CHAPTER I

INTRODUCTION AND BACKGROUND

1.1 Problem definition

Most organic chemical products are derived from petrochemicals. About 95% of total organic chemical manufacture is at present based on petroleum and natural gas. Petroleum is a mixture of a tremendous number of organic compounds of different basic structures with various molecular weights. Most of them are hydrocarbons. Synthetic organic chemicals have undergone at least one chemical reaction such as oxidation, hydrogenation, halogenation, sulfonation or alkylation. Consequently, hydrocarbon derivatives which contain oxygen or other hetero-atoms are important intermediates in organic synthesis and in petrochemical industry. However, the future promised further substantial increases in demand. A great deal of effort has been expanded in attempts to advance a quite new process based upon catalytic epoxidation which will yield such as product selectivity. Many investigations of epoxidation reactions have been examined for appropriate and viable catalysts on selective epoxidation for over 20 years. Most of catalysts that used for the selective epoxidation are fallen into the utilization of transition metal complex catalysts. Although the epoxidations by peracids or peroxides are generally unselective, proceeding a complex mixture of potentially valuable refinery of separation and low percentage yields in terms of electron poor alkenes.[1] In addition, many reactions were occupied the attention of an expensive catalyst and vigorous conditions such as high temperature, high pressure, acid-base conditions in order to achieve the success.

Just as a whole set of reactions in several biological systems was reported to be able to oxidize hydrocarbons under mild conditions to provide products selectively. Cytochrome P-450 enzyme is remarkably used for hydroxylation of alkanes and oxidation of alkenes.[2] Some researches revealed the improvement in applying Cytochrome P-450 enzyme practically for the epoxidation of styrene.[3] More than

half of all enzymes have metal ions in their structures, these are called metalloenzymes. Thus, extensive efforts have been devoted to mimic these remarkable abilities of biological systems.

1.2 Literature review on the epoxidation of alkenes

Epoxide, an important chemical intermediate in organic process industry can be produced by epoxidation of alkenes.[4] Epoxides are raw materials for a wide variety of chemicals such as glycols, alcohols, carbonyl compounds[5], alkanolamines and polymers such as polyesters, polyurethanes, and epoxy resins.

Epoxides are cyclic ethers with three-membered ring. Oxygen is added to carbon-carbon double bonds to form epoxides. The simplest epoxide, ethylene oxide is one of the oldest-established ethylene-based petrochemicals. It has been made in USA since about 1925. In 1930, improvement using Ag catalyst was employed in the process. Ethylene oxide is prepared industrially by direct air oxidation of ethylene over a hot silver catalyst.[6]

$$CH_2{=}CH_2 \quad + \quad O_2 \quad \xrightarrow[\text{Ag catalyst}]{250\text{-}330^\circ C} \quad \underset{O}{CH_2{-}CH_2}$$
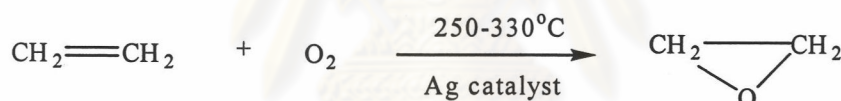
The most widely used method for synthesizing epoxides is the reaction of alkene with an organic peroxy acid (or peracid) and peroxide.

1.2.1 Literature review on the epoxidation of alkenes with peroxy acids

The reaction of alkenes with peroxy acid to produce epoxides has been known for almost 90 years.[7] It provides the most convenient method for the preparation of epoxide. Epoxidations with commercially available peroxy acids such as peroxyacetic acid, peroxybenzoic acid, peroxyfluoroacetic acid, m-chloroperoxybenzoic acid[8] and m-nitroperoxybenzoic acid are among well-known examples. Oxygen atom transferred from a peroxy acid to an alkene is facilitated by electron-donating substituents on the carbon-carbon double bond and electron-withdrawing groups on the peroxy acid.
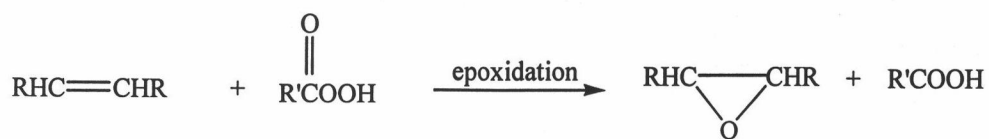
Bach and co-workers[9] reported the epoxidation of 1-nonene by *m*-chloroperbenzoic acid (*m*-CPBA) in the presence of either CCl_3COOH (TCA) or CF_3COOH (TFA) in benzene. Reaction rates were monitored by following the formation of 1,2-epoxynonane and it was found that the reaction was second order and the addition was stereospecific of oxygen. Some typical epoxidations with peroxy acids are shown below.
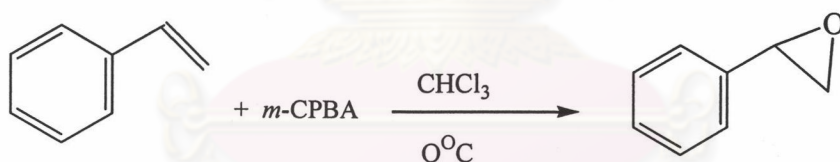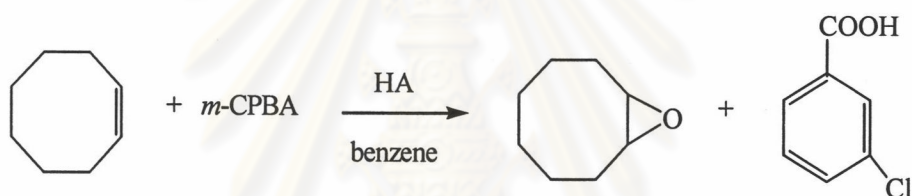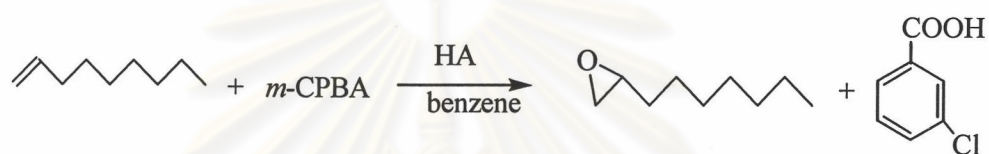
Polyolefinic alcohols were reported to be epoxidized regioselectively and gave excellent yields by using monoperoxyphthalate (MMPP) at the controlled pH of water. Both MMPP and *m*-CPBA affected the epoxidation of allylic alcohols, no significant improvement was obtained by replacing *m*-CPBA with MMPP.[10] The choice of the preferred MMPP for the epoxidation of alcohol also depended on the increasing of the amount of epoxides.


