CHAPTER I

INTRODUCTION

Petrochemical industries become more important manufacture in Thailand. About 95% of total organic chemical manufacture is at present based on petroleum and natural gas. Petroleum is a mixture of hydrocarbons of different basic structures with various molecular weights. There are many reactions were reported to convert these abundant compounds to the desired products. Synthetic organic chemicals have undergone at least a chemical reaction such as oxidation, hydrogenation, halogenation, sulfonation or alkylation. Hydrocarbon derivatives containing oxygen or other heteroatom are important intermediates in organic synthesis and in petrochemical industry.

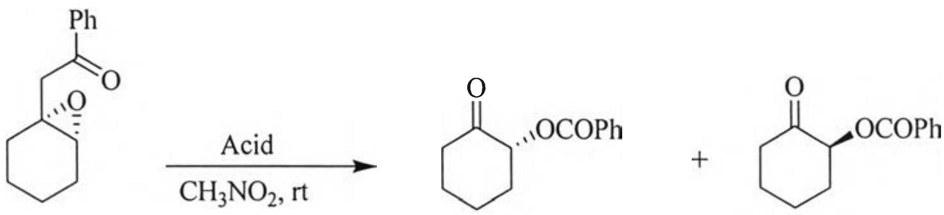
Epoxides are one of the most useful and versatile intermedieate substrates in organic synthesis due to their high reactivity [1] and easy availability through a wide variety of methods [2], and also undergo numerous modes of subsequent transformation. While epoxides are frequently employed as electrophiles in ring-opening nucleophilic addition reactions [3], another common, useful and atom-economical reaction is isomerization to form other functional groups. In the presence of a strong and bulky base, an epoxide may undergo a deprotonation-elimination sequence to form an allylic alcohol [4] frequently with high stereoselectivity. More commonly, epoxides react with Lewis acids to form carbonyl compounds, generally *via* hydride, alkyl, or aryl 1,2-migration pathways [5]. The synthetic applications of epoxides have been the subject of a number of recent and thorough reviews [6].

1.1 Literature review on the rearrangement of epoxides

Epoxide, and important chemical intermediate in organic process industry can be produced by epoxidation of alkenes [7]. Epoxide are raw materials for a wide variety of chemicals such as glycols, alcohols, carbonyl compounds [8], alkanolamines and polymers such as polyesters, polyurethanes, and epoxy resins. Among epoxide-transformations, the rearrangement of epoxides such as those bearing aryl-, vinyl-, silyl-, and trialkyl-substituents to carbonyl compounds is a well-investigated reaction, and leading references can be found in several articles [**9**].

1.1.1 Literature review on the rearrangement of epoxides by acid

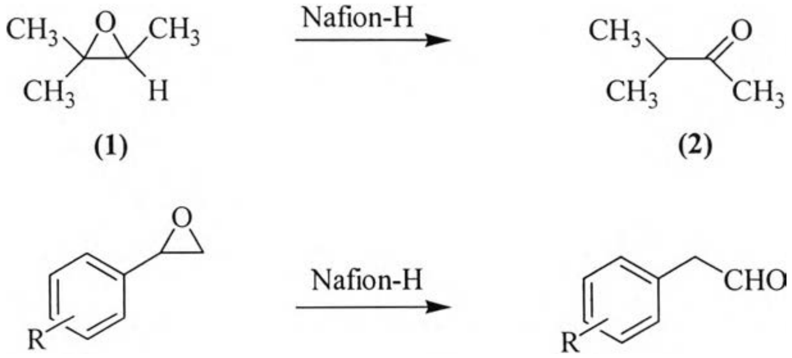
In 1998 Zhu and colleagues reported the enantioselective synthesis and stereoselective rearrangements of enol ester epoxides by acid catalyst. Enol ester epoxides can rearrange to R-acyloxy ketones or aldehydes under acidic such as H_2SO_4 or thermal conditions.



(R) (S)

Under thermal conditions, these epoxides rearrange highly stereoselectively with inversion of configuration [**10**].

