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Abstract of thesis entitled "Olefins Epoxidation Catalyzed by Ruthenium Porphyrins Using Dioxygen as Oxidant"

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Abstract

$Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ were synthesized by reacting $Ru^{II}(TDCP)(CO)(MeOH)$ and $Ru^{II}(TMP)(CO)(MeOH)$ with m-chloroperoxybenzoic acid in dichloromethane.

$Ru^{VI}(P)O_2$ complexes are effective in epoxidation of olefins. The turnover rates by $Ru^{VI}(TDCP)O_2$ are lower than that of corresponding reactions catalyzed by RuVI(TMP)O2. Both catalysts are deactivated after the reaction by the formation of a stable Ru(II) carbonyl species.

Kinetics studies showed that the intermediates are cationic 3-membered species. A concerted oxygen insertion mechanism is proposed.

List of Figures

List of Tables

List of Abbreviations

ABBREVIATION	FULL NAME
CH_2Cl_2	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquine
EtOH	Ethanol
GC	Gas Chromatography
H_2TDCP	5,10,15,20-meso-tetrakis(2,6-dichlorophenyl)-21H-23-H-porphyrin
H_2TMP	5,10,15,20-meso-tetramesityl-21H-23-H-porphyrin
H_2TPP	5,10,15,20-meso-tetraphenyl-21H-23-H-porphyrin
IR	Infrared
m-CPBA	m-Chloroperoxybenzoic acid
MeOH	Methanol
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
$Ru^{VI}(P)O_2$	*trans*-dioxoruthenium(VI) porphyrin complex
UV	Ultra-violet
WCOT	Wall Coated Open Tubular

Content

Chapter 4 Results and Discussion

Chapter 1 Introduction

1.1 General Background

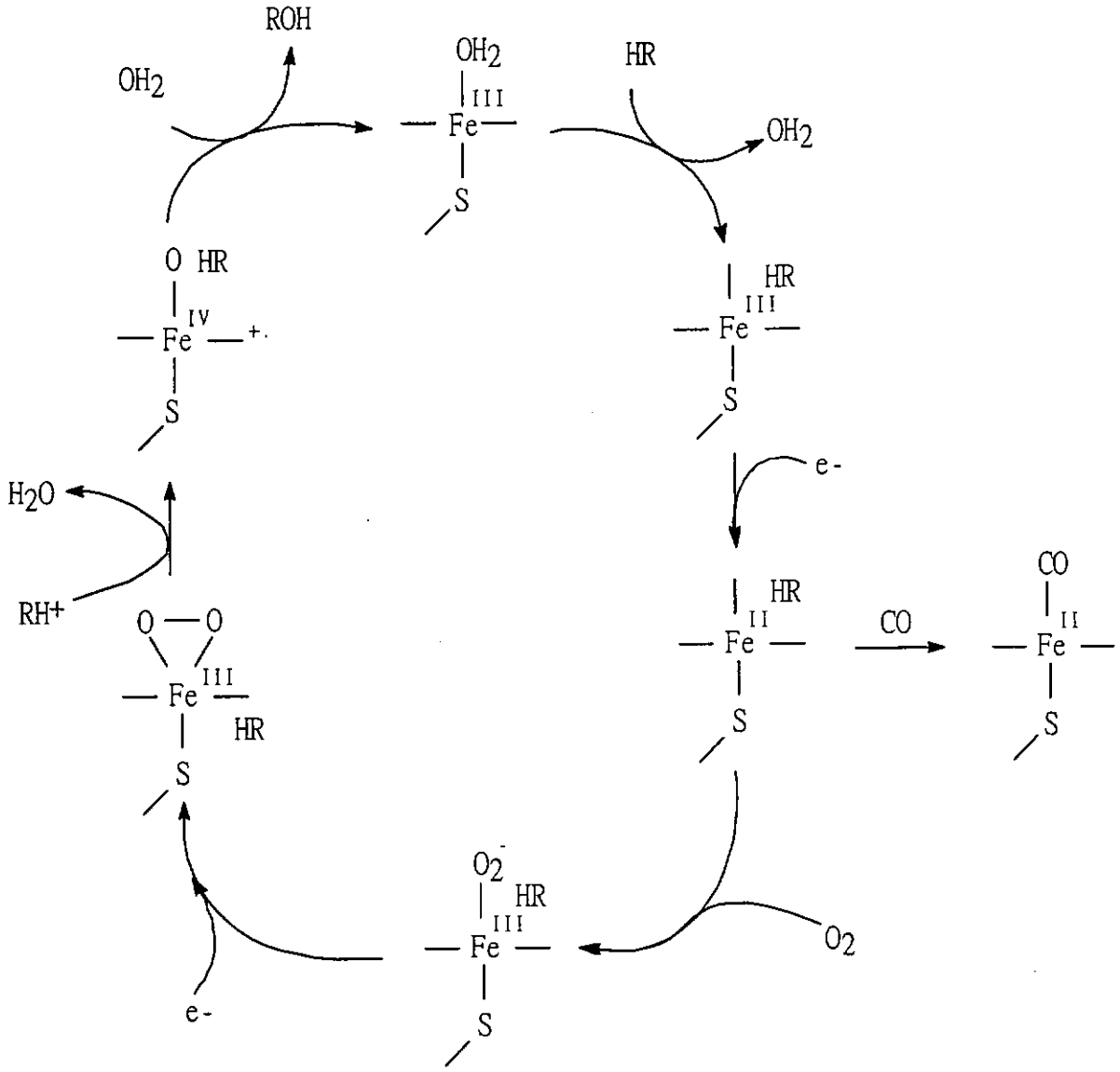
Selective oxidation of hydrocarbons is an important aspect of chemical industries and living organisms. They include production of fine chemical in chemical industries and biological processes such as detoxification, biosyntheses and even metabolism, inside our bodies. Oxygenated products, e.g. alcohols, carboxylic acids and epoxides etc., from natural products are important in many chemical industries or even human beings.