78% yield
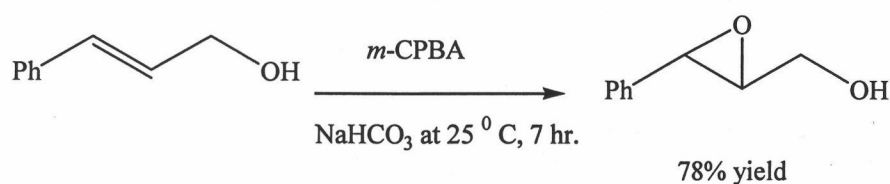
In addition, Carison and colleagues[11] reported that peroxybenzimidic acid appears to be a relatively indiscriminate reagent and was not the reagent of choice for selective epoxidation of polyunsaturated substrates. Peroxybenzimidic acid appeared to be less selective than other peroxy acids for the epoxidation of olefins. For example, the comparative epoxidation study of 4-vinylcyclohexene and limonene with *m*-CPBA and peroxybenzimidic acid was demonstrated. The epoxidation of limonene with *m*-CPBA gave predominantly 1,2-epoxide in 87% yield while peroxybenzimidic acid is less selective reagent for the epoxidation of double bonds than are peracids. The epoxidation of 4-vinylcyclohexene with *m*-CPBA furnished 1,2-epoxide in 88% yield and 7,8-epoxide in 2% yield.
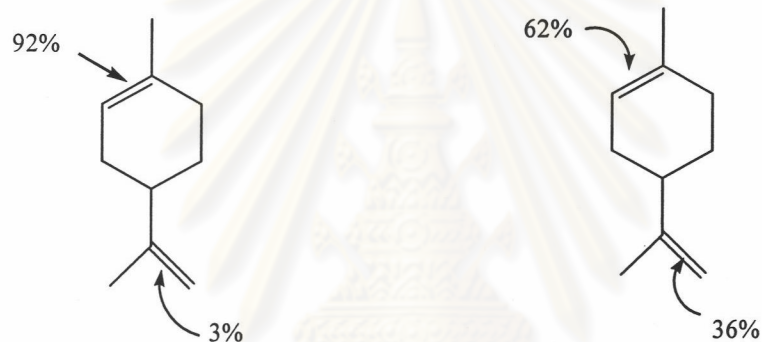
limonene attacked by *m*-CPBA   limonene attacked by peroxybenzimidic acid
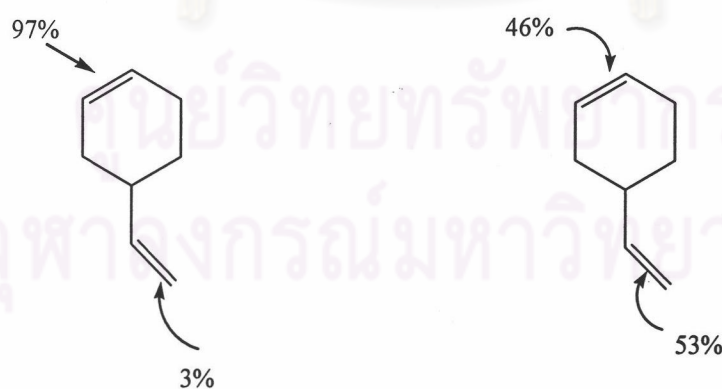
4-vinylcyclohexene attacked by *m*-CPBA   4-vinylcyclohexene attacked by peroxybenzimidic acid

