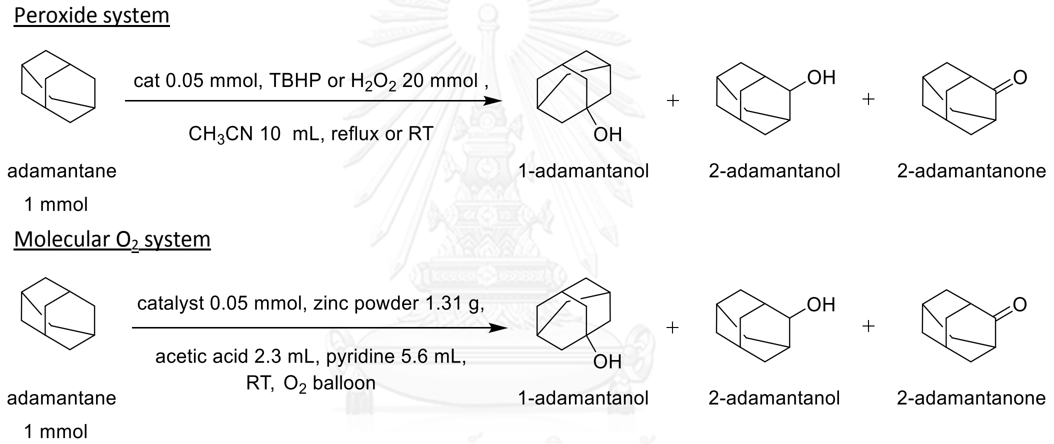
The comparison of three oxidation systems of cyclododecane demonstrated that zinc-pyridine-acetic acid-O_2 system gave the best yield of corresponding ketone and total yield of desired products. Considering the selectivity of ketone to alcohol ratio, the highest selectivity was achieved from TBHP system.

3.11 Selectivity study

3.11.1 Oxidation of adamantane

Another interesting substrate that should be investigated was adamantane. Previous model substrates (cyclohexane and cyclododecane) contained only secondary carbon (2° C). Adamantane consists of 16 hydrogen and 10 carbon atoms and can be described by only two sites as tertiary carbon (3° C) 4 equivalent sites and secondary carbon (2° C) 6 equivalent sites.

The oxidation of adamantane was explored in three systems: TBHP, H_2O_2 and zinc/acetic acid/O_2 systems. Optimized conditions for three systems are shown below.



The expected products from the oxidation reaction were 1- and 2-adamantanol and 2-adamantanone. 1-Adamantanol was an alcohol product at 3° C while 2-adamantanol and 2-adamantnone were alcohol and ketone products at 2° C, respectively. If the reaction proceeded smoothly, three oxidation products should be observed. Selectivity was measured in terms of 2° C to 3° C oxygenated product ratios. The results are summarized in Table 3.8.

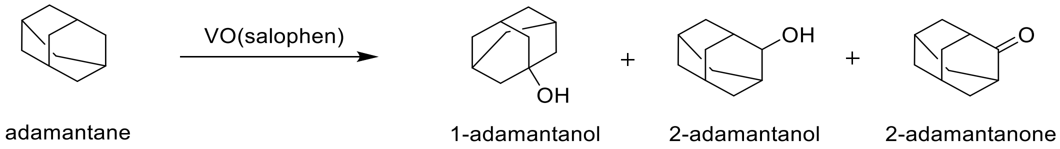


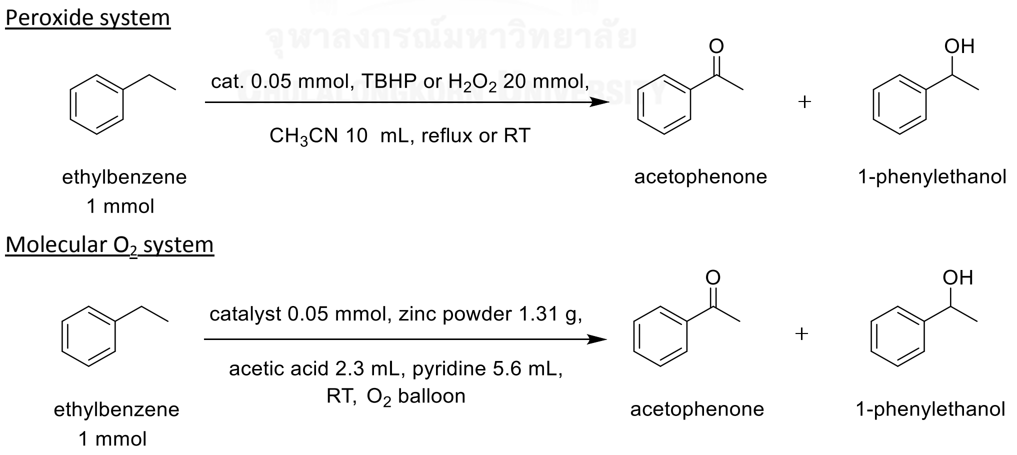
Table 3.8 Oxidation of adamantane

Entry	Oxidizing agent (mmol)	Temp (°C)	Solvent	% Yield			Ratio of C2/C3
				2-none	1-nol	2-nol	
1	70% TBHP (20)	Reflux	CH_3CN	9	23	2	0.16
2	30% H_2O_2 (20)	RT (35)	CH_3CN	4	6	3	0.39
3	zinc/acetic acid/O_2 (20)	RT (35)	pyridine	10	2	2	2.00

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP, 30% H_2O_2 or zinc/acetic acid/O_2, CH_3CN 10 mL, 24 h

The oxidation of adamantane in three systems gave different results in yield of products and C2/C3 ratio of oxygenated product. Considering about position of C-H bond that could be oxidized without concerning of functional group, in TBHP system, 2° C-H oxidized products (11%) were obtained less than 3° C-H oxidized products (23%). Adamantane molecule has twelve 2° C-H bonds and four 3° C-H bonds. Therefore, 3° C oxidized products per 3° C-H bond was 5.75 and 2° C oxidized products per 2° C-H bond was 0.92. In conclusion, it was revealed 0.16 C2/C3 ratio of oxygenated product. Radical reactions involving free radicals show a C2/C3 ratio between 0.05 to 0.15. For example, Fe(II)-Y catalyzed adamantane oxidation in TBHP system, the C2/C3 ratio (0.05-0.30) is closest to the expected C2/C3 ratio for radical reactions. [89] For H_2O_2 systems, 1-adamantanol was also major product with 0.39 C2/C3 ratios. While that in peroxide systems preferred the oxidation at 3° C, the oxidized product in zinc/acetic acid/O_2 was selectively occurred at 2° C. The ratio of C2/C3 of oxygenated product was 2.0. The difference of C2/C3 ratio in peroxide and zinc/acetic acid/O_2 system implied the different mechanistic pathway of oxidation reaction.

3.11.2 Oxidation of ethyl benzene



Ethyl benzene is important in petrochemical industry as an intermediate in the production of styrene, the precursor to polystyrene, a common plastic material. Ethyl benzene has two types of carbons as 1° and 2° C therefore the oxidation would give different ketone or alcohol or aldehyde. The expected products might be the one that was oxidized at benzylic position.

Selectivity was measured in terms of ketone to alcohol ratio. The results of the oxidation of ethyl benzene are displayed in Table 3.9.

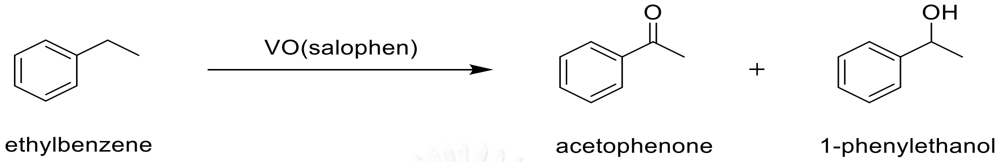


Table 3.9 Oxidation of ethyl benzene

Entry	Oxidizing agent (mmol)	Temp (°C)	Solvent	% Yield		Ratio of none/nol
				(none)	(nol)	
1	70% TBHP (20)	reflux	CH_3CN	14.0	4.0	3.5
2	30% H_2O_2 (20)	RT (35)	CH_3CN	8.3	1.1	7.5
3	zinc/acetic acid/O_2 (20)	RT (35)	pyridine	3.0	1.3	2.3

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP, 30% H_2O_2, zinc/acetic acid/O_2, CH_3CN 10 mL, 24 h

(none) acetophenone **(nol)** 1-phenylethanol

For the oxidation of ethyl benzene, the major product was acetophenone while the minor was 1-phenylethanol. The reaction product at 1° C was not detected. The selectivity was around 2 to 7, especially in H_2O_2 system gave the best selectivity for ketone formation. This reaction alternatively oxidized at 2° benzylic position. In this case, carbon radical at benzylic position was very reactive resulting in the oxidation taken place at this position. Nevertheless, zinc/acetic acid/O_2 system seemed not to be a good system for ethyl benzene oxidation considering from %yield of products obtained in 24 h.

From the investigation of these two alkanes, it can be concluded that the reaction in peroxide system occurred selectively at 3° more than 2° and 1° C, respectively. The assumption was an intermediate of reaction was carbon radical. Generally, 3° carbon radical is more stable than 2° carbon radical indicated that 3° C-H bond was more reactive than 2° C-H bond. Moreover, according to bond dissociation energy (BDE) of C-H bond, 1° C-H bond was the strongest bond and 3° C-H bond was the weakest. Therefore, the results were supported that selective oxidation in peroxide system occurred *via* radical pathway.

In conclusion, the oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in peroxide system was selectively produced ketone. Therefore, these three catalytic systems (TBHP, H_2O_2 and O_2) revealed the unique characteristics for ketone formation as a major product together with small amount of accompanying alcohol.

Conclusion of the developed system

VO(salophen) acted as efficient catalyst in saturated hydrocarbon oxidation in TBHP and H_2O_2 system. The developed system revealed that ketone was selectively as a major product. Comparing two types of peroxide, TBHP displayed a better catalytic activity more than H_2O_2. For selectivity study of adamantane and ethyl benzene, it can be concluded that reaction in peroxide system occurred *via* radical process.

Part 3 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in peroxide system

Besides oxovanadium(IV) Schiff's base complexes, oxovanadium bearing picolinic acid and its derivatives have been interested with regard to their oxidizing properties. In fact, the well-characterized V(V) peroxo complexes, e.g., $[(Dipic)VO(O_2)\cdot H_2O]^{-}NH_4^{+}$ [90], $[VO(O_2)_2NH_3]^{-}NH_4^{+}$ [90] and related complexes, [91-93] are anionic species and generally insoluble in organic solvents. However, vanadium compounds have been widely used as catalysts for the oxidation of olefins by H_20_2 or ROOH. [94, 95] They are generally less efficient and selective catalysts than molybdenum compounds for the epoxidation of unactivated olefins, [96] but highly active and selective for allylic alcohol. [97] This part focused on the oxidation reaction catalyzed by the synthesized oxovanadium(IV) picolinate complexes in TBHP system.