In the past, oxidation of hydrocarbons was achieved by reacting substrates with molecular oxygen over supported metals at high temperatures and/or sometimes elevated pressures. However, undesirable products, e.g. over-oxidized products, are always present together with the desired products because of the radical chain reaction nature of the oxidation reactions. The high bond energies of C-H and C-C bonds limited the efficiency of these oxidation reactions. The small difference in bond dissociation energy between C-H bond in terminal methyl groups and secondary or tertiary groups made the reaction less selective.

Therefore, there are needs for developing effective oxidizing systems in order to overcome the problems and control the final outcomes of the reactions.

1.2 Control of Oxidation Reaction

Without carrying out reactions under high temperatures and pressures, enzymes inside living organisms can effectively oxidize substrates under moderate conditions. Enzymes like monooxygenases have the abilities to hydroxylate non-activated C-H bonds in hydrocarbons. These enzymatic reactions involve electron donors, which are commonly found as NADPH, and oxygen sources. These monooxygenases utilize reductive activation of O_2 where 1 O-atom is reduced to H_2O and the second O-atom becomes available within a high-valent metal-oxo species for the oxygenation process (Fig. 1.1).[1]



Simplified reaction:

$$RH + O_2 + NADPH + H^+ \xrightarrow{\text{P-450}} ROH + H_2O + NADP^+ \qquad \text{-Eq.1}$$

Fig 1.1: Reaction cycle for cytochrome P-450.[2]

Cytochrome P-450, which got its name from the characteristic absorption at 450 nm, [3] is a well-known ubiquitous membrane bound monooxygenase enzyme found in tissues of various animals: in liver, lung, kidney and curtis. It has been extensively investigated for its ability to oxidize hydrocarbons.[4][Miss1] Reactions include oxidation of steroids, vitamins, fatty acids, drugs, pesticides and carcinogens. Those reactions are important in normal physiological functions in living organisms.[5] General P-450 catalyzed reactions are listed in Table 1.1.[6] The distinguishing substrate selectivity and activity exhibited by the cytochrome P-450 enzymes produce a stimulating effect on synthesizing modeling systems to mimic the oxygenation reactions of this enzymes and hence develop a biomimetic approach to the search for purely chemical catalysts.[7, 8]