The stereoselectivity of epoxidations with peroxy acids has been well studied. The stereospecific *syn*-addition was consistantly observed. The epoxidation of

dihydrophthalic acid derivatives were therefore believed to be a concerted processes. Apparently, neighboring functional groups influenced the direction of the attack of the peroxy acid. Addition of oxygen occurred preferentially anti attack of the molecules. Allylic carboxylic acids and carboxylates are also effective *syn*-directing groups. For certain substrates such as *trans*-1,2-dihydrophthalic acid, the epoxidation yielded only *cis*-monoepoxide[12] while the epoxidation of dimethyl *trans*-1,2-dihydrophthalate furnished 9:1 mixture of *cis*- and *trans*-epoxide.[13] A free carboxylic acid was a more effective *syn*-directing group than a carboxylic ester. As *trans*-1,2-dihydrophthalate, there should be no steric or conformation preferences for *syn*- or *anti*-epoxidation to the carboxylate substitutents. Therefore, the epoxidation of *trans*-1,2-dihydrophthalate proceeded in 90% stereospecificity to monoepoxide. In addition, the result presented that a carboxylate group exerted a *syn*-directive and the effect of stereoselectivity of peroxy acid for epoxidation would afford preferentially *cis*-epoxide.
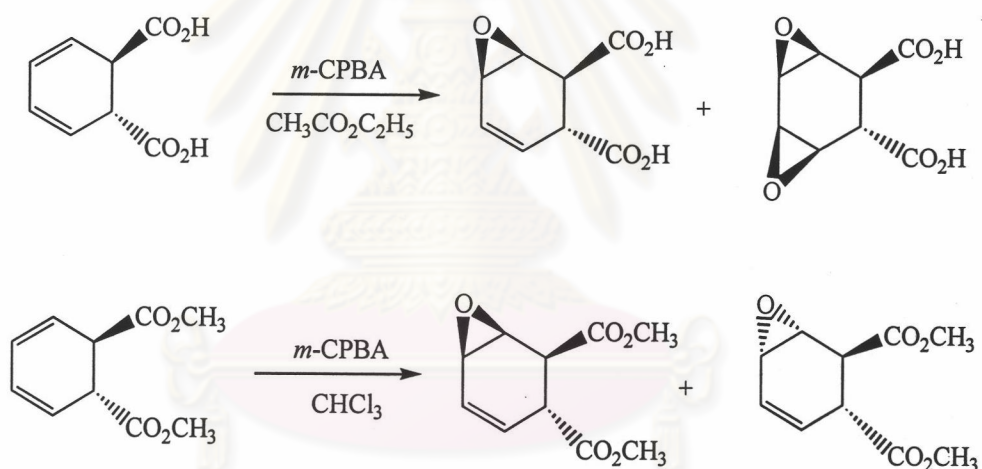
Furthermore, the epoxidation of *trans*-5,6-diacetoxycyclohexa-1,3-diene gave 2:1 mixture of *cis*- and *trans*- monoepoxides.[13] The oxidation of allylic acetates was not very stereospecific but generally gave more *cis*- epoxides than expected on the basis of steric interactions alone. Carboxylate was a better *syn*-directing group than allylic acetates but was not as effective as hydroxyl groups. The relative order of effectiveness for *syn*-directing allylic substituents was $-OH > -CO_2H > -CO_2R > -OCOR$. The stereospecific directive effect of allylic hydroxyl groups was due to the stabilization of the transition state leading to *cis*- epoxides by hydrogen bonding to the peracid. This interaction was more effective when the directing group was in the pseudoequatorial position.

1.2.2 Literature review on the epoxidation of alkenes with peroxides

Besides peroxy acids, hydroperoxides are used in epoxidation of alkenes especially, hydrogen peroxide and *tert*-alkyl hydroperoxides. Hydrogen peroxides are available to use for epoxidation. A dilute aqueous solution of hydrogen peroxide (H_2O_2) is the oxygen source for alkene epoxidation and it generates water and oxygen as by products.[14,15] Only a few alkenes undergo epoxidation reaction using H_2O_2 alone. Since the transfer of an oxygen atom from a molecule of H_2O_2 to alkene is a dehydration, numerous dehydration agents have been used in epoxidation systems.[16] During study on epoxidation using the fructose-derived ketone, many cases of epoxidations be used of H_2O_2 as a primary oxidant combined with organic reagents such as nitriles.[17] In the system which composed of nitriles, it was catalyzed by hydrotalcites. Among amides used for epoxidation, isobutyramide was found to be commonly used in the reaction.

The epoxidation of α,β-unsaturated ketones using H_2O_2 under strongly alkaline conditions with bases such as NaOH, Na$_2$CO$_3$, KOH and K$_2$CO$_3$ was still the most common procedure. Moreover, the use of bases was undesirable because they were hazardous and led to the production of a vast amount of wastes. For the hydrotalcite catalysts ($Mg_{10}Al_2(OH)_{24}CO_3$), which had been developed with H_2O_2 as oxidant, could conveniently used for epoxidation. Epoxidation of α,β-disubstituted ketones, pulegone, using benzonitrile and H_2O_2 in the presence of hydrotalcites gave epoxyketone 93% yield. In this epoxidation, hydrotalcite catalysts efficiently transform hydrogen peroxide into the perhydroxyl anion as an active species.[18]