3.12 Oxidation of cyclododecane catalyzed by oxovanadium(IV) picolinate complexes

The efficiency of prepared $VO(pic)_2$, a non-ligated catalyst ($VOSO_4\cdot 5H_2O$) and a commercially available catalyst vanadyl acetylacetonate ($VO(acac)_2$) was comparatively examined for the oxidation of cyclododecane.

Among three oxovanadium(IV) complexes, the prepared $VO(pic)_2$ exhibited the highest activity. Cycloalkane could be oxidized in the presence of this catalyst better than $VOSO_4{\cdot}5H_2O$. Comparing with $VO(acac)_2$, the synthesized catalyst also gave higher yield of the desired product than the commercial one as exhibited in Figure 3.18.

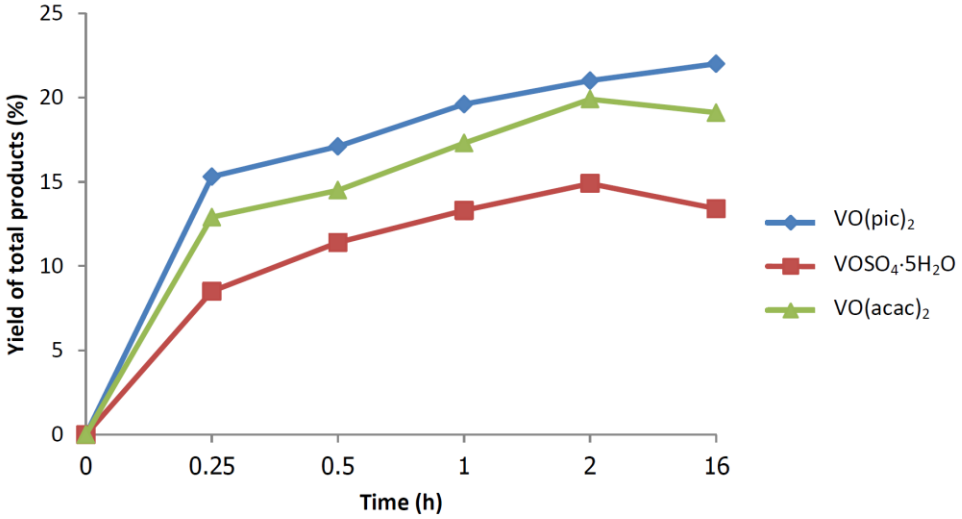


Figure 3.18 Effect of catalyst on the oxidation of cyclododecane

The results demonstrated that synthetic complex was an efficient catalyst. As described before that electron-withdrawing interaction with the vanadium exhibited positive potentials whereas electron-donating interactions led to negative potentials.[32] Therefore, oxovanadium bearing picolinate ligand gave higher activity than acetylacetonate ligand and sulfate, respectively due to its electron-withdrawing interactions with vanadium.

Further study on the comparison among three systems (TBHP, H_2O_2 and zinc/acetic acid/O_2) and three types of complex catalysts (VO(acac)$_2$, VO(pic)$_2$ and VO(salophen)) were explored. The results are presented in Table 3.10 and Figure 3.19.

Table 3.10 Effect of catalyst on the oxidation of cyclododecane in three systems

Entry	Catalyst	System	Yield (%)		Ratio of none/nol
			(none)	(nol)	
1	VO(acac)$_2$	30% H_2O_2	7.4	5.6	1.32
2		zinc/acetic acid/O_2	17.5	5.4	3.24
3		70% TBHP	12.6	4.3	2.93
4	VO(pic)$_2$	30% H_2O_2	1.4	0.7	2.00
5		zinc/acetic acid/O_2	26.2	8.1	3.23
6		70% TBHP	20.2	4.7	4.30
7	VO(salophen)	30% H_2O_2	9.8	5.4	1.81
8		zinc/acetic acid/O_2	21.7	6.9	3.14
9		70% TBHP	17.1	3.1	5.52

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP (20 mmol), 30% H_2O_2 (20 mmol) or zinc/acetic acid/O_2 (20 mmol), 24 h

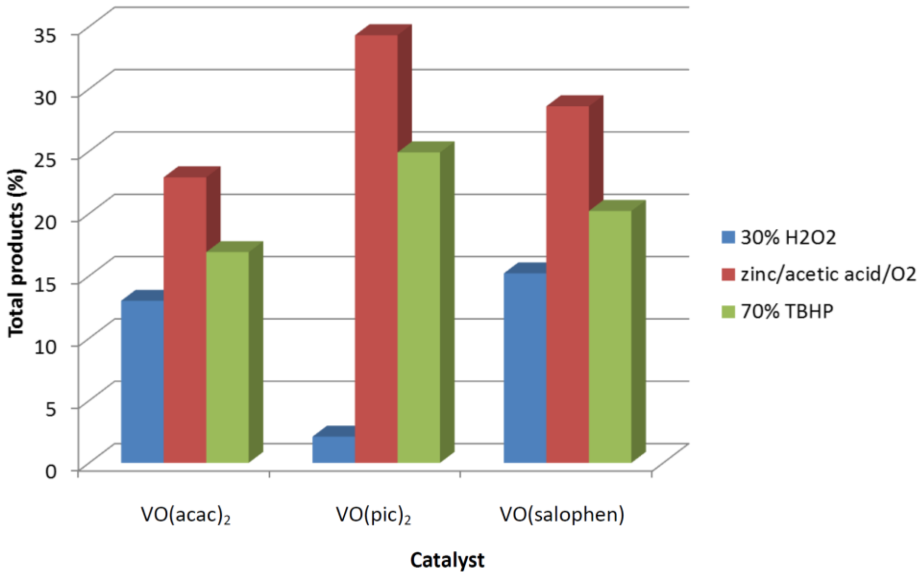


Figure 3.19 Effect of catalyst on the oxidation of cyclododecane in three systems

VO(pic)$_2$ gave the highest yield in both TBHP (24%) and zinc/acetic acid/O_2 (34%) systems. VO(salophen) provided the yield of desired products in higher value than H_2O_2 system but lower than VO(pic)$_2$. VO(acac)$_2$ exhibited as the lowest efficient catalyst among three different complexes. It can be noted that in H_2O_2 system VO(pic)$_2$ was not efficient catalyst that gave very small amount of corresponding ketone (1.4%) and alcohol (0.7%). Due to the interactions between ligand and vanadium, VO(pic)$_2$ and VO(salophen) reactivity were higher than VO(acac)$_2$. Comparing oxovanadium bearing N,O-ligand between VO(pic)$_2$ and VO(salophen), picolinate ligand had electron-withdrawing interactions to vanadium higher than salophen ligand. Consequently, VO(pic)$_2$ acted as catalyst more effective than VO(salophen).

Considering the selectivity of ketone to alcohol formation, in TBHP system both $VO(pic)_2$ and VO(salophen) contributed high selectivity in entries 6 and 9 (Table 3.10). In H_2O_2 system, using of any oxovanadium complexes showed the lowest selectivity of ketone to alcohol product in every case. For zinc/acetic acid/O_2 system, the selectivity was moderate between those two systems. In the past decade, Mimoun found that the oxidation of cyclohexane by $(pic)VO(O_2)\cdot 2H_2O$ gave cyclohexanol as a major product. [33] Shul'pin and others later reported several effective vanadium catalyst systems. [54] Mechanistic studies suggest that the free hydroxyl/alkoxy radical was the active oxidant in many of these C–H oxidation reactions. [55] With modest yields and selectivities, the synthetic utility of most reported vanadium catalysts is rather limited.

3.13 Kinetic study

This research focuses on the use of $VO(pic)_2$ as catalyst on the oxidation of cyclododecane in peroxide system. From previous study that TBHP was more efficient oxidant than H_2O_2 therefore the selected oxidant used for further study would be TBHP. The results are presented in Figure 3.20.

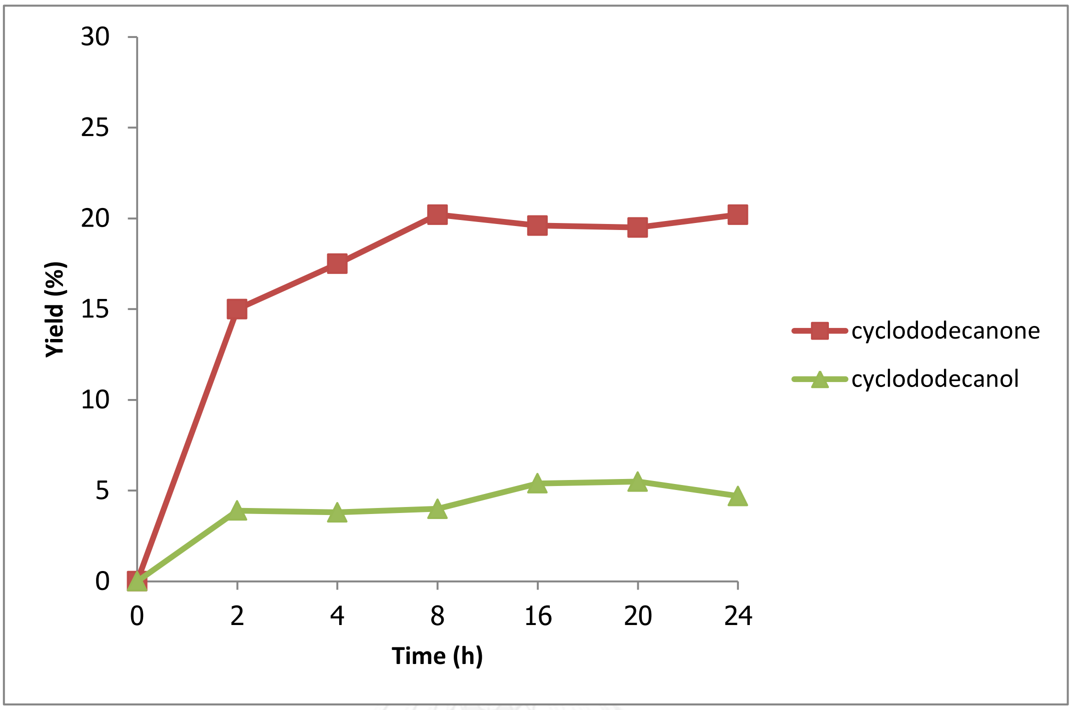


Figure 3.20 Kinetic study of the oxidation of cyclododecane catalyzed by $VO(pic)_2$

From Figure 3.20, cyclododecanone was selectively obtained as a main product and occurred rapidly within 2 h. Cyclododecanol also produced in the first 2 h, but less than cyclododecanone and slightly increased until 24 h. From this kinetic study, it implied that ketone and alcohol were generated in parallel pathway. Half-life of ketone and alcohol formation was 80 min. Comparing with VO(salophen) catalyzed oxidation reaction in TBHP system in part 2, it was observed that rate of cycloalkane oxidation catalyzed by $VO(pic)_2$ was faster than the reaction catalyzed by VO(salophen). Another work reported that the oxidation of cycloalkane catalyzed by vanadium peroxo complexes provided low yield of alcohol within 4-5 h. [33] Kozlov also studied about zeolite-encapsulated vanadium picolinate peroxo complexes active for catalytic hydrocarbon oxidations using H_2O_2 in CH_3CN and found that alcohol was a major product with low yield in 24 h. [98]

3.14 Optimum condition for cyclododecane oxidation

3.14.1 Effect of the amount of catalysts

The amount of catalyst was an important parameter that needed to be evaluated. $VO(pic)_2$ was selected as a catalyst and cyclododecane was used as a model substrate. The other parameters were controlled to be constant and the effects of the amount of catalyst are displayed in Figures 3.21.