In 1998 Prakash and colleagues reported that Nafion-H, a perfluorinated resin sulphonic acid was found to be an efficient and simple catalyst for the isomerization of epoxides to ketones or aldehydes depending on the nature of the substituents on the epoxide carbons. The reaction is very straightforward which give the products in high yield.

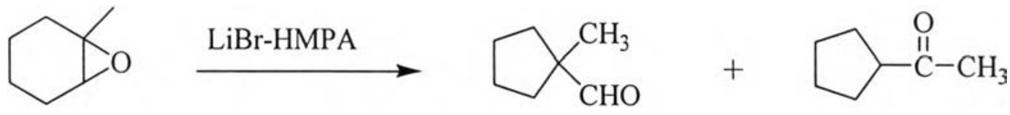


(1) (2)

Isoamylene oxide (**1**) gave isopropyl methyl ketone (**2**) and styrene oxide and its derivatives gave phenylacetaldehyde. Cyclic systems such as cyclohexene oxide, cycloheptene oxide, and cyclooctene oxide did not undergo ring opening under these conditions. Reaction after 24h did not afford the desired product [**11**].

1.1.2 Literature review on the rearrangement of epoxides by salt base

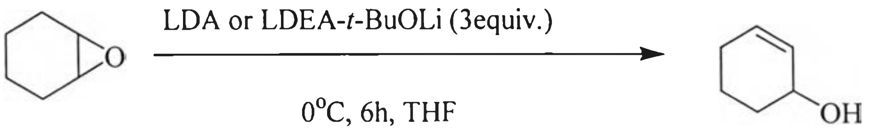
In 1971 Rickborn and Gerkin reported that lithium bromide is solubilized in benzene by the addition of equivalent amount of hexamethylphosphoramide (HMPA) or other phosphine oxide. The resultant complex is an efficient catalyst for the rearrangement of epoxides to aldehydes and/or ketones. Evidence is presented which supports a mechanism involving the lithium salt of the bromohydrin as an intermediate in the LiBr-catalyzed rearrangement.



(3) 95% **(4)** 5%

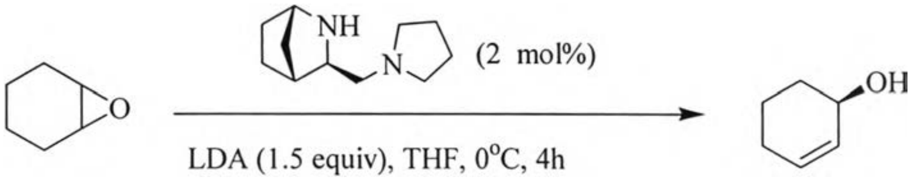
An interesting observation was made using 1-methylcyclohexene oxide as the substrate lithium bromide in benzene by the addition of equivalent amount of hexamethylphosphoramide (HMPA) as a catalyst produce major product (**3**) and minor product (**4**). The lithium salt catalyzed rearrangement of epoxides involves very mild conditions and a degree of selectivity depending on the nature of the epoxides and the choice of lithium salt to use as a catalyst [**12**].

In addition 1997 Saravanan and colleagues reported that a variety of epoxides were synthesized from the corresponding olefins. The deprotonation reaction was carried out in THF. It was found that there is some effect of *t*-BuOLi ion the deprotonation reaction. It was observed that the combination of *tert*-butoxide (*t*-BuOLi) and lithium diethylamide (LDEA) enhanced the isolated yield of 2-cyclohexen-1-ol in the deprotonation reaction of cyclohexene oxide.



The effect of *t*-BuOLi in the rearrangement of epoxides with LDA and LDEA, There is an appreciable increase in the isolated yield of the product. The drawback with the method was that it did not show any effect on acyclic epoxides [**13**].