93 % yield
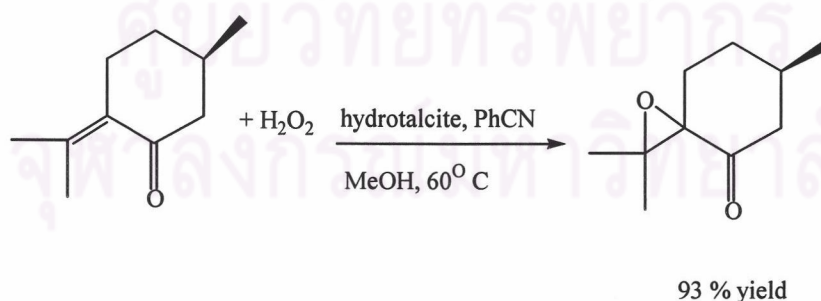
Developing the epoxidation reactions employed amides, H_2O_2 and hydrotalcites in the system indicating that isobutyramide was the most effective in the system. For instance, increasing isobutyramide in this system directive effected on the yields of

the corresponding epoxide. Cyclooctene oxide was obtained with 84% yield. Common alkenes gave excellent yields of the corresponding epoxides with almost a stoichiometric amount of isobutyramide. On the other hand, in the case of a terminal alkene like 1-octene as a substrate, a large excess of the amide was necessary to attain a high yield of the epoxide. The regioselectivity in the epoxidation of alkenes having different types of double bonds was strongly dependent on types of amide used. The regioselectivity study on the epoxidation of 4-vinylcyclohexene provided 1,2-epoxy-4-vinylcyclohexene with 97% yield in the case of propionamide, while the use of isobutyramide gave the small amounts of terminal epoxides and also gave 1,2-epoxide with 84% selectivity.[19]

$$\xrightarrow[\text{propionamide},H_2O_2]{Mg_{10}Al_2(OH)_{24}CO_3}$$
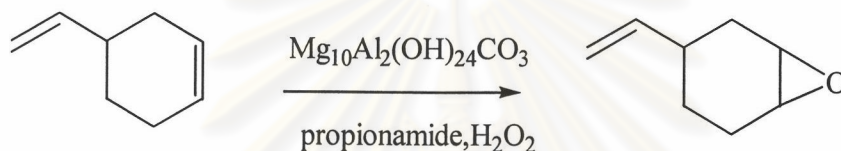
The generalized stereoselective epoxidation of allylic alcohol by *tert*-butylhydroperoxide in the presence of titanium(IV)isopropoxide, $Ti(OPr^i)_4$, and tartrate esters to the epoxide constitutes a seminal landmark in metal-mediated asymmetric oxidation. In the Sharpless asymmetric epoxidation,[20] allylic alcohols were converted to optically active epoxides more than 90% ee, by treatment with *t*-BuOOH, titanium tetraisopropoxide and optically active diethyl tartrate.

In comparison with titanium catalyst, the complex $VO(acac)_2$ or $VO(OPr^i)_3$ was the catalyst of choice for stereoselective epoxidation of allylic alcohols. Only double bonds proximal to the alcohol were epoxidized under high rate acceleration. For example, in Sharpless asymmetric epoxidation protocol of allylic alcohols had proven to be an extremely useful means of synthesizing enantiomerically enriched compounds.[21] To explore further epoxidation of various substituted aryl alcohols, the epoxidation of 3,3-disubstituted allylic alcohols using catalytic $VO(OPr^i)_3$ (5 mmol%) proceeded smoothly to yield the corresponding epoxides in moderate to good yields with mediocre selectivities. On the other hand in the case of 2,3-disubstituted allylic alcohols, irrespective of bearing aromatic groups, a uniformly high degree of enantioselectivities around 90% yield was obtained.

80%
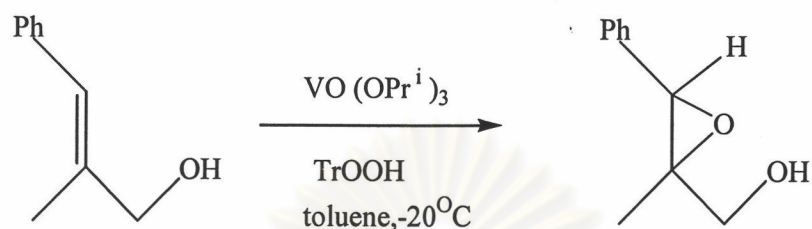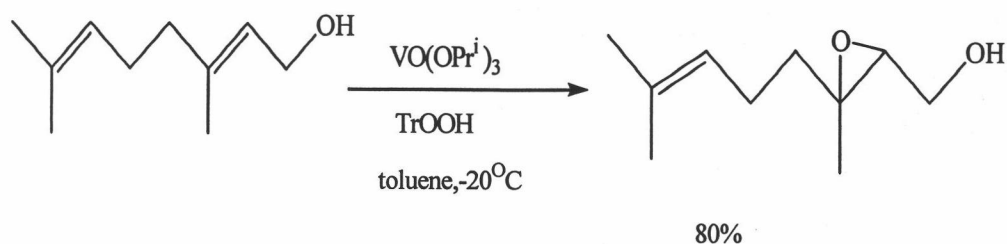
*TrOOH = triphenylmethyl hydroperoxide

The productivity of vanadium catalysts for 1-cyclopentenylmethanol was superior to the stoichiometric epoxidation with the titanium tartrate,[22] chiral vanadium catalysts for asymmetric epoxidation of allylic alcohols proceeded good yields with high selectivity.