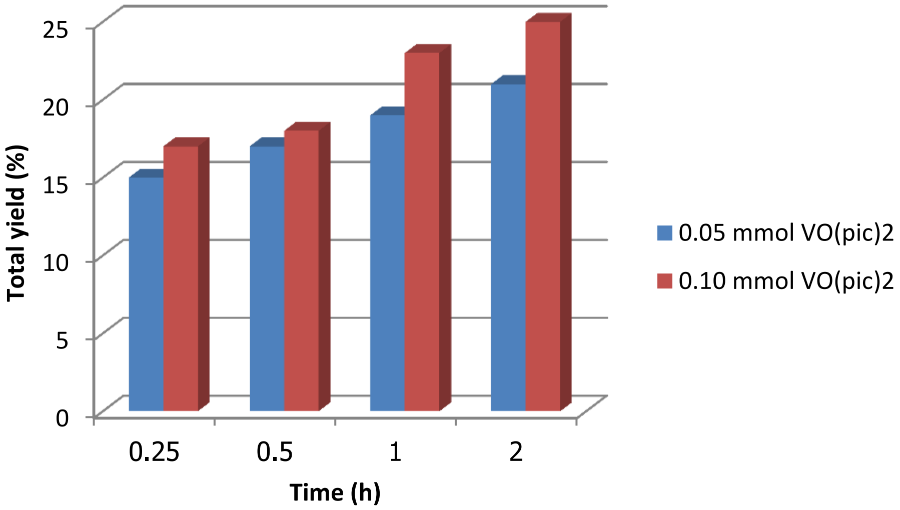


Figure 3.21 Effect of the amount of catalysts

It was found that the increased amount of catalyst did not affect to %yield of products significantly. When increasing amount of catalyst, yield of product was increased only 2-3%. Therefore, 0.05 mmol of VO(pic)$_2$ per 1 mmol of substrate was sufficient for this oxidation system.

3.14.2 Effect of amount of oxidant

As clearly seen in previous study that TBHP had a crucial role and affected to the yield of desired products. Therefore the amount of TBHP was explored to examine its effect on yield and selectivity. The results are presented in Figure 3.22.

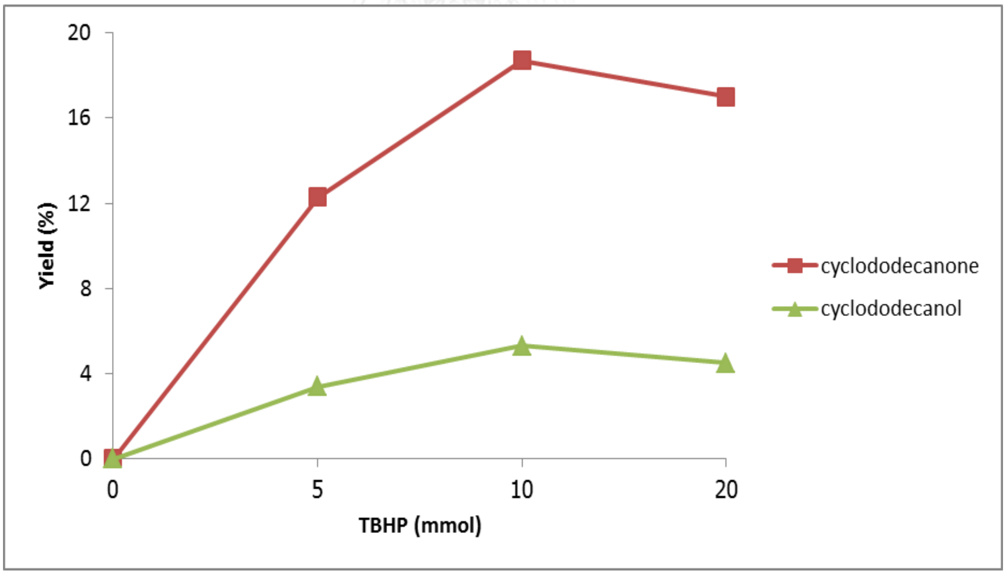


Figure 3.22 Effect of amount of TBHP on oxidation of cyclododecane

Considering from product yield observed in reaction, the yield was higher when amount of TBHP increased. The excess amount of oxidant was slightly reduced total amount of products. It revealed that the appropriate amount was 10 mmol.

3.14.3 Effect of solvent

Another important feature that needs to be evaluated is the selectivity. The selectivity of this system was dependent on solvent. Nine solvents were used as summarized in Table 3.11.

Table 3.11 Variation of solvent

Entry	Solvent	Yield (%)		none/nol ratio
		(none)	(nol)	
1	CH_3CN	19.6	4.6	4.26
2	$CHCl_3$	9.2	10.3	0.89
3	isooctane	3.5	2.3	1.52
4	CH_2Cl_2	6.2	5.1	1.22
5	CH_3OH	-	-	-
6	$C_2H_4Cl_2$	8.2	3.4	2.41
7	CH_3COCH_3	12.1	3.8	3.18
8	CCl_4	5.0	3.6	1.39
9	THF	-	-	-

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP (10 mmol), solvent 10 mL, reflux 2 h

To explore the effect of solvent on the yield of desired products and selectivity, the results are presented in Figure 3.23.

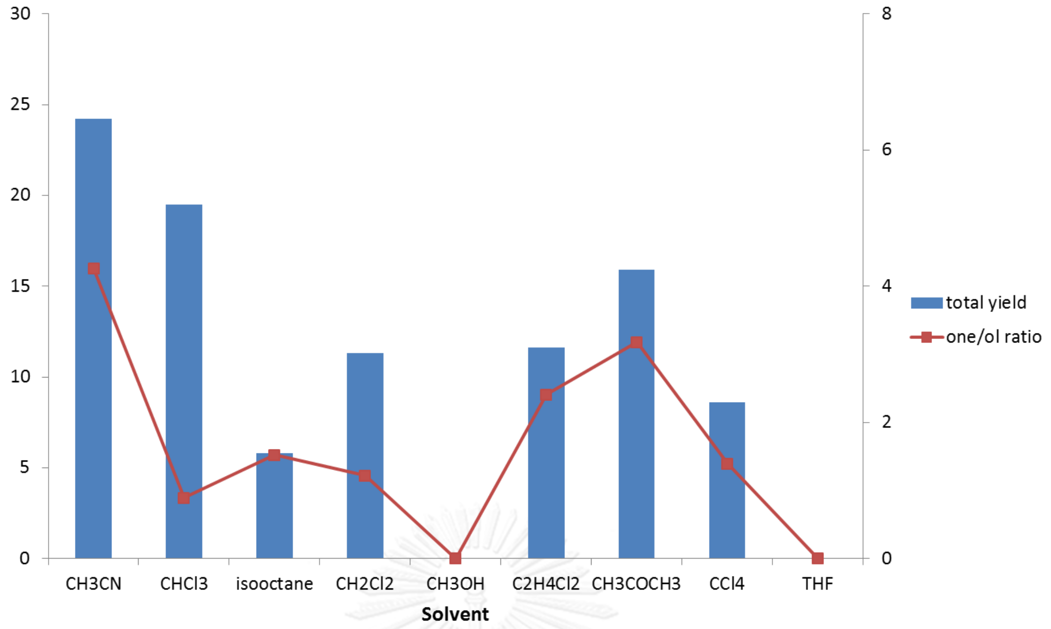


Figure 3.23 Effect of solvent on oxidation of cyclododecane

CH_3CN gave the highest total yield (24%) and best selectivity (4.26) for ketone formation. Using too high polar solvent, the oxidation did not occur. When using low polar solvent, both yield and selectivity were decreased. The appropriate reaction media was moderate to high polar solvent. The proper solvent system could act as reaction media that enhanced the selectivity of product formation. In this case, CH_3CN was suitable for ketone formation. Another literature reported that the conversion was affected from solvent system. [88] The results also showed that CH_3CN was the best solvent with oxovanadium hydrazone Schiff's base complexes. Solvents with high polarity gave better conversion but some solvents would deactivate the catalyst because strong coordination with the vanadium center, such as DMF, which had high coordinating ability. However, this literature did not concern about selectivity of product(s).

3.15 Conclusion of the optimized conditions for cyclododecane oxidation

The factors affected to yield and selectivity of corresponding ketone and alcohol can be concluded in Table 3.12.

Table 3.12 Optimum condition study for cyclododecane oxidation

Entry	Catalyst (mmol)	Solvent	Recovery	Yield (%)		none/nol ratio
				(none)	(nol)	
1	0.05	CH_3CN	72.2	19.6	4.6	4.26
2	0.10	CH_3CN	69.8	23.1	5.7	4.05
3	0.05	$CHCl_3$	74.9	9.2	10.3	0.89
4	0.05	isooctane	86.9	3.5	2.3	1.52
5	0.05	CH_2Cl_2	87.2	6.2	5.1	1.22
6	0.05	CH_3OH	102.4	0	0	-
7	0.05	$C_2H_4Cl_2$	82.7	8.2	3.4	2.41
8	0.05	CH_3COCH_3	81.4	12.1	3.8	3.18
9	0.05	CCl_4	96.1	5.0	3.6	1.39
10	0.05	THF	102.8	0	0	-

Reaction conditions: substrate (1 mmol), catalyst (0.05 mmol), 70% TBHP (10 mmol), solvent 10 mL, reflux 2 h

It was found that ketone was selectively obtained as main product and occurred rapidly within 2 h. From entries 1 and 2, the amount of catalyst did not affect on the yield of products significantly. Therefore, the selected amount of catalyst for further study was 0.05 equivalents to substrate.