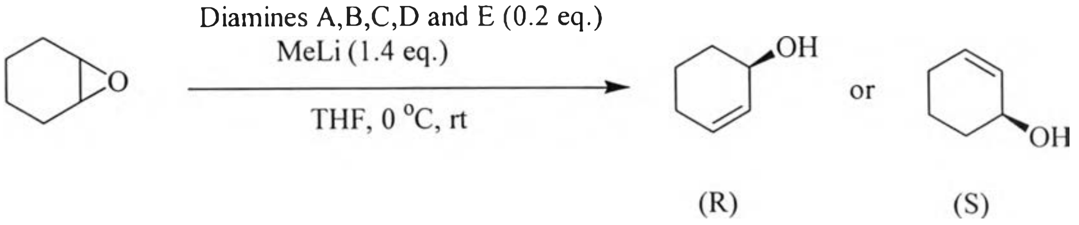
In 2002 Bertilsson and Andersson reported that the use of chiral base for the asymmetric (1*S*,3*R*,4*R*)-3-(pyyrrolidinyl)methyl-2-azabicyclo[2.2.1]heptane catalyzed rearrangement of cyclohexene oxide to (1*R*)-cyclohex-2-en-1-ol. No significant improvement of the reaction protocol was achieved although some interesting trends were observed. The enantioselectivity in the cyclohexene oxide rearrangement was however markedly improved by slow addition of the achiral base.

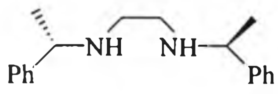


The achiral base had great influence on the reaction outcome of the catalytic asymmetric lithium amide-mediated rearrangement of epoxides. No clear correlation between enantioselectivity and conversion could be detected, which might indicate that the achiral base has an additional role in the reaction. Of the bases investigated, LDA remains superior. However, in the presence of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), n-BuLi reacts with similar efficiency. By keeping the concentration of achiral base low during the reaction, the enantioselectivity can be significantly improved [**14**].

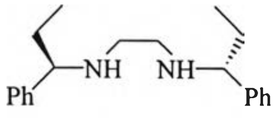
In 2004 Equey and Alexakis reported that cyclohexene oxide can be rearranged with good levels of induction (up to 68% ee) with substoichiometric amounts of chiral bases derived from readily available diamines.

The substituents of the amine moiety improved the enanioselectivity for the base-mediated epoxide rearrangement of cyclohexene oxide [**15**].

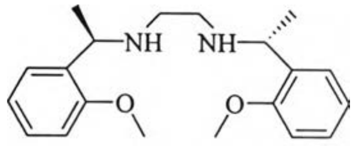




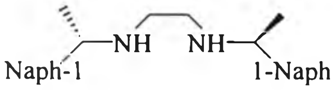
A (S,S)



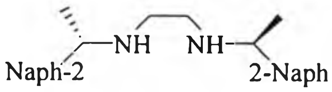
B (R,R)



C (R,R)



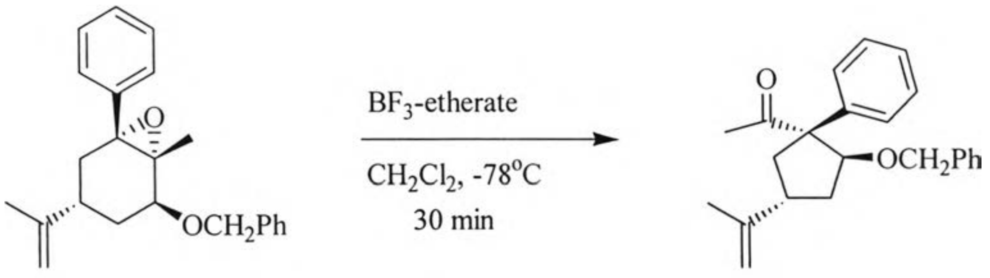
D (S,S)



E (S,S)