Some epoxidation reactions of alkenes with H_2O_2 using trifluoroacetone (CF_3COCH_3) as discussed earlier proceeded good yields of epoxides under mild conditions.[9] An effective epoxidation system involved trifluoroacetone, the procedure provided a simple route to prepare valuable epoxide.[7] Furthermore, some epoxidation reaction of alkenes with peroxide as proposed earlier gave steroselective yields in basic media. An average yield of epoxide was obtained under high reaction conditions.

1.2.3 Literature review on the epoxidation of alkenes catalyzed by metal complexes

Catalysis has been successfully used in the chemical industry for hundreds of years. Many large-scale industrial processes were carried out with the aids of catalysis. Most industrial synthesis and all biological reactions also require catalysts.[23] The catalysts influenced the selectivity of chemical reactions. This means that completely different products were obtained from a given starting material by using different catalyst system. Similar to other organic transformations, the catalyst plays an important role in the oxidation reaction. The selective activation of particular

varieties of C-H bonds and the oxidation process were controlled after the desired substitution has been achieved. Heterogeneous and homogeneous catalysts were both used in industries. Toward this objective, there was an attempt to develop the homogeneous catalysts to use in the oxidation reaction. In homogeneous catalysis, catalyst, starting materials and products were present in the same phase. The homogeneous catalysts have a higher degree of dispersion in the reaction media than heterogeneous catalysts since each individual atom was catalytically active. In heterogeneous catalyst, only the surface atoms were active.[24] Moreover, the most prominent feature of homogeneous transition metal catalysts can offer high molar catalytic efficiencies, under mild conditions, tolerance to many types of organic functionality, and high selectivities can be achieved. Refer to their high degree of dispersion, the homogeneous catalysis provided a higher activity per unit mass of metal than heterogeneous catalysts and high mobility of the molecules in the reaction mixture. The most prominent features of homogeneous transition metal catalysts were the high selectivity. Most of the petrochemical processing, the thermal stability [25] and the solvent effects of transition complexes in liquid phase[26] were also the significant parameters to be considered.

The use of organometallic compounds in which a central metal atom was coordinated by ligand was utilized for many reactions in order to enhance high yield and activate the reaction. The attempt to modify new strategies for the selective oxidation for hydrocarbons continued being an important aim for both academic and industrial point of view. During the last 15 years, metalloporphinates have been shown to be excellent models for biological and bioinorganic chemistry.[27]

The alkene epoxidations and hydroxylations catalyzed by metalloporphyrin have been widely invoked as the biomimetic reactions of Cytochrome P-450.[28,29] These reactions were often recognized by remarkable regio- and stereoselectivities. The systematic structural variation of the porphyrin ligands has proved to be a useful strategy to achieve electronic and steric tuning of the catalysts.[30] Moreover, the highly enantioselective epoxidation of unfunctionalized alkenes has also been developed by using chiral metalloporphyrin catalysts.[31,32,33] As would be expected for the reactive intermediates, recently the reactive metal–oxo (M=O) intermediates of some oxometalloporphyrin complexes of Cr, Mn, and Fe have been explored extensively.[34,35]

The elegant results that *in situ* generated iron(III)peroxo porphyrin complexes were powerful nucleophiles capable of epoxidizing electron-deficient alkenes. In

cytochrom P-450 and aromatase enzymes and iron(III) peroxo phorphyrin complex were the reactive species responsible for the aldehyde deformation and aromatization reactions. The epoxidation of *cis-* and *trans-*stilbenes with oxidants such as *m*-CPBA was effectively catalyzed by *meso*-tetrakis(pentafluorophenyl)-porphinato)iron(III) chloride [Fe(TPFPP)Cl] afforded good yields of a mixture of products which consisted of 88:11 ratio of *cis-* to *trans-*stilbene oxide.[36]

In the epoxidation of alkenes catalyzed by *meso*-tetakis(pentafluorophenyl)-porphinato)iron(III)chloride [Fe(TPFPP)Cl] and *m*-CPBA in aprotic solvent, cyclooctene oxide 92% yield, *cis*-stilbene oxide 86% were obtained, but *trans*-stilbene was found to be unreactive under these conditions. The iron(III) tetrakis (pentafluorophenyl)porphyrin chloride was proved to be an excellent catalyst for the epoxidation of cyclooctene by *t*-BuOOH (90% yield of cyclooctene oxide in CH_2Cl_2/CH_3OH 25:75 by volume). In the reaction of hydrogen peroxide, *tert*-butyl hydroperoxide and *m*-CPBA with norbornene as a substrate catalyzed by iron(III) tetrakis(pentafluorophenyl)porphyrin chloride produced epoxide in 60-65% yields.[37]

Moreover, the epoxidation of alkenes catalyzed by manganese porphyrins has recently been reported.[32] The manganese derivatives of chiral porphyrin catalyst were the most effective asymmetric catalysts in the epoxidation system. Monosubstituted alkenes were epoxidized by magnesium monoperoxyphthalate, like with other oxygen donor, and catalyzed by tetra-2,6-dichlorophenylporphinatomanganese(III)acetate. Alkene conversion was nearly completed within 0.5-5 minutes at 0°C and provided good yields (60-93%). In addition, the epoxidation by threitol-strapped manganese porphyrins catalyzed for *cis*-disubstituted alkenes gave optical yield up to 88% *ee* and proceeded greater than 80% conversion to oxidized products when iodosylbenzene was used as an oxidant. These were the highest *ee* in the epoxidation of these olefins such as styrene, *p*-chlorostyrene, α-methyl styrene and 1,2-dihydronaphthalene. While *mono-* and *cis*-disubstituted alkenes were epoxidized with high degree of stereoselectivity, *trans*-disubstitued alkenes were poor substrates. For example, the epoxidation using threitol-strapped manganese porphyrins by iodosylbenzene as an oxidant was shown below.