For the study of oxidizing agent, when increasing the amount of TBHP from 5 to 10 mmol, the yield of products were increased and started to decrease at 20 mmol. The highest yield of products was obtained at 10 equivalents of TBHP to substrate.

Another important feature was the selectivity. The selectivity of this system was also dependent on solvent. Nine solvents were examined (entries 1, 3-10). CH_3CN gave the best selectivity for ketone formation and the highest yield of total products. Using CH_3OH or THF as polar solvents, the oxidation did not occur since no product was detected and obtained 100% of recovery. When using low polar solvent CCl_4, both yield and selectivity were achieved in small amount. Therefore, the proper solvent system that could provide high selectivity and yield was moderate to high polar solvent.

The oxovanadium(IV) picolinate complex showed higher catalytic activity for the oxidation reactions. The effectiveness of the catalytic system was strongly dependent on various parameters such as temperature, solvent, and oxidant.

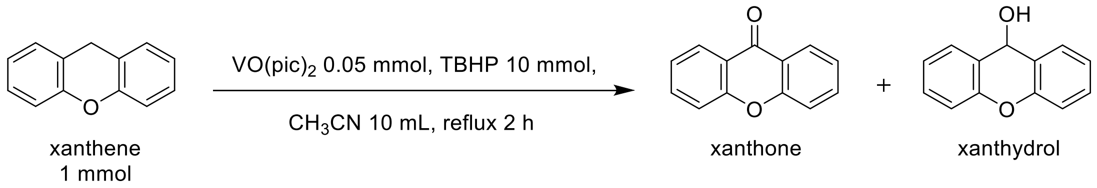
3.16 Catalytic activity of other substrates

Other saturated hydrocarbons were selected to investigate under the optimized conditions. Cyclooctane, adamantane, ethyl benzene, propyl benzene, xanthene, tetralin and diphenylmethane were oxidized under optimized conditions. Catalytic activities of other substrates are summarized in Table 3.13.

Table 3.13 Selective oxidation of other substrates

Entry	Substrate	Recovery	Products (none, nol)	Remarks
1	cyclododecane	72	cyclododecanone (20), cyclododecanol (5)	none/nol (4)
2	cyclooctane	78	cyclooctanone (14), cyclooctanol (1)	none/nol (14)
3	adamantane	49	2-adamantanone (12), 1-adamantanol (34), 2-adamantanol (3)	C2/C3 (0.15)
4	ethyl benzene	69	acetophenone (18), 1-phenylethanol (3)	none/nol (6)
5	propyl benzene	57	propiophenone (14), 1-phenylpropanol (1)	none/nol (14)
6	xanthene	0	xanthone (101)	-
7	tetralin	0	tetralone (39), 2,3-dihydronaphthalene-1,4-dione (26)	-
8	diphenylmethane	51	benzophenone (50)	-
9	acenaphthene	0	acenaphtoquinone (30), unknown (12)	-

From the results shown in Table 3.13, the oxidation of cycloalkane (entries 1-2) displayed the same trend even the number of carbons was changed from 12 to 8. It meant that size of cycloalkane did not affect to the oxidation reaction. In entry 3, adamantane oxidation occurred at 3° C more than 2° C position and gave three types of products, 1- and 2-adamantanol and 2-adamantanone. The C2/C3 ratio of oxidized product of adamantane was 0.15. Due to the assumption that the oxidation reaction in peroxide system occurred *via* radical process and 3° C radical was more stable than 2° C radical, therefore, 3° C oxidized product could be produced easier than 2° C oxidized product. For aromatic compounds (entries 4-9), ethyl benzene, propyl benzene, xanthene, tetralin, diphenylmethane and acenaphthene, the C-H oxidation proceeded rapidly at benzylic position. This can be expected because the benzylic position was the most active compared with other positions in the molecule. Moreover, ketone was selectively as a main product in high yield and high selectivity. Especially, xanthene oxidation could occur quantitatively of xanthone within 2 h.



Yield (%) 101 0

From the better results of benzylic compound oxidation comparing with alkane oxidation, it was revealed that benzyl radical occurred easier than alkyl radical. Benzyl radical was more stable than alkyl radical due to its resonance effect. Therefore, more stable benzyl radical could occur rapidly and resulted in high yield of product.

Comparing with previous literature in 2012 Xia and co-workers reported Cp_2VCl_2-catalyzed benzylic oxidation in TBHP. [99] This catalytic system provided moderate to high yield of selective benzylic C–H oxidation with no competing aromatic oxidation but need to prolong the reaction under mild conditions for 5 days.

3.17 Chemoselectivity study

Another feature that needs to study in this catalytic system was the chemoselectivity. Ten additives were used in this study whether effect to yield of desired product(s) and none/nol ratio. The results are summarized in Table 3.14.

Table 3.14 Chemoselectivity study

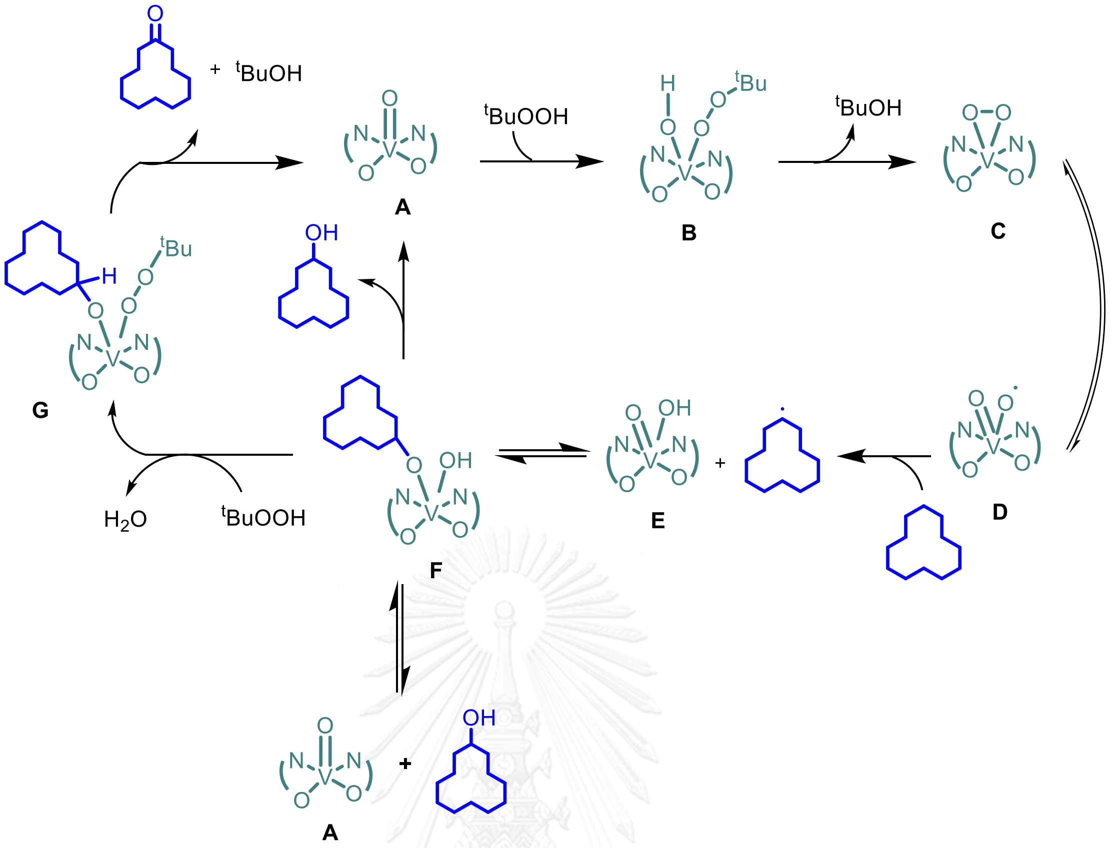
Entry	Additives	Recovery	% yield at 2 h		none/nol ratio
			(none)	(nol)	
1	None	72.2	19.6	4.6	4.26
2	Absolute ethanol	71.1	15.8	3.5	4.51
3	Isopropanol	70.1	19.9	4.2	4.74
4	Hydroquinone	63.1	7.1	3.1	2.29
5	Triphenylphosphine	71.5	17.3	3.9	4.44
6	Ascorbic acid	71.9	12.1	6.1	1.98
7	Aniline	65.5	10.1	3.5	2.89
8	Methyl salicylate	84.7	15.5	4.5	3.44
9	Triethylamine	100	1.9	1.0	1.90
10	Anisole	61.9	19.7	3.7	5.32
11	Ethylene glycol	70.7	20.1	3.9	5.15

Reaction conditions: substrate (1 mmol), additive (1 mmol), catalyst (0.05 mmol), 70% TBHP (10 mmol), CH_3CN 10 mL, reflux 2 h

It could be seen from Table 3.14 that there were two groups of additives. The first group was those that caused increasing of ketone to alcohol ratio which were absolute ethanol, isopropanol, PPh_3, anisole and ethylene glycol. The last group was those that decreased ketone to alcohol ratio including hydroquinone, ascorbic acid, aniline, methyl salicylate and trimethylamine. In case of hydroquinone, aniline and trimethylamine, the observed yield also decreased with lessen selectivity. This chemoselectivity study exhibited different trend with that of O_2 system. From this study, it implied the different pathway of oxidation reaction mechanism.

3.18 Mechanistic study

Besides the informative results guided of the mechanistic pathway derived from chemoselectivity study, the selectivity study of other substrates in the oxidation reaction also showed that this cycloalkane oxidation proceeded *via* radical reaction. The mechanism was proposed as shown below in Scheme 3.2. Firstly, oxovanadium(IV) complexes **(A)** was activated by TBHP to generate complexes **(B)** followed by elimination of ^{t}BuOH to form unstable peroxovanadium complexes **(C)**. The peroxovanadium complexes **(C)** could be switched to complexes **(D)**. After that, cycloalkane was reacted with complexes **(D)** and cycloalkyl radical intermediate was generated and coordinated with complexes **(E)** to form complexes **(F)**. Finally, alcohol and ketone products were yielded in parallel pathways from complexes **(F)**. In case of ketone, complexes **(F)** would react with TBHP to form complexes **(G)** and then complexes **(G)** eliminated ketone and ^{t}BuOH to reproduce oxovanadium(IV) complexes **(A)**.