Successful isolation of cytochrome P-450 revealed that the active center is a porphyrin iron complex in equilibrium between a hexacoordinate low-spin Fe (III) form and a high-spin pentacoordinate Fe(III) form.[9] Iron porphyrins, which are synthetic analogues to the active center of heme-containing enzymes, are then used as a studying model to elucidate the chemistry of cytochrome P-450 catalyzed hydrocarbons oxidation.[10]

Table 1.1 Typical P-450 reactions[11]

Reaction type	Simplified example	Typical substrate
Aliphatic Hydroxylation	Cyclohexane ⟶ cyclohexanol	Pentobarbital
Aromatic Hydroxylation	Benzene ⟶ Phenol	Phenobarbital
Alkene Epoxidation	Cyclohexene ⟶ Cyclohexene oxide	Aldrin
N-Dealkylation	$CH_3N(H)CH_3 \longrightarrow CH_3NH_2 + H_2C{=}O$	Methadone
O-Dealkylation	$C_6H_5OCH_3 \longrightarrow C_6H_5OH + H_2C{=}O$	Codeine
Oxidative Deamination	$(CH_3)_2CHNH_2 \longrightarrow (CH_3)_2C{=}O + NH_3$	Amphetamine
S-Oxidation	$CH_3SCH_3 \longrightarrow (CH_3)_2S{=}O$	Chlorpromazine
Reductive Dehalognation	$C_6H_5CH_2Br \longrightarrow C_6H_5CH_3$	Halothane

1.3 Oxidation of Hydrocarbons

1.3.1With Donors of Active Oxygen

Various oxygen sources had been used in iron porphyrins catalyzed oxidation. They included iodosobenzenes[1b] and its derivatives,[12] hypochlorites,[13] hydrogen peroxides,[14] alkylhydroperoxides,[15] molecular oxygen[16] and N-amine oxides.[17] Iodosobenzene was first used by Ullrich et al. and Groves et al. The reactivity and effectiveness of hydrocarbon oxidation catalyzed by metalloporphyrin using iodosobenzene was well published. The product yield, selectivity and kinetics were found to be dependent on the nature of the metalloporphyrin, the oxygen donor and the axial ligand. Apart from the use of N-oxide in metalloporphyrin catalyzed oxidation, nitrous oxide[18] was studied by Groves and his coworkers in ruthenium porphyrin system.

1.3.2With Dioxygen Accompanied With Reducing Agent

In an attempt to protect the environment and reduce the cost of the catalytic reactions, there is an increasing interest in using molecular oxygen as an external oxygen source in metalloporphyrins catalyzed hydrocarbons oxidation. Attempts were made to mimic the biological oxidative system. To construct a realistic model of this system, chemists developed hydrocarbon oxidation systems using dioxygen coupled with a reductant. Tobushi and Yazaki[19] first utilized dihydrogen on colloidal platinum

as a reducing agent to mimic the chemistry of monooxygenase. Other reducing agents, such as sodium ascorbate, zinc powder and dihydropyridine, and electrochemical methods were also adopted. Studies of the oxidation of hydrocarbons by the aid of a reducing agent revealed the fact that product selectivity and kinetics are determined by the nature of the metalloporphyrin and the electron- and proton-donor.

1.3.3With Dioxygen Without Reductant

Molecular oxygen is an abundant and inexpensive reagent that can be utilized in a variety of useful oxidation reactions. Nonetheless, it is environmental friendly in nature. However, the biradical property of molecular oxygen will lead to radical chain reaction and finally, lack of product selectivity. By coordination to a metal center, this undesirable property can be eliminated. Ellis and Lyons[20] studied *meso*-porphyrin complexes of Mn-, Fe-, Cr- with azide as an axial ligand in the catalyzed autooxidation of *iso*-butane into alcohol.