threitol-strapped porphyrins

CH_2Cl_2, 25°C

82% yield, 70% ee
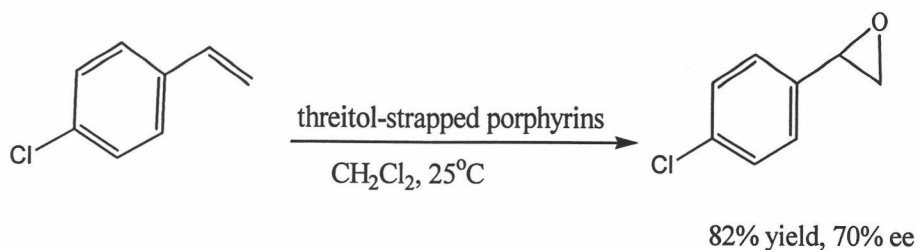
Catalysis was achieved by means of transition metal complexes with common oxygen sources while the stereoselectivity may be controlled either by an optically active oxidizing species or by a chiral substrate.[33] Stereocontrol using the diasteroselective epoxidation of chiral allylic alcohols had proved to be used of transition metal in the system.[34] Several catalytic [Ti(OiPr)$_4$/ TBHP[20], VO(acac)$_2$ /TBHP[34, 35], and non catalytic (DMD, m-CPBA)[36, 37, 38] methods have already been extensively studied. The valuable information on the geometry of the oxygen transfer process has been required. The mentioned catalytic oxidants including peroxy- and peroxo-metal complexes were catalyzed by metal(Salen) or metal(porphyrin) complexes.[33]

The epoxidation of chiral allylic alcohols catalyzed by iron(porphyrin) complexes, 4-phenylpyridine N-oxide (PPNO) as an oxidant, this system was capable to epoxidize chiral allylic alcohols such as 1-methylgeraniol providing the oxidized product with iodosylbenzene as the oxygen source. The high *threo* diastereoselectivity was obtained for the 3,4-epoxide as a major product. Because an analogous was related to 1,3-allylically strained alcohol, these experimental findings supported the hydrogen bonding between the allylic hydroxy group and the oxo-metal intermediate as attractive interaction. In comparison, the oxidants such as Ti(OiPr)$_4$/TBHP which were involved for metal-alcoholate bonding provided higher preference of 3,4-epoxide, than the characteristic hydrogen bonding systems, m-CPBA and dimethyldioxirane (DMD) favored with 7,8-epoxide regioisomer. As the results, the epoxidation of chiral allylic alcohols was accomplished by utilizing high valent oxo-metal complexes to enchance the reactivity. The results established that the hydroxy-directed epoxidation of chiral allylic alcohols were effectively catalyzed by iron(porphyrin) complexes. The highly *threo*-diastereoselective epoxide formation was controlled by synergistic combination of 1,3-allylic strain and hydrogen bonding.[33]

The oxidation of (+)-limonene with the Cl$_2$pyNO as an oxidant in CH$_2$Cl$_2$ system was catalyzed by ruthenium *meso*-tetrakis (2,6-dichlorophenyl)porphyrin, [Ru^{II}(TDCPP)(CO)(EtOH)], the *cis*–1,2-epoxide was predominantly produced greater than 8,9-epoxide. However, the oxidations of (+)-limonene afforded *trans*-1,2-epoxide as minor product.[39]

In recent years has witnessed significant advance in the study of the epoxidation catalyzing by oxoruthenium (Ru=O) complexes. The class of ruthenium porphyrin complexes played promising selectivities towards organic oxidant using dioxygen[40], as well as other mild oxidizing reagents such as N$_2$O[41] and 2,6-dichloropyridine *N*-oxide (Cl$_2$pyNO).[42]

In alkene epoxidation, using manganese complex bearing the optically active salen ligand [*N,N*-bis(*S*)-3-(1-phenylpropyl) salicylidene]-(1*R*,2*R*)-1,2-diphenylethylenediaminato] was found to be an effective catalyst for the enantioselectivity of 50% *ee* for the epoxidation reaction of 1-phenyl-1-propene.[43] The chiral (salen) manganese(III) complex, [(8S,8′S)-3,3′-bis[(1R)-1-phenylpropyl]-4,4′-dimethyl-8,8′-diphenylsalen] manganese(III) complex was remarkable for the epoxidation of stilbene.[44] Effectively chiral Mn(salen) and Fe porphyrin complexes have been investigated,[45] in chiral manganese salen complexes substituted in the third position with bulky silyl group (TMS, TBDMS) catalyzed the epoxidation of unfunctionalized olefins in moderate to high *ee*'s. Absolute selectivities for styrene oxide 18% (R) *ee* and 33% (R) *ee* was obtained at the substituent in the 3 position, respectively. The variation of the oxidizing agent was also studied and it was efficiently catalyzed by chiral (salen) Mn(III) complexes in alkene epoxidations.[46] However, the combination of *m*-CPBA and NMO were found to be particularly effective for low temperature reactions. In enantioselective epoxidation of unfunctionalized alkenes under anhydrous low temperature conditions, alkenes which were either water-soluble or decompose in the presence of aqueous bleach were also studied for the epoxidation reaction.[46]