1.1.3 Literature review on the rearrangement of epoxides by Lewis acid

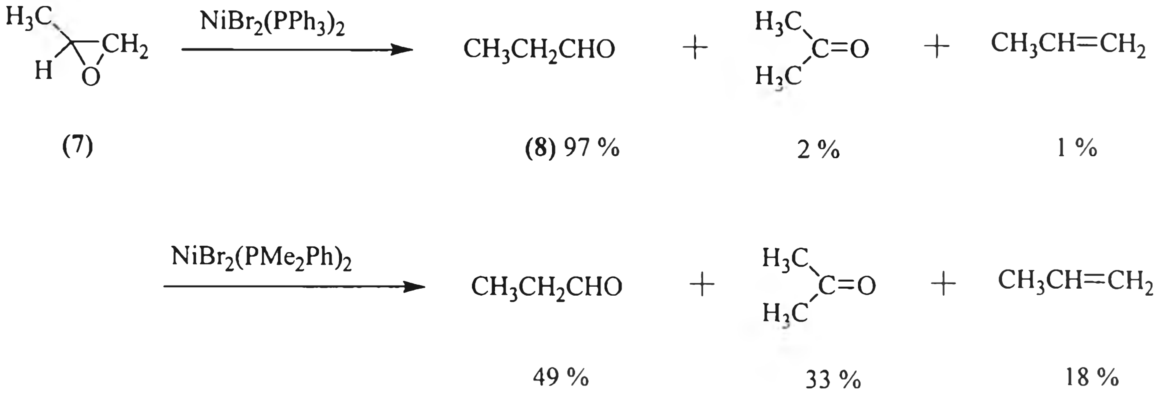
In recent years, emergence of Lewis acid as a catalyst for affecting a variety of chemical transformations in chemo-, regio-, and stereoselective fashion prompted use to initiate a systematic study. Lewis acid-catalyzed rearrangement of epoxides to carbonyl compounds is a well-known reaction in organic chemistry. It is generally explained that this reaction proceeds by coordination of a Lewis acid molecule on the oxygen atom, fission of a C-O bond to form an electron-deficient carbon center at the more substituted carbon atom, and migration of a substituent to the adjacent carbon center with concomitant formation of a carbonyl compound. For instance in 1999 Neef and colleagues reported that use of boron(III) fluoride etherate catalyze to the rearrangement of epoxides [**16**].



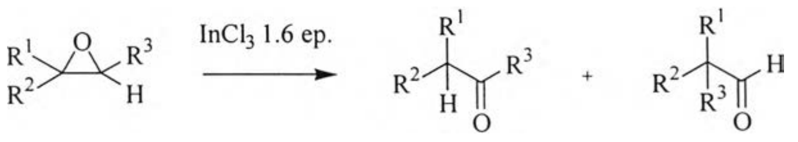
(5) **(6)** 85%

The BF_3-etherate treatment of benzyl ether-protected epoxy alcohol (**5**) proceeded with clean and high yield formation of a single ring-contracted ketone (**6**).

In 1986 Miyashita and colleagues reported that $NiBr_2(PPh)_3$ catalyze rearrangement of 1,2-epoxy-propane (7) to propionaldehyde (**8**) under mild conditions, while $NiBr_2(PMe_2Ph_2)_2$ gave a mixture of acetone, propylene and aldehyde. Regioselectivity for a C-O bond cleavage of epoxide is determined by the nature of the ligand coordinated to the metal center [17].



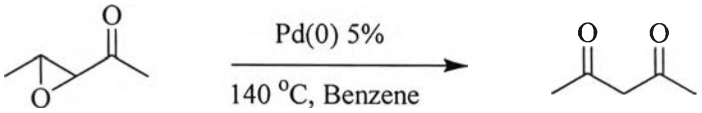
Moreover in 1998, Ranu and Jana reported that use of indium(III) chloride as a catalyst on the rearrangement of epoxides. A simple and efficient procedure for the rearrangement of substituted epoxides catalyzed by $InCl_3$ has been developed. Aryl-substituted epoxides isomerize with complete regioselectivity to form a single carbonyl compound via cleavage of the benzylic C-O bond. The reactions are simple, fast, and high yielding. This procedure is very mild compared to those catalyzed with BF_3 and other Lewis acids and compatible with several acid-sensitive functionalities. This protocol provides a highly selective synthesis of substituted benzylic aldehydes and ketones.