1.4 Choose of Metal as Metal-oxo Complexes

Oxo-metals such as chromates, manganates were chosen for stoichiometric oxidation reactions with hydrocarbons.[21] The catalysts were commonly supported-metal with metal-oxo bond and the metal center is in a high valence state. Those oxo-metal complexes can effectively oxidize the hydrocarbons in relatively mild conditions especially in liquid phase reactions.

The metal used for model compound should has a higher and stable oxidation state for metal-oxo complexes. Late transition metals was not chosen as they tend to form μ -oxo instead of terminal oxo complexes.[22] So, we limited our choice to period 4 and 5 elements.

Under these circumstances, organometallic oxo complexes then received intensive attention in metal-catalyzed hydrocarbons oxidation.[23] Hydrocarbon oxidations catalyzed by iron-substituted metalloporphyrins have been studied intensively in the past decades.[24, 6c] However, the intrinsic reactivities and labilities of the intermediate during the reaction hindered further and detailed studies of the underlying mechanisms of oxygen transfer.

1.5 Proposed Mechanisms of Oxygen Transfer

High-valent Iron-oxo species have been suggested to be the active intermediates in many oxygen transfer reactions, e.g. iron porphyrin systems. Several mechanism for the catalyzed oxygen atom transfer were previously proposed (see Fig. 1.2):

(i) Direct Oxygen Atom Transfer

This mechanism was proposed by Collman et al. in the study of the oxygenation of styrene by Fe- or Mn-porphyrin complexes.[25]

(ii) Free Radical Addition Followed by a Fast Ring Closure

The lack of stereospecificity in the reaction product suggested the mechanism to be addition of metal-oxo to C=C bond. This gives rise to an open-chain of metal-oxo-carbon radical species.[26] It was argued against by the work done by Bruice and Castellino.[27] They showed that a neutral radical species cannot be a discrete intermediate.

(iii) Reversible Metalleoxetane Formation

This mechanism was initially proposed by Sharpless et al. in the study of the oxidation of olefins by chromyl chloride.[28] Metalleoxetane was considered to be a possible transition state in metalloporphyrin-catalyzed epoxidations although it's lifetime should be greater than $10^{-12}s^{-1}$.[29] The presence of rearrangement products and N-alkylhemins argued against this theory.

(iv) Electrophilic Addition and Fast ring Closure

The linear correlation of rate of alkenes epoxidation with ionization potential of alkenes found by Traylor[30] suggested an electron transfer mechanism. This is also a general pathway demonstrated by cytochrome.[31]

(v) Electron Transfer Followed by a Collapse to a Radical or to a Carbocation

Proposed by Bruice and Castellino[32] using a *cis*-olefin with *trans*-2, *trans*-3-diphenylcyclopropyl substitutents to trap possible radical-cation intermediate. The mechanism was proposed based on the presence of rearrangement products.

(vi) Bridged Metal-oxo Complex

Proposed by Jorgensen[33] and co-workers based on theoretical grounds. N-alkylation complexes isolated by Traylor and Dolphin[34] supported this mechanism.