Moreover, in the enantioselective epoxidation of unfunctionalized alkenes catalyzed by active Mn(III) salen in the presence of molecular oxygen and pivalaldehyde, *N*-alkylimidazoles was effective axial ligands to proceed optically active epoxides with high enantioselectivities such as 1,2-dihydronaphthalene derivatives and 2,2-dialkyl-2H-chromene derivatives were converted into the corresponding optically active epoxides with 60-92% enantiomeric excess.[47]

A series of heteropolymetalates especially with low-valent transition metals such as maganese(II), cobalt(II) have been shown efficiency for the catalysis of oxygen transfer reaction in the epoxidation of alkenes. Nevertheless, up to now catalytic epoxidation using transition metal substituted polyoxometalates(TMSPs) was limited to alkenes, with one exception where a manganese(III)substituted heteropolyanion, $[\alpha\text{-MnBrP}_2\text{W}_{17}\text{O}_{61}]^{8-}$, catalyzed the oxidation of R-(+)-limonene. In this reaction, the relative high turnovers were obtained with good regioselectivity of 1,2-limonene oxide. Epoxidation of substrate with species of the non heteropolymetalates, Ishii-Venturello system ($\text{H}_3[\text{PW}_{12}\text{O}_{40}]\cdot X\text{h}_2\text{O}/ \text{H}_2\text{O}_2/ \text{PTC}$) led to 90-100% conversion to 1,2-limonene oxide, nevertheless these systems work stoichiometrically and diepoxides have been produced. For using manganese substituted in heteroporphyrin, $[\text{Mn}^{III}(\text{H}_2\text{O})_3)_2(\text{WO}_2)_2(\text{BiW}_9\text{O}_{33})_2]^{10-}$ as a catalyst for the epoxidation of this substrate, the results exhibited the excellence in regioselectivities >99% yield and very high turnovers even with only a small molar of hydrogen peroxide. Nevertheless, the difficulty of synthesis is one of the problems limiting the use of metal porphyrins as catalysts in hydrocarbon oxidations. The developing for other classes of catalysts such as salen for investigation in epoxidation reaction has been emerged. As its ligand framework was similar to that of porphyrin, it has been well known that metal salen complexes could catalyze the epoxidation of alkenes using iodosylbenzene or m-CPBA as an oxygen atom donor.[48]

The vanadyl salen complexes coupled with TBHP as an oxidant could selectively oxidize cyclohexene to cyclohexene oxide under mild conditions at 80°C, 1 atm of O_2 with 80% yield. The initial autooxidation of cyclohexene generated allylic hydroperoxides. The vanadyl complexes decomposed the intermediate organic peroxide by cleavage or as electrophilic oxygen-transfer reagents by promoting heterolytic peroxide cleavage. Homolytic cleavage of peroxide by either oxovanadium(IV) or oxovanadium(V) furnished 2-cyclohexen-1-ol and 2-cyclohexen-1-one. The cyclohexene oxide was a major product in this system. Furthermore, the autooxidation by simple vanadyl salts such as VO(acac)$_2$ or VOSO$_4$ under these conditions was much slower and occurred only at allylic positions. The oxovanadium(V) complex catalyzed the epoxidation to yield cyclohexene oxide in moderate yield while the utilization of oxovanadium(IV) catalyst, the effect of the epoxidation rate depended on TBHP decomposition in Haber-Weiss cycle. The result

was attributed to the substituent: with electron withdrawing group the reaction was found to increase both the reduction potential, metal-oxoelectrophilicity and hence the catalytic activity.[49]

Epoxidation of alkenes by iodosylbenzene as an oxygen source and catalyzed by manganese(III)salen complexes exhibited the high catalytic ability in dichloromethane, 4-phenylpyridine N-oxide (PPNO) as additive. Allylic alcohols such as 1,1-dimethyl-1,2-dihydronaphthalen-2-ol selectively epoxidized to mainly enone. For utilizing Mn(III)salen complex as a catalyst, cyclic allylic alcohol was preferentially transformed to the ($2R$-) configuration of cis-epoxide : $trans$-epoxide, 80:20 ratio. Under the same reaction conditions, (Z)-4-phenyl-3-buten-2-ol was epoxidized by this catalyst yielding (R-) configured allylic alcohol in 46% ee, while (S) enantiomer was epoxidized to the ($2S,3R,4S$)-cis-epoxide in 73% ee and the ($2S,3R,4S$)-$trans$-epoxide in 80% ee. The following substrate is shown below.[34]

Recently, it was found that calix[4]pyrrole ligands have acquired special importance because of their efficiency. It was useful to make anion binding agents and especially neutral substrates.[50,51] Calix[4]pyrroles provided useful precursors which play important role in the chemistry of biological processes.[52,53] The epoxidation reaction examined in this research were proceeded by the use of cobalt calix[4]pyrrole complexes. The consideration derived from the structure of ligands is somewhat similar to porphyrin skeleton, in which be used in oxidation and biochemical systems.