Scheme 3.2 Proposed mechanistic pathway for oxovanadium(IV) picolinate complexes-catalyzed cycloalkane oxidation in peroxide system

Conclusion of the developed system

The synthetic oxovanadium(IV) picolinate complex exhibited good catalytic activity in terms of %yield of desired product and selectivity of ketone formation. For application with other substrates, oxovanadium(IV) picolinate complex still displayed competent activity for oxidation reaction especially in benzylic compound oxidation. In addition, this oxidation system occurred *via* radical pathway.

Part 4 Bromination of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in peroxide system

Alkyl bromides are well-known intermediates in chemical industry. Although numerous methods have been developed, the direct bromination of alkanes is certainly the ideal way to produce alkyl bromides. Various reagents have been investigated including Br_2, NBS, Cl_3CSO_2Br, CBr_4, Et_4NBr, $BrCCl_3$, and Br_2/HgO. [100]

Generally, the bromination of saturated hydrocarbons proceeds through radical abstraction of hydrogen atoms and trapping with bromide, whereas the bromination of aromatic and unsaturated hydrocarbons is induced by electrophilic addition of Br_2 and/or a cationic bromide. [101] However, the direct bromination of non-activated C–H bonds is still a challenging task. Although Br_2, CBr_4, R_4NBr and LiBr have been reported to serve as bromine sources for the bromination of saturated hydrocarbons, these reactions exhibit low selectivity or reactivity. [102] In this part, the selective bromination of saturated hydrocarbons catalyzed by synthesized vanadium catalyst was focused.

3.19 Optimum condition for cyclododecane bromination

3.19.1 Effect of amount of brominating agent

$BrCCl_3$ was first selected as a brominating agent. The reaction conditions were the same as those described in part 3. Therefore, the amount of $BrCCl_3$ was investigated to determine whether it affected to the yield of the corresponding products. The results are accumulated in Table 3.15.

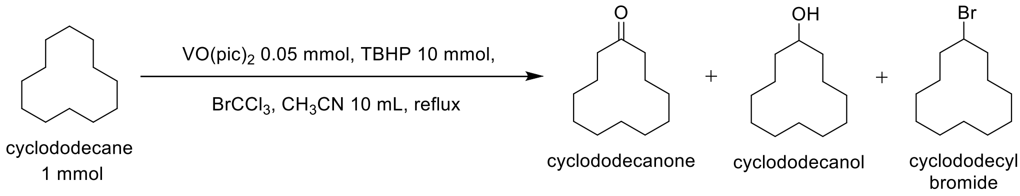


Table 3.15 Effect of amount of brominating agent

Entry	$BrCCl_3$ (mmol)	Yield (%)				MB
		(cane)	(none)	(nol)	alkyl bromide	
1	0	69.5	20.2	4.7	-	94.4
2	1	51.2	7.6	3.5	37.8	100.1
3	3	38.5	1.2	0.42	59.7	99.8
4	5	36.6	0.61	0.53	54.1	91.8

Reaction conditions: cyclododecane (1 mmol), $BrCCl_3$, $VO(pic)_2$ (0.05 mmol), 70% TBHP (10 mmol), CH_3CN 10 mL, reflux 24 h

The selectivity of alkyl bromide product and yield were better when the amount of brominating agent in the system increased. In the absence of brominating agent, alkyl bromide was not occurred. Using 1:1 substrate to brominating agent ratio, alkyl bromide could be detected in 37.8% yield. When the ratio was changed to 1:3 and 1:5, the amount of alkyl bromide was higher with trace amount of oxidation product and the final yield was around 60%. Higher selectivity of alkyl bromide to oxidized product could be obtained when increasing amount of $BrCCl_3$.

3.19.2 Effect of amount of oxidant

Besides brominating agent, another crucial parameter was an oxidant. Therefore the amount of TBHP was explored and the results are displayed in Table 3.16.

Table 3.16 Effect of amount of TBHP

Entry	TBHP (mmol)	Yield (%)				MB
		(cane)	(none)	(nol)	alkyl bromide	
1	0	94.5	0	0	0	94.5
2	5	36.7	1.39	0.36	46.6	85.1
3	10	37.5	0.50	0.60	45.5	84.1
4	15	39.5	1.40	1.33	40.2	82.4
5	20	38.6	1.61	1.92	41.2	83.3

Reaction conditions: cyclododecane (1 mmol), $BrCCl_3$ (5 mmol), $VO(pic)_2$ (0.05 mmol), 70% TBHP, CH_3CN 10 mL, reflux 2 h

In the absence of oxidant, alkyl bromide was not occurred. When using 1:5 and 1:10 substrate to oxidant ratio, alkyl bromide could be detected approximately 45-46% yield. With 1:15 and 1:20, the amount of alkyl bromide was slightly lower and yield was around 40%. Therefore, the excess amount of TBHP could not affect significantly to bromination process. The optimum of TBHP used in system as 1:10 gave the highest amount of alkyl bromide with trace amount of oxidation product.

3.19.3 Effect of reaction time

Besides brominating agent and oxidant, the reaction time was also studied. As clearly seen in previous study, the desired products were obtained rapidly within 2 h. %Yield of desired products *vs* reaction time is presented in Table 3.17.

Table 3.17 Effect of reaction time

Entry	**Time (h)**	**Yield (%)**				**MB**
		(cane)	**(none)**	**(nol)**	**alkyl bromide**	
1	1	47.5	0.50	0.60	45.5	94.1
2	2	44.3	0.93	0.15	47.8	93.2
3	8	37.7	0.72	0.51	57.0	95.9
4	24	36.6	0.61	0.53	54.1	91.8

Reaction conditions: cyclododecane (1 mmol), $BrCCl_3$ (5 mmol), $VO(pic)_2$ (0.05 mmol), 70% TBHP (10 mmol), CH_3CN 10 mL, reflux

High yield was observed within 2 h of reaction time (47.8%). Even the reaction time was prolonged to 24 h, %yield of alkyl bromide was slightly increased. The final yield was around 55%. Half-life of this reaction was lower than 1 h indicated that this bromination proceeded very fast.

3.19.4 Effect of type of brominating agent

Type of brominating agent was the next parameter to investigate. Variation of brominating agent could make difference in terms of yield and selectivity for alkyl bromide production. The results are shown in Table 3.18 and Figure 3.24.

Table 3.18 Effect of type of brominating agent

Entry	Brominating agent	Yield (%)				MB
		(cane)	(none)	(nol)	alkyl bromide	
1	$BrCCl_3$	62.9	7.7	3.9	16.5	91.0
2	HBA	66.4	0.78	0	36.7	103.9
3	CBr_4	60.3	3.33	0	29.6	93.2
4	NBS	65.3	12.0	2.2	16.9	96.4
5	Br_2	62.3	6.3	1.4	26.2	96.2

Reaction conditions: cyclododecane (1 mmol), brominating agent (1 mmol), $VO(pic)_2$ (0.05 mmol), 70% TBHP (10 mmol), CH_3CN 10 mL, reflux

Five brominating agents were examined: $BrCCl_3$, HBA, CBr_4, Br_2 and NBS. HBA was the best brominating agent that gave the highest yield (36.7%) of bromination product. The other four brominating agents gave around 20-30% yield. HBA and CBr_4 could furnish alkyl bromide as a main product with trace amount of accompanying ketone. For further investigation, HBA should be the valuable choice of brominating agent.

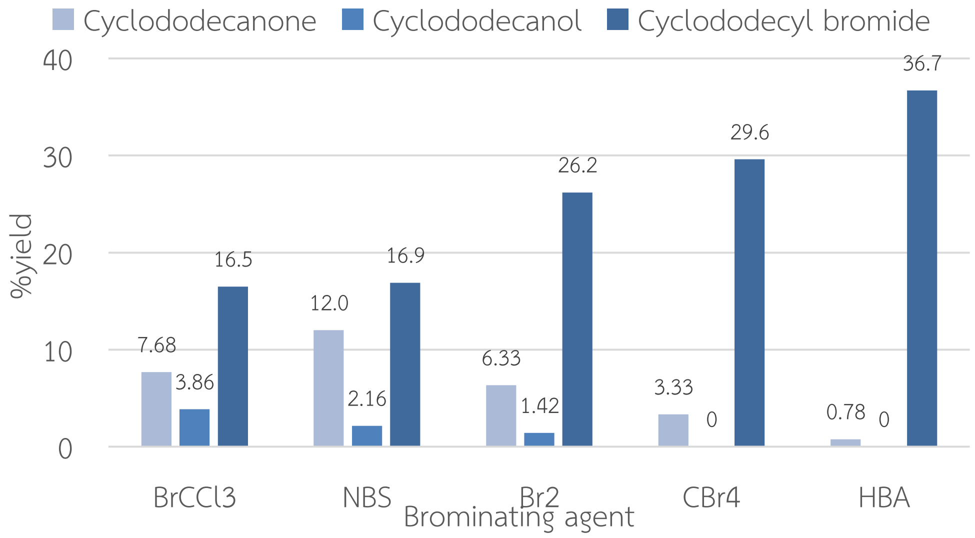


Figure 3.24 Variation of brominating agent

At the same amount of brominating agent (1 mmol), HBA gave the highest yield of alkyl bromide, 36.7%. Considering the structures of all brominating agents, HBA had 6 bromine atoms per 1 molecule. Therefore, the highest number of bromine atom in HBA affected to bromination reaction. Many bromine sources in its molecule may assist the production of alkyl bromide. Moreover, bromine radical could generate from HBA easily because co-radical product generated together with bromine radical was very stable. In addition, the different yield might be affected from bond dissociation energy or BDE of each brominating agent. BDE of $BrCCl_3$, NBS, Br_2 and CBr_4 are 218, 281.6, 193.87 and 209 kJ/mol, respectively. [103, 104] High value of BDE refers to high bonding strength that caused difficulty to generate bromine radical in reaction system.

3.20 Optimum condition for cyclododecane bromination using HBA

3.20.1 Effect of amount of HBA

The variation of amount of HBA was examined to find the best ratio of substrate to brominating agent that could provide high yield of alkyl bromide with less amount of HBA used: 1:0, 1:1, 1:3 and 1:5. The results are presented in Figure 3.25.