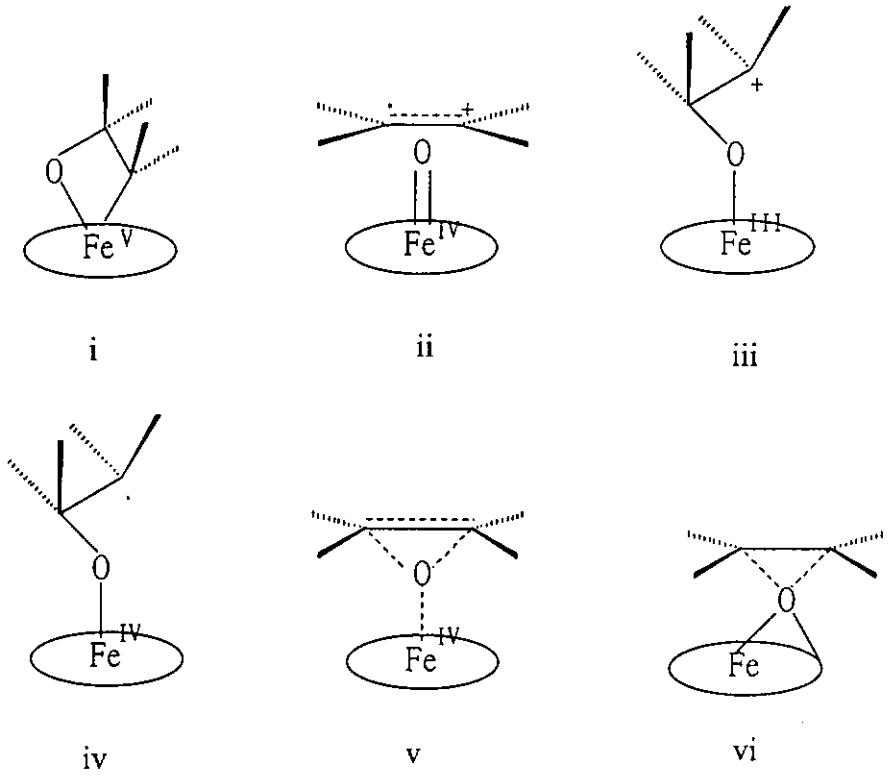


Fig. 1.2. Proposed intermediates in the epoxidation of olefins catalyzed by iron prophyrins. i) metallaoxetane, ii) alkene-derived π-radical cation, iii) carbocation, iv) carbon radical, v) concert insertion of an "Oxene" into the C=C bond of alkene, and vi) bridged metal-oxo complex.

Other possible active oxidants that can be generated in the H_2O_2, PhIO, m-CPBA and O_2/aldehyde reaction have been proposed (Fig. 1.3). Iron-hydroperoxide complex, compound II, is generated by the complexation of H_2O_2 with an Fe cyclam complex.[35] Complex III is an active intermediate in Lewis acid metal-catalyzed epoxidation using iodosobenzene.[36] The iodine(III) center was found to be the electrophilic center for reaction with the electron-rich olefin double bond. Complex IV is formed by the

complexation of m-CPBA with an iron complex.[37] Complex V is a peroxy radical formed in O_2/aldehyde-metalloporphyrin system.[38] Olefins were oxidized to give corresponding epoxides. Complex VI[39] has been synthesized as models for cytochrome P-450. It was found to be nucleophilic in nature.