Throughout the nature, animal kingdom and substances often use pyrroles to bind cations such as oxygen atom. Chlorophylls and heme are the common substrates that consist of magnesium and iron in porphyrin skeleton. Moreover, the ability of porphyrins as a catalyst was well-known.[45] In addition, the basic skeletons of porphyrin are easy to modify, generate analogues with expanded, contracted,

variations in the number and orientation of the constituent pyrroles. It is also possible to generate close congenors of porphyrins that are nonaromatic. In particular, these modifications can produce polypyrrole macrocycles that act as anion-binding agent. This special property is discussed within the framework of prototypic system such as calixpyrroles.[54] Certain polypyrrole macrocycles unlike porphyrins can act as highly efficient anion binding receptors.[55, 56, 57]

Calix[4]pyrroles (*meso*-octaalkylporphyrinogens) are stable tetrapyrrolic macrocycles first synthesized in the 19th century by Baeyer *via* acid-catalyzed condensation of pyrrole with acetone to produce *meso*-octamethylcalix[4]pyrrole.[58] In the early 1970s, Brown reported a refined procedure that permitted them to obtain tetraspirocyclohexylcalix[4]pyrrole.[51,52] Recently Floriani and coworkers have made an extensive study on the chemistry of metal complexes of various deprotonated octaalkylporphyrinogens.[59,60] Although porphyrinogen (5,10,15,20,22,24-hexahydroporphyrin (H_4L)) is a well known precursor of porphyrin, its chemistry has never been explored. This is mainly due to its instability since it spontaneously forms porphyrin, the oxidation reaction being facile due to the presence of hydrogen atoms in the *meso*(5,10,15,20-) positions. However, a stable form of porphyrinogen has been known for more than a century[61] with alkyl groups at each *meso* positions. Recent investigations by Floriani and coworkers on the use of 5,5,10,10,15,15,20,20-octaalkylporphyrinogen in coordination and organometallic chemistry led to the discovery of their curiousity characteristics.[62]

The importance in the catalytic epoxidation by metalloporphyrinogen complexes under mild condition will be explored. The interested metal calix[4]complex with a variety of six ligands of calix[4]pyrrole that the *meso*-substituted porphyrinogens is noteworthy due to its facile synthesis.[62] The *meso*-octaalkylporphyrinogen ligand is easily converted by the reaction with *n*-BuLi in tetrahydrofuran. The chemistry of lithium is well documented in coordination, organometallic and organic chemistry. Owing to the variety of its interaction modes with hetero and carbon atoms.[63] Lithium derivatives of porphyrin-based ligands are widely investigated. The synthesis and characterization of the lithium derivative of 5,5,10,10,15,15,20,20- octaalkylporphyrinogen (H_4L) and its solvent-dependent forms including the reaction with tetrahydrofuran (THF). This synthesis of H_4L has been found in nineteenth century but its use in coordination and organometallic chemistry

is far more recent.[62,63] The binding of tetraanion to transition metals has been achieved *via* the tetralithium intermediate.[60,63]

$$H_4L + 4LiBu^n \xrightarrow[-BuH]{THF} LLi_4 \cdot 4THF$$
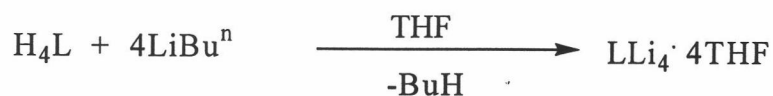
In order to obtain metal complexes of H_4L, a procedure often employed tetraanion in this synthesis to combine metal.[64] In addition to the electronic flexibility, the use of tetraanion has advantage that it stabilized high oxidation states of metals and favors the intramolecular interaction between unsaturated metal and *meso*-alkyl substituents. In terms of catalysis for epoxidation of alkenes, in contrary to the case of porphyrin, porphyrinogen is able to use the periphery for binding metal atom and substrates such as neutral molecules.

Recent literature review has been revealed that cobalt(III) complexes derived from Schiff base catalysts were found to be effective to afford epoxides, respectively.[43,44] Continued studies on the aerobic epoxidation of alkenes catalyzed by cobalt(II)complex found that an aldehyde acted as an excellent reductant when used with molecular oxygen at room temperature.[45] Although there have been some investigations on the use of cobalt complex for catalytic epoxidation of alkenes, there is no report on the utilization of cobalt(II) calix[4]pyrrole complex as a catalyst. This research concerned with the selectively catalytic epoxidation by cobalt(II) calix[4]pyrrole complexes under mild conditions. Moreover, the regioselectivity of this developed system was investigated. The outcome of this work will certainly amplify the use of cobalt(II) calix[4]pyrrole complexes in the catalytic epoxidations.

1.3   The goal of this research

The aims of this research can be summarized as follows.

1.   To synthesize calix[4]pyrrole ligands and cobalt(II) calix[4]pyrrole complexes.

2.   To study the optimum conditions for alkene epoxidations by using cobalt(II)calix[4]pyrrole complexes as catalyst at room temperature.

3.   To apply the optimum conditions for the epoxidations of some selected alkenes.