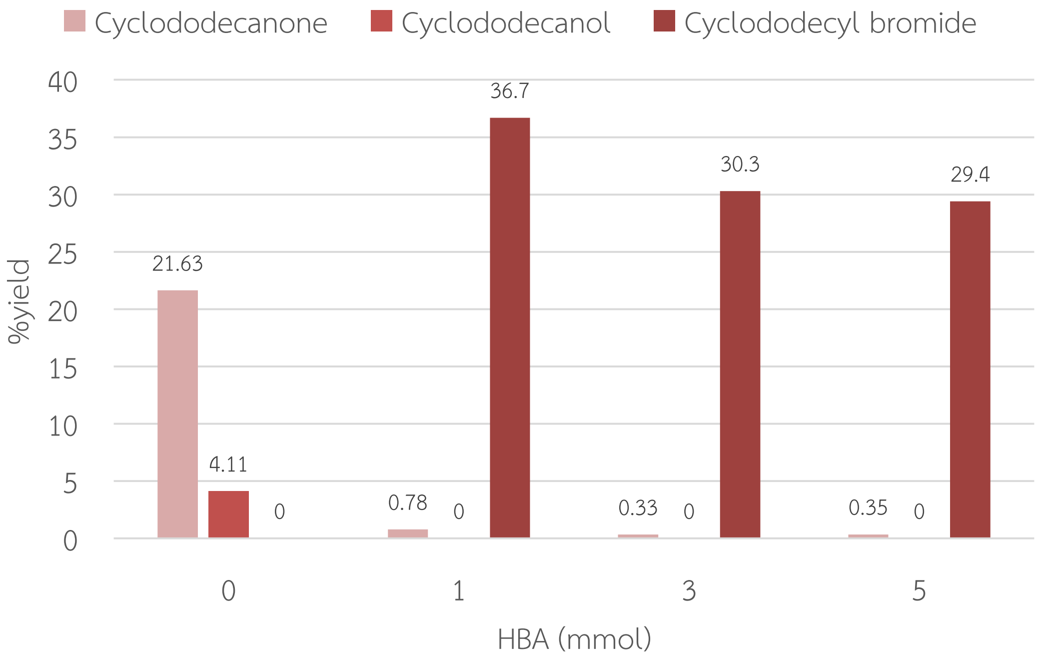


Figure 3.25 Effect of amount of HBA

From Figure 3.25, the ratio that provided the highest amount of alkyl bromide (36.7%) was 1:1. When increasing the ratio to 1:3 and 1:5, it was revealed that alkyl bromide was lessened. This might be due to the excess amount of HBA affected to the reactivity of catalyst resulted in decreasing of alkyl bromide. Bromine radical could coordinate with the complex consequently lower activity of catalyst. Another reason was a large amount of HBA could produce too many bromine radicals, therefore the radicals could form Br_2 resulted in reducing of active bromine radical. On the other hand, 1:1 ratio furnished more amount of product than the others. It can thus be concluded that 1:1 ratio of substrate to HBA was enough to generate bromine radical for bromination reaction effectively.

3.20.2 Effect of solvent

Another parameter that should be considered was solvent system. Eight solvents examined were MeOH, isooctane, CH_2Cl_2, $CHCl_3$, CCl_4, 1,2-DCE, acetone and CH_3CN. The effects of solvent are displayed in Figure 3.26.

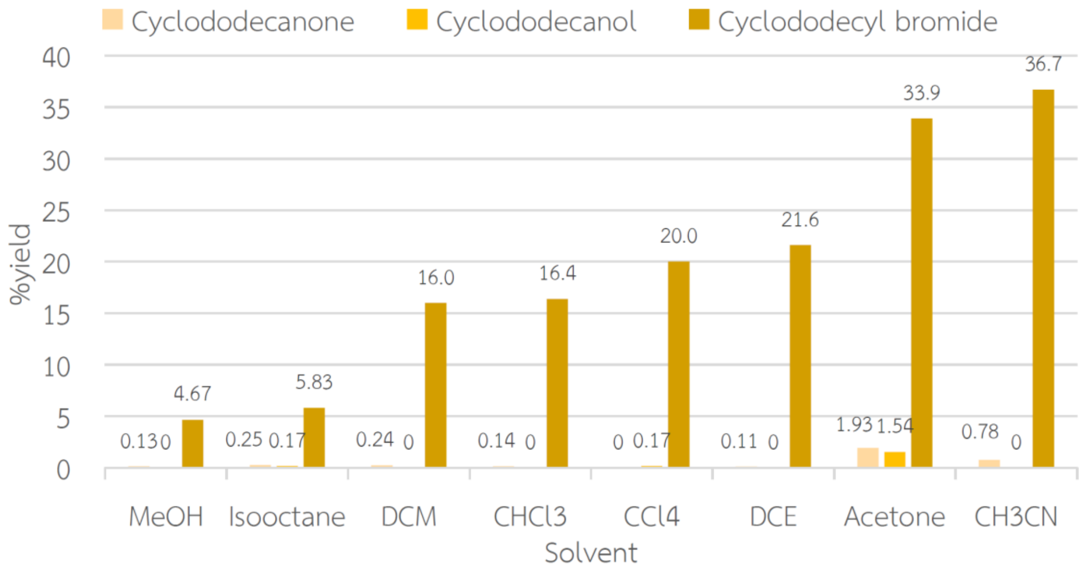


Figure 3.26 Effect of solvent

It was found that CH_3CN was the best solvent which gave the highest amount of alkyl bromide, and the next one was acetone. Both solvents were high polar solvents which could dissolve substrate and catalyst completely. However, CH_3CN was the most proper because fewer amounts of side products (ketone and alcohol) occurred comparing with acetone. CH_2Cl_2, $CHCl_3$, CCl_4 and 1,2-DCE provided alkyl bromide in moderate yield because of low polarity property. For MeOH and isooctane, alkyl bromide obtained in very less amount due to the fact that both solvents could not dissolve all compounds. Therefore, the most proper solvent was CH_3CN and the second choice was acetone.

3.20.3 Effect of amount of oxidant

From previous study, the amount of oxidant could affect to the production of alkyl bromide. Therefore, the amounts of TBHP were investigated: 0, 3, 5, 10 and 15 mmol. Effects of TBHP are exhibited in Figure 3.27.

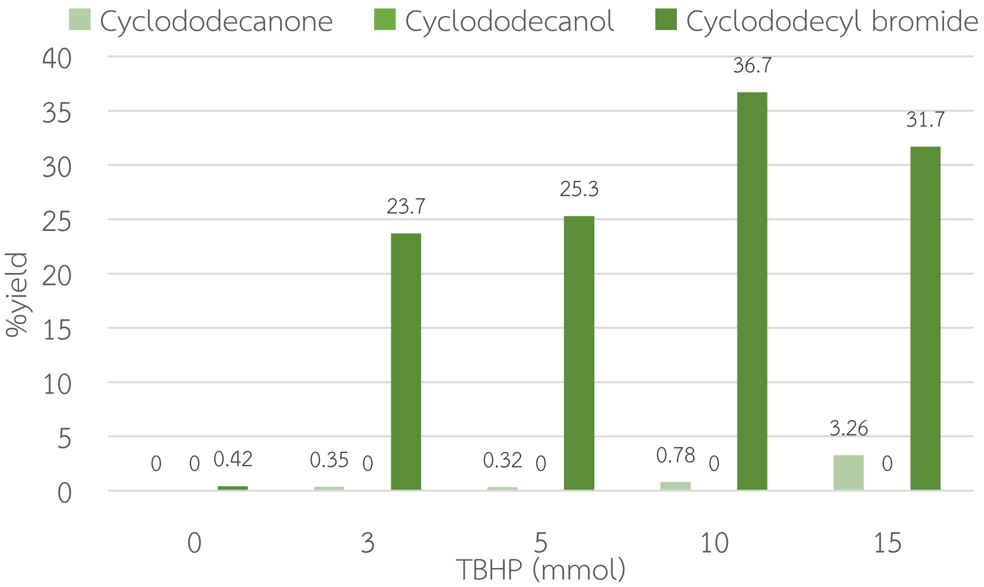


Figure 3.27 Effect of TBHP

As seen in Figure 3.27, the highest yield of alkyl bromide was gained at 10 mmol of TBHP. Reducing to 3 and 5 mmol of TBHP resulted in decreasing of alkyl bromide. Due to the role of TBHP in reaction was C-H bond activator that facilitated reaction process to be occurred fruitfully. In the absence of TBHP, alkyl bromide was observed in very trace amount. It can be noted that lack of TBHP would give small amount of alkyl bromide. In case of excess of TBHP, 15 mmol, the amount of alkyl bromide was lower than 10 mmol of TBHP used but the amount of ketone was higher. It might be because the excess amount of TBHP used may cause oxidation reaction occurred competitively with bromination reaction in parallel affected to lessening of alkyl bromide production. Consequently, 10 mmol of TBHP used was the most effective amount for synthesis of alkyl bromide.

3.21 Kinetic study of alkyl bromide synthesis catalyzed by oxovanadium(IV) picolinate complexes using HBA

Most of chemical reactions concerned with the rate of reaction. The outcome of kinetic study would imply half-life of the reaction which is a significant factor to reflect the kinetic of the system. The reaction with less half-life would proceed faster. The rate of reaction and half-life of alkyl bromide production in 6 h was explored. Time intervals for this study were 0.5, 1, 2, 4, and 6 h. The results are shown in Figure 3.28.