R^1, R^2, R^3 = H, alkyl or phenyl

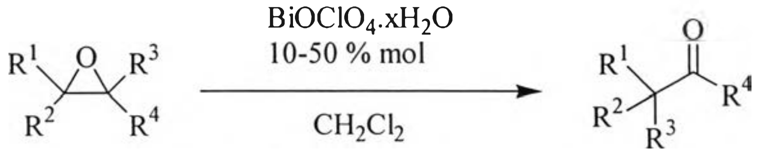
A wide range of structurally varied epoxides were subjected to rearrangement with $InCl_3$ by simple procedure to provide the corresponding carbonyl compounds in good yield. For instant 1-aryl-, 1,1-diaryl-, 1,1-alkyl and aryl-substituted underwent rearrangement by exclusive hydride shift to give the respective aryl-substituted acetaldehyde as the only isolable compound. While the rearrangement of tri- and tetrasubstituted aryl epoxides selectively producing the corresponding methyl ketone [18].

In 1997 Kulasegaram and Kulawiec reported the isomerization of monoalkyl-substituted epoxides to ketone compounds using a palladium(0) catalyst [**19**] generated from Pd(OAc)$_2$ [**20**]and tertiary phosphines, and that rearrange aryl-substituted epoxides to benzylic aldehydes or ketones, depending on the substitution pattern.



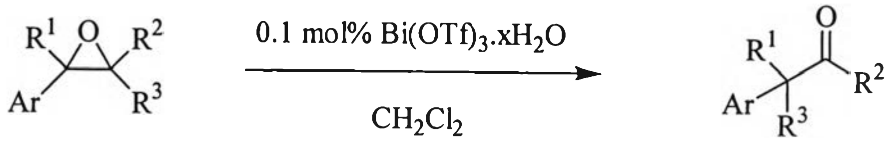
In both of this reaction, the products are formed in high yield under mild conditions with complete chemoselectivity for the indicated functional group [**21**].

Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis due to their low toxicity. In an earlier study, In 1999, Anderson and colleagues reported that aryl-substituted epoxides and aliphatic epoxides with a tertiary epoxide carbon undergo smooth rearrangement in the presence of 10-50 mol% bismuth(III) oxide perchlorate, BiOClO$_4$.xH$_2$O, to give carbonyl compounds. The rearrangement is regioselective with aryl-substituted epoxides and a single carbonyl compound arising from cleavage of benzylic C-O bond is formed [**22**].



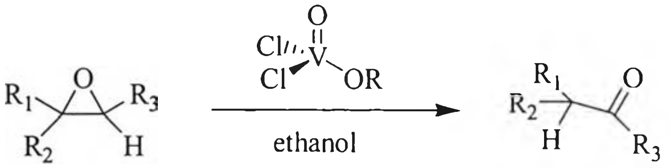
The rearrangement of both *cis*- and *trans*-stilbene oxides gave diphenylacetaldehyde as the only product in high yield. Nevertheless, rearrangement of styrene oxides did not give a very pure product. While starting material was seen to disappear by TLC in 15 min, the crude product appeared to be very impure and attempted purification gave very low yields (15%) of phenylacetadehyde.

In addition 2001 Bhatia and colleagues reported that aryl-substituted epoxides undergo smooth rearrangement in the presence of bismuth(III) triflate, Bi(OTf)$_3$.xH$_2$O (0.1 mol%). Bismuth triflate is a highly efficient catalyst for rearrangement of aromatic epoxides to carbonyl compounds.



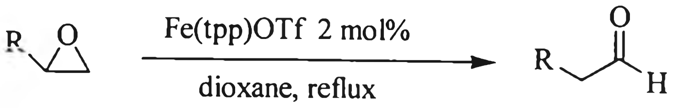
Aryl-substituted epoxides undergo smooth rearrangement in the presence of 0.01-0.1 mol% $BiOClO_4.xH_2O$. The reaarangement is regioselective with aryl-substituted epoxides, and products arise from cleavage of the benzylic C-O bond. The highly catalytic nature of this method coupled with the fact that the reagent is relatively non-toxic, easy to handle and inexpensive make it an attractive alternative to more corrosive and toxic Lewis acids, such as BF_3Et_2O, currently used to effect epoxide rearrangement [**23**].