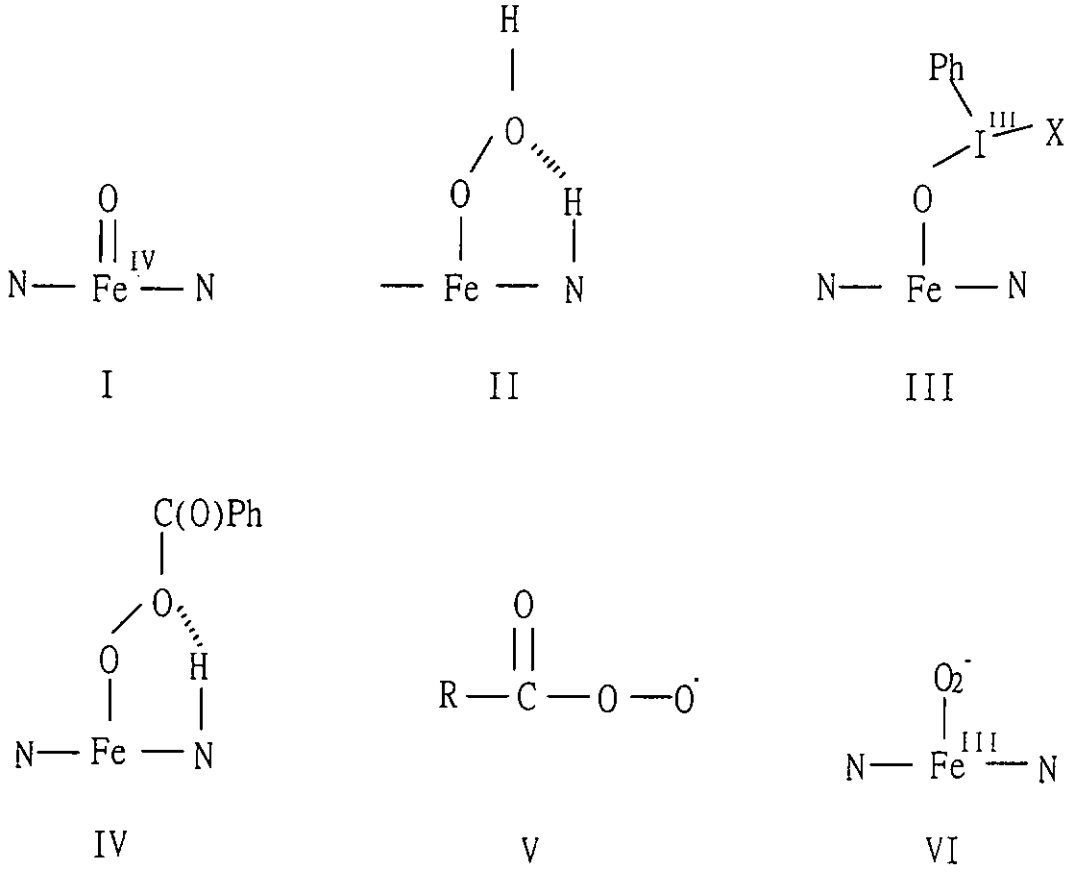


Fig. 1.3: Possible intermediates in metal-catalyzed oxygenation reactions.

1.6 Use of Biomimetic Ligands

In order to develop an effective oxidizing agent, the metal itself in the organometallic complex should be sufficiently stable in a single change of oxidation state during the reaction. It prevents any further oxidation of products obtained by the metal ion in the intermediate state. Chromic acid oxidizes cyclobutanol and gives ring cleavage products instead of the desired cyclobutanone.[13a] As a result, multi-anionic clelating ligands were used to stabilize the metal ions making the whole metal-oxo complexes stable throughout the reaction.

Several types of anionic ligands were used in previous studies.[40] They all have the characteristic property that they are resistant to oxidation by the central metals or the external oxidants. In metalloporphyrin systems, electron-withdrawing groups are frequently employed as the choice of substitutents on the phenyl ring of the tetraphenyl-porphyrin molecules to prevent electrophilic attack by third parties to the porphyrin rings.[41] Also, the central metal should have vacant sites for the binding of oxidants or substrates after binding to an anionic complexing ligand.

To mimic the substrate selectivity and product regio-selectivity of the cytochrome P-450, sterically hindered porphyrinato-ligands have been elucidated.[42] TMP, TDCP are the mostly concerned synthetic models and were utilized frequently in modeling the heme environment. In Meunier's studies of olefin epoxidation catalyzed by ruthenium porphyrin,[43] TMP derivative was found to be more selective than TPP analogue. Over

95% selectivity was obtained in TMP system while only around 70-90% was found in TPP system. The overall epoxide yield for TMP was also higher than TPP too. In Suslick's studies of regioselective epoxidation reaction of dienes with Mn-porphyrin,[44] a series of sterically hindered porphyrin complexes are shown to be shape-selective. The substitutents have the function of preventing bi-molecular deterioration[45] of the complexes and fine-tuning the complexes activities.[46]

Since asymmetric oxidation of hydrocarbons has been a hot topic in recent years, various enantioselective epoxidation catalysts have been elucidated. Mansuy[47] synthesized a "basket-handle" iron porphyrin and used it to catalyze the epoxidation of p-chlorostyrene into (R)-epoxide with 50% e.e. Collman[48] utilized a threitol-strapped manganese porphyrin to catalyze the epoxidation reaction of unfunctionalized olefins. Up to 88% e.e. was obtained in the epoxidation of 1,2-dihydronaphthalene. Groves[49] has prepared a chiral, vaulted binaphthyl porphyrin which was found to be a good stereoselective catalyst in asymmetric oxygenation of alkanes, alkenes and alkyl sulfides.