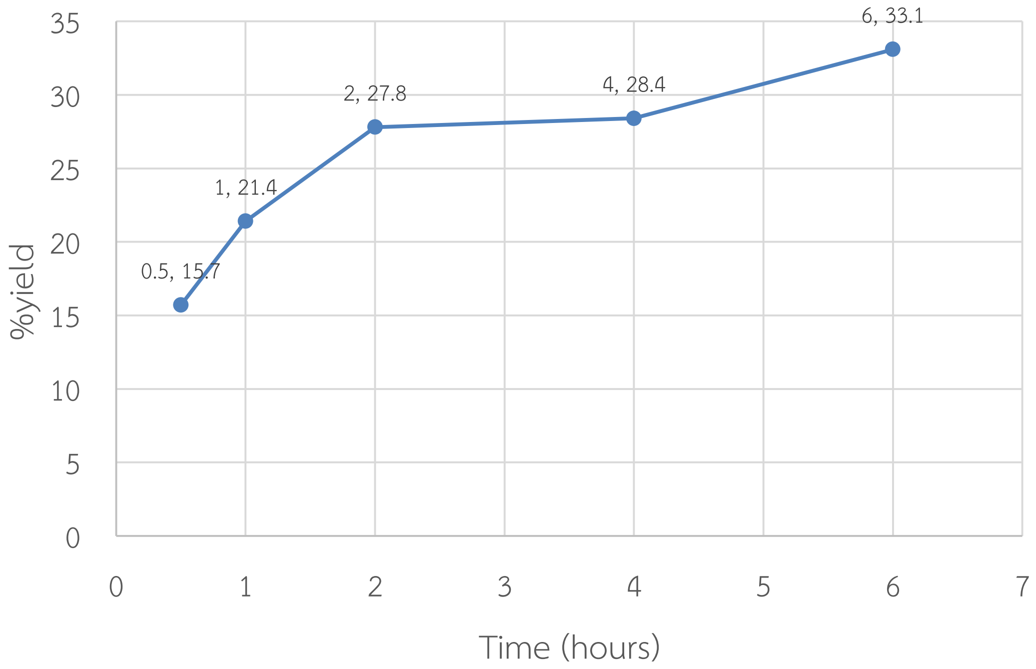


Figure 3.28 Kinetic study of bromination reaction

From Figure 3.28, the yield of alkyl bromide at 6 h was 33.1% hence the half-life of this reaction was 34.2 min which emphasized that this bromination system proceeded very fast. In previous literatures, Smirnov reported the bromination of saturated hydrocarbons with CBr_4. Cycloalkanes and alkanes were brominated for 5-10 h in moderate yield at high temperature (150-180 $^{\circ}$C). [105] In 2013 Nishina and co-workers disclosed the saturated hydrocarbons bromination through radical reactions induced by LEDs irradiation. [101] Alkyl bromide was produced in low to moderate yield within 24 h.

3.22 Variation of alkanes in alkyl bromide synthesis catalyzed by oxovanadium(IV) picolinate complexes using HBA

From previous study, a model substrate- cyclododecane consisted of only 2° C. Replacing with bromine atom at any position of cyclododecane resulted in the same product. Thus, the bromination of other alkanes will provide the scope of the reaction. Six selected alkanes or other organic compounds with alkyl chain were used. The selected substrates were adamantane, dodecane, ethyl benzene, acetophenone, 2,4-dimethylpentane and isooctane.

Table 3.19 Variation of alkanes in bromination reaction

Entry	Substrate	Products	Remarks
1	adamantane	1-adamantanol (7.74), 1-bromoadamantane (3.66), 2-bromoadamantane (12.3)	C2/C3 (0.36)
2	ethyl benzene	acetophenone (34), 1-phenylethanol (10)	none/nol (3.4)
3	dodecane	dodecanol (7.38)	-
4	acetophenone	ND	-
5	2,4-dimethylpentane	ND	-
6	isooctane	ND	-

The oxidation of adamantane could prove a position of carbon where the reaction occurred. The major product from this oxidation revealed the same as that from previous work, *i.e.*, 1-adamantanol and trace amount of other products, 2-adamantanol and 2-adamantanone. [106] The assumption implied that an intermediate was carbon radical. Generally, 3° carbon radical is more stable than 2° carbon radical and indicated that 3° C was more reactive than 2° C.

For the bromination of adamantane, 7.74% yield of 1-adamantanol, 3.66% of 1-bromoadamantane and 12.3% of 2-bromoadamantane were observed. In the system, the amount of TBHP was more than HBA that caused oxidation reaction at 3° C of adamantane resulted in alcohol product still occurred in this reaction. Besides the reaction at 3° C, 2-bromoadamantane was formed. Even though 2° C could react slower than 3° C but a higher site of 2° C compared with 3° C would trap Br_2 easily. Considering the position of carbon being oxidized without concerning of functional groups, 2° C oxidized products were obtained less than 3° C ones resulted in 0.36 C2/C3 ratio which higher than C2/C3 ratio (0.15) in TBHP oxidation system.

The bromination of ethyl benzene was explored yielding the main products of acetophenone (34.0%) and 1-phenylethanol (10.3%) which were oxidized products from 2° C (benzylic position). The brominated product was not obtained in this experiment. This might be due to benzylic position was very reactive but HBA in system was not enough and active to trap radical and turn into alkyl bromide product.

From the investigation of two alkanes, it can be concluded that reaction occurred selectively at 3° C more than 2° C and 1° C, respectively. According to bond dissociation energy (BDE) of C-H bond, 1° C-H bond was the strongest bond and 3° C-H bond was the weakest bond among three types of C-H bonds. [107] Therefore, the results were supported this theory.

Other alkanes were dodecane, acetophenone, 2,4-dimethylpentane and isooctane (entries 3-6). The bromination of dodecane was observed in optimized conditions. Only dodecanol was detected from reaction mixture but achieved in many isomers due to many positions of the substrate being involved.

Finally, the bromination of acetophenone, 2,4-dimethylpentane and isooctane were examined. The bromination of those substrates could not proceed in this system. It was observed that no product obtained from bromination reaction. An expected major product from 2,4-dimethylpentane and isooctane might be an alkyl bromide produced from 3° C position of alkane. Jiang reported the bromination promoted by unactivated MnO_2 occurred exclusively at the 3° C when all CH_3, CH_2, and CH groups were present in one molecule. [100]

3.23 Chemoselectivity of alkyl bromide synthesis catalyzed by oxovanadium(IV) picolinate complexes using HBA

To study chemoselectivity of alkyl bromide synthesis catalyzed by oxovanadium(IV) picolinate complex, substrate was changed to cyclododecanol.

Reaction proceeded under optimized conditions with 1:10 ratio of cyclododecanol to HBA in CH_3CN for 6 h under refluxing temperature. The results are presented in Figure 3.29.

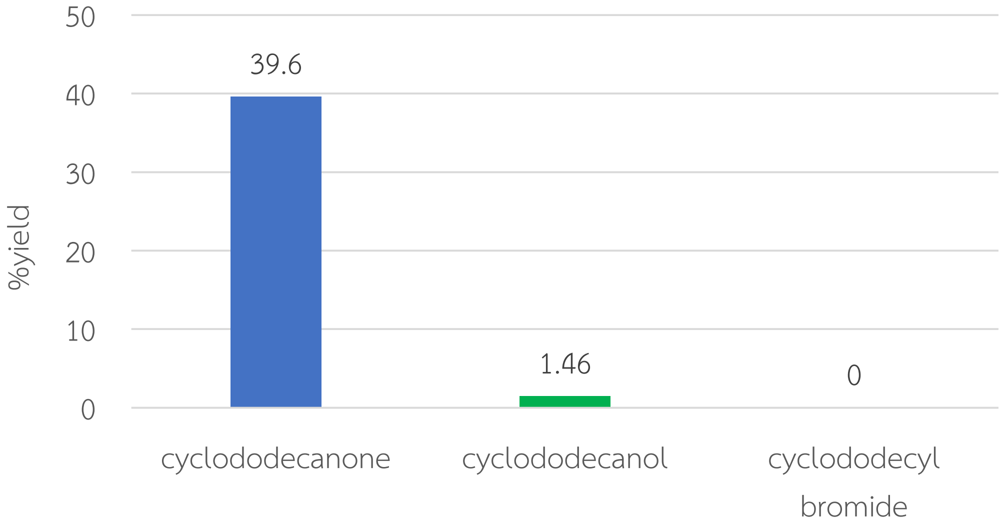


Figure 3.29 Bromination of cyclododecanol

The major product from the bromination of cyclododecanol was cyclododecanone with the absence of cyclododecyl bromide. It unveiled that cyclododecanol did not react with HBA but oxidized and turned into cyclododecanone. From the less amount of cyclododecanol that could detect in reaction, it can be judged that cyclododecyl bromide did not occur *via* alcohol intermediate.

Further study was the competitive bromination under the same conditions as previous study. Selected substrates were different in functional groups as cyclododecane and cyclododecanol. The results are displayed in Figure 3.30.

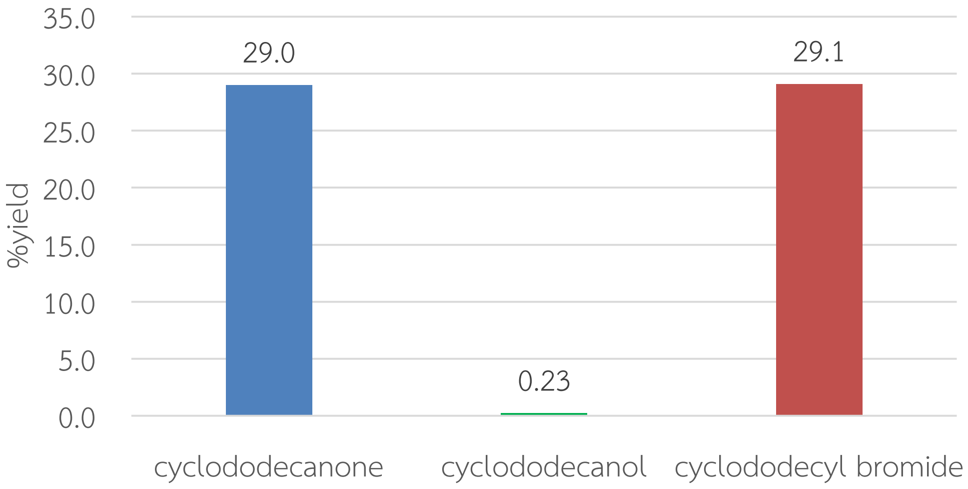


Figure 3.30 Bromination of cyclododecane and cyclododecanol mixture

From Figure 3.30, main products were cyclododecanone and cyclododecyl bromide. Comparing with previous experiment that had only one alcohol substrate, it can be presumed that alkyl bromide produced from alkane and no alcohol product obtained in this reaction system.

To confirm the assumption that alkyl bromide generated from alkane, another experiment was carried out. The competitive bromination was explored using alkane and alcohol with different carbon atoms in molecule. The bromination of cyclododecane-cyclohexanol and that of cyclododecanol-cyclohexane were investigated and the results are accumulated in Figure 3.31.