Moreover, in 2000 Fernando and colleagues were reported that high valence vanadium complexes induce the selective rearrangement of epoxides. The monosubstituted epoxides are isomerized with complete regioselectivity each forming a single carbonyl compound exclusively.



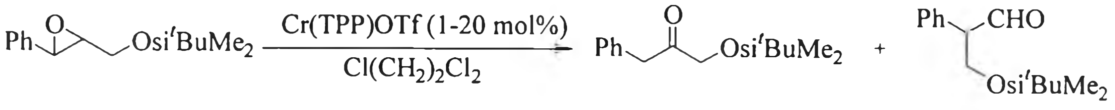
Under their conditions, the rearrangement of epoxides by vanadium complex, addition to the C-O bond of mono-substituted and 1,1-disubstituted epoxides promoted their rupture, and hydrogen migration occurred selectively producing the corresponding aldehydes [**24**].

From many literature cite was observed are isomerization reactions of epoxides having a simple monoalkyl-substituent to the corresponding aldehyde and/or methyl ketones [**25**], In particular, reports on a regioselective catalytic version of the isomerization to aldehydes are very limited [**26**]. In 1996, Takanami and colleagues reported that development of novel and synthetically useful chemical properties of metalloporphyrin works as a mil and characteristic Lewis acid catalyst in the rearrangement of small-ring heterocycles [**27**]. Iron(III) tetraphenylporphyrin, Fe(tpp)OTf, is an efficient catalyst for the regioselective rearrangement of simple monoalkyl-substituted epoxides into the corresponding aldehydes.

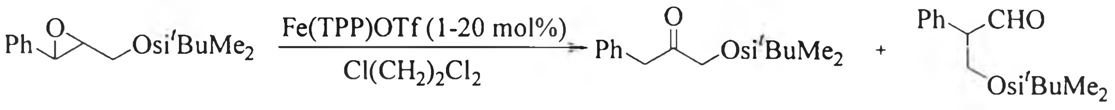


The Fe(tpp)OTf catalyst has several advantages such as it stable, crystalline solid is more convenient to handle, use less amount of catalyst, high yield and almost complete regioselectivity [**28**].

Not only that in 2004 Kohji and colleagues reported that a highly regio- and stereoselective rearrangement of epoxides (**9**) to aldehydes (**11**) with a porpyrin-based Lewis acid catalyst, chromium(III) tetraphenylporphyrin triflate, Cr(TPP)OTf, in low catalyst loading (1-20 mol %) under very mild conditions. While using Fe(TPP)OTf as a catalyst in rearrangement of epoxide (**9**) gave only ketone (**10**) in high yield [**29**].



(**9**) (**10**) 0 % (**11**) 97 %



(**9**) (**10**) >99 % (**11**) 0 %

Moreover, the present catalytic method complements Fe(TPP)OTf-catalyzed the rearrangement of epoxides (**9**) into ketones (**10**) *via* hydrogen migration [**30**], ketones (**9**) and aldehyde (**11**) can selectively of a simple choice of Fe(III) and Cr(III) central metal ions of the porphyrin catalysts.

From these literatures, epoxides are one of the most intermediate in the organic industry process. The importance in the catalytic rearrangement by Lewis acid under mild condition will be explored. Conversion of epoxides to carbonyl compound is another important process in petrochemical industry. The search for cheap, simple and selective frequency focuses on the ligand of iron. An interesting example is Fe(acac)$_3$ catalyst for the rearrangement of epoxides in the short period of time and mild condition. These iron salts and complexes are inexpensive. Catalytic efficiency of these complexes was screened using the rearrangement of styrene oxide as a model substrate reaction. After the reaction was optimized, it will be applied to a variety of different epoxides.

1.2 The goal of this research

The aims of this research can be summarized as follows.

1. To study the optimum conditions for epoxide rearrangement by using $FeCl_3$ and $Fe(acac)_3$.
2. To apply the optimum conditions for the rearrangement of some selected epoxides.