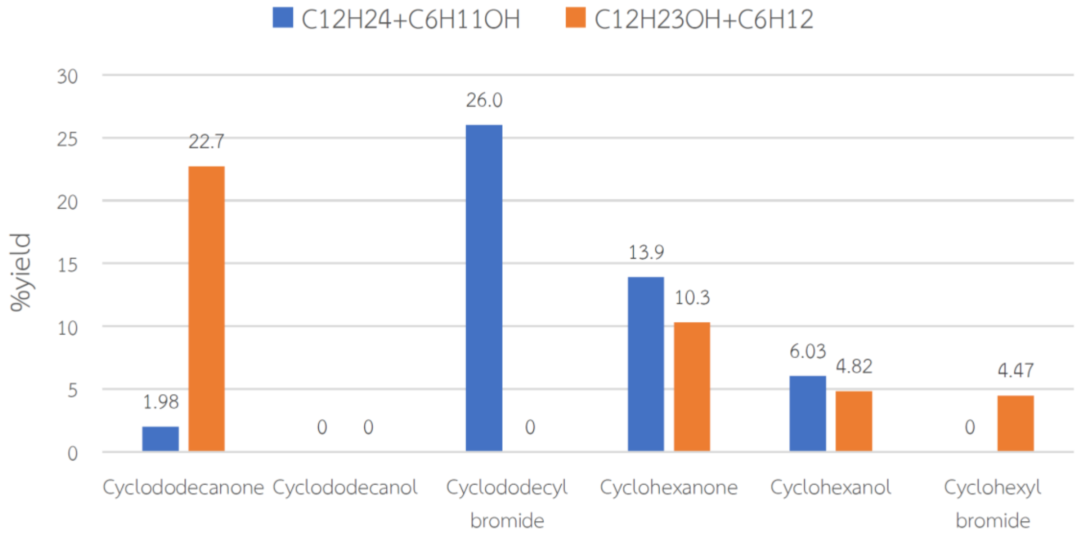
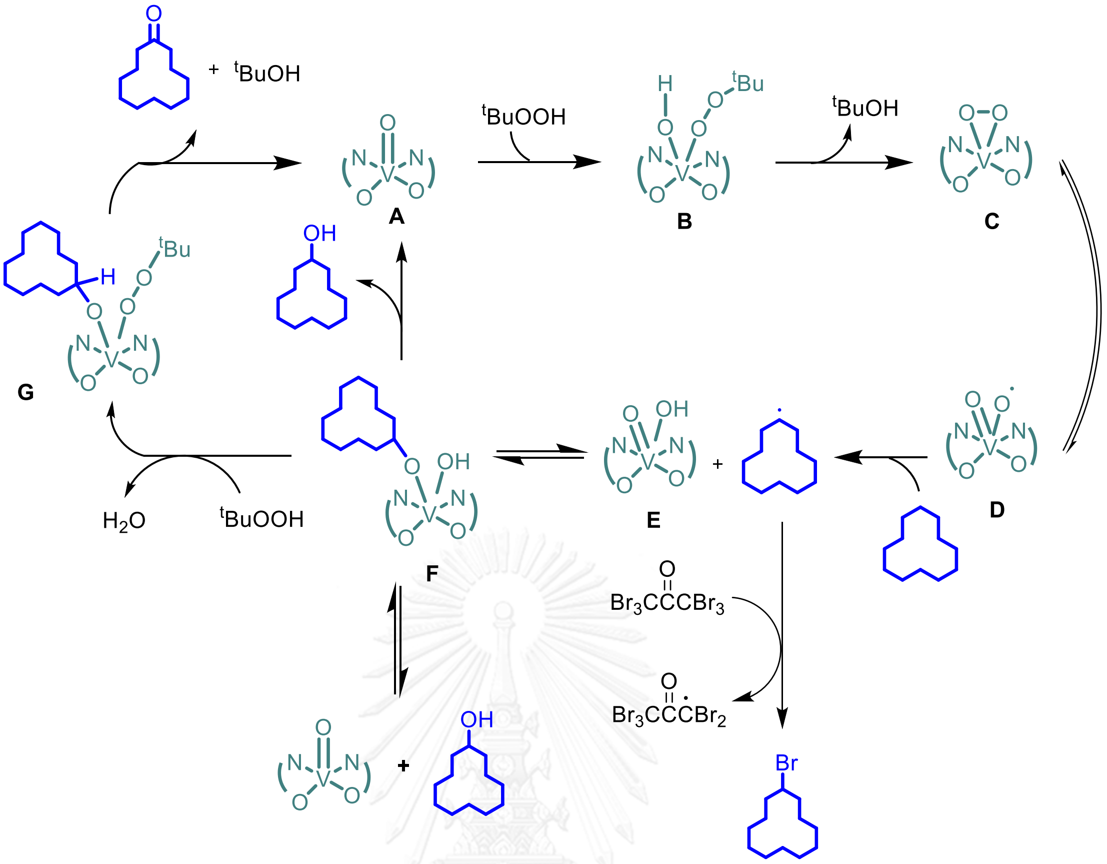


Figure 3.31 Bromination of alkane and alcohol mixture

The reaction between cyclododecane and cyclohexanol gave only cyclododecyl bromide. Similarly, the reaction between cyclododecanol and cyclohexane gave only cyclohexyl bromide. Therefore, it can be concluded that alkyl bromide occurred *via* alkane directly. These results indicated that bromination catalyzed by oxovanadium(IV) picolinate complex was selectively functionalized to alkane more than alcohol.

3.24 Mechanistic pathway of bromination catalyzed by oxovanadium(IV) picolinate complexes using HBA

The bromination using oxovanadium(IV) picolinate complexes occurred *via* C-H bond activation by metal. From all results, the oxidation and bromination pathways catalyzed by oxovanadium(IV) picolinate complexes were occurred *via* radical process. The proposed mechanisms are summarized in Figure 3.38. Firstly, oxovanadium(IV) complexes **(A)** was activated by TBHP to generate complexes **(B)** followed by elimination of ^{t}BuOH to form unstable peroxovanadium complexes **(C)**. The peroxovanadium complexes **(C)** could be switched to complexes **(D)**. After that, cycloalkane was reacted with complexes **(D)** and cycloalkyl radical intermediate was generated and coordinated with complexes **(E)** to form complexes **(F)**. Finally, alcohol and ketone products were yielded in parallel pathways from complexes **(F)**. In case of ketone, complexes **(F)** would react with TBHP to form complexes **(G)** and then complexes **(G)** eliminated ketone and ^{t}BuOH to reproduce oxovanadium(IV) complexes **(A)**. For bromination product, after cycloalkyl radical was generated, bromine from brominating agent would be trapped and finally yielded alkyl bromide product.



Scheme 3.3 Reaction pathways of oxidation and bromination catalyzed by oxovanadium(IV) picolinate complexes

Conclusion of the developed system

Adding HBA under optimized conditions provided bromination. Alkyl bromide was produced in moderate yield without any oxidation products at suitable ratio of HBA to substrate. This bromination reaction was selectively functionalized to alkane more than alcohol. Alkyl bromide was yielded *via* radical reaction.

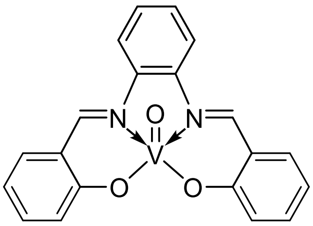
CHAPTER IV

CONCLUSION

The development of homogeneous Schiff’s base and picolinate oxovanadium(IV) catalysts for the oxidative functionalization of saturated hydrocarbons was disclosed. The selection of a suitable oxidizing agent and oxovanadium(IV) complexes, along with optimized reaction systems, could provide efficient oxidative transformations of saturated hydrocarbons and other substrates.

4.1 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff’s base complexes in O_2 system

The oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff’s base complexes in zinc-pyridine-acetic acid system under O_2 atmospheric pressure was preliminary studied from the effect of nine different Schiff’s base complexes. All prepared complexes could be an efficient catalyst with different extent. VO(salophen) exhibited good activity in terms of %yield of desired product and selectivity.



Bis(salicylaldehyde)*N,N'*-*o*-phenylenediimine-vanadium (IV)

Under optimized conditions, ketone was selectively achieved as a main product. The outcome from chemoselectivity study provided an important clue for the mechanistic pathway for this developed oxidation system. The proposed mechanism was proceeded *via* non-radical reaction.

4.2 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) Schiff's base complexes in peroxide system

VO(salophen) was used to study further in saturated hydrocarbons oxidation in TBHP and H_2O_2 system. The optimum study revealed that ketone was selectively as a major product. Comparing two types of peroxide, TBHP displayed a better catalytic activity more than H_2O_2 resulted in higher yield of products and selectivity. The comparison of three oxidation systems of cyclododecane demonstrated that zinc-pyridine-acetic acid-O_2 system gave the best yield of corresponding ketone and total yield of desired products. Considering about the selectivity of ketone to alcohol ratio, highest selectivity was achieved from TBHP system. For catalytic activity of other substrates, adamantane and ethyl benzene, it can be concluded that reaction in peroxide system occurred *via* radical pathway.

4.3 Oxidation of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in TBHP system

The prepared oxovanadium(IV) picolinate complex exhibited good catalytic activity especially the selectivity of ketone formation. Ketone was produced as selective product in high yield within 2 h. The selectivity of this system was also depended on solvent. CH_3CN gave the best selectivity for ketone formation and highest yield of total products. For application with other substrates, oxovanadium(IV) picolinate complex still displayed competent activity for oxidation reaction. Furthermore, chemoselectivity study implied that this oxidation system occurred *via* radical reaction.

4.4 Bromination of saturated hydrocarbons catalyzed by oxovanadium(IV) picolinate complexes in TBHP system

Adding brominating agent under optimized conditions provided bromination. HBA acted as an efficient brominating agent in this system. Alkyl bromide was produced in moderate yield without any oxidation products at suitable ratio of HBA to substrate. Chemoselectivity study indicated that bromination catalyzed by oxovanadium(IV) picolinate complex was selectively functionalized to alkane more than alcohol. Alkyl bromide was yielded *via* radical process.

From all the results studied, synthetic oxovanadium(IV) Schiff's base and picolinate complexes were efficient catalysts for selective oxidation of saturated hydrocarbons in both O_2 and peroxide systems. Comparing the efficiency and selectivity for saturated hydrocarbons oxidation by using Schiff's base oxovanadium(IV) and picolinate oxovanadium(IV) complexes, $VO(pic)_2$ exhibited higher catalytic activity than VO(salophen). In addition, HBA could convert the activation process to furnish alkyl bromide efficiently. Chemoselectivity study implied the clues of reaction mechanism. In zinc-pyridine-acetic acid-O_2 system, the reaction occurred *via* non-radical pathway while the oxidation in peroxide system proceeded *via* radical pathway.

Suggestion for future work

The selective oxidation of other saturated hydrocarbons to observe the stereoselectivity of the system should be carried out. Furthermore, other types of hydrocarbons may be important to investigate under this developed system. In addition, the modification of this catalytic system for bromination reaction that could be applied to other organic compounds should be evaluated for expanding the scope of this reaction.

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