1.7 Ruthenium-constituted Metalloporphyrins

Product yields, rates of reaction, substrates selectivity are all dependent on the nature of central metal ions in the complexes, the presence of axial ligands and the nature of oxygen donors.[50]

The mechanism of these metalloporphyrin catalyzed hydrocarbon oxidation reactions involve the formation of high-valent oxo-metal porphyrin complexes, M=O.[1c] Various metal-oxo porphyrin complexes have been investigated and some of them like Titanium, Vanadium, were found to be unsuccessful oxygen transfer agents although they are stable in the high-valence state.[51] Cr-oxo porphyrins[52] are stable but showed little oxygen transfer activity when compared to Mn-[53] or Fe- porphyrins, despite the fact that their oxo species are quite labile in nature.[54]

Nevertheless, the periodic relationship between ruthenium and iron allowed chemists to use ruthenium-constituted metalloporphyrins as a studying analogue to mimic the mechanism of oxidation effected by cytochrome P-450. The ability of forming a stable metal-oxo species of ruthenium, which was achieved by the aid of the sterically encumbered porphyrin ligands, making it a hot topic in metalloporphyrin catalyzed hydrocarbon oxidation reactions. High-valent oxo-ruthenium complexes were well accepted as good potential catalysts[55] in the oxidation of hydrocarbons.[56]Groves and his co-workers demonstrated that $Ru^{VI}(TMP)O_2$ species were capable of catalyzing aerobic oxidations.[57]

In this work, ruthenium constituted metalloporphyrins with sterically bulky porphyrin ligands, TMP and TDCP, using dioxygen as the external oxidant were chosen as a studying model to probe the steric and electronic effect in the hydrocarbon epoxidation reactions. Detailed mechanism was discussed.

Chapter 2 Experimental Section

2.1 Reagent and Material

Dichloromethane (A.R., ACROS), chloroform (A.R., ACROS), hexane (99%, ACROS) were firstly washed with conc. H_2SO_4(aq.), neutralized and then distilled from CaH_2. *trans*-Stilbene was recrystallized from ethanol and dried under vacuum. Olefins were passed through short column of neutral Al_2O_3(s) immediately before use. Oxygen (high purity, HKO) was used as received without further treatment. Other solvents and reagents were used without further purification.

2.2 Physical Measurements

2.2.1 Nuclear Magnetic Resonance Spectra Analysis

Nuclear magnetic resonance spectra were recorded using an Brücker 400MHZ nuclear magnetic resonance spectrometer. Chemical shifts were measured either with reference to the residual proton peak of the solvent or to the signal of TMS. Quantitative measurements were done by area integration of the individual peak area.

2.2.2 Ultra Violet-Visible Spectra Analysis

UV-Visible spectra were recorded on a Hewlett Packard 8452-A, photo-diode array spectrophotometer equipped with a microcomputer for data processing.

2.2.3 Infra Red Spectra Analysis

Infra red spectra were recorded with Nicolet, Magna 750 FT-IR spectrophotometer. The data were recorded by a microcomputer. Spectra for ruthenium porphyrins were obtained by using KBr pressed-disc method. IR spectra for olefins or other oxidation products were obtained as thin-film with NaCl cells.

2.2.4 Gas-Chromatographic Analysis

GC analysis were carried out on an Hewlett Packard 5730A gas-chromatograph with flame-ionization detector and cool on-column injector. Chromatographic separation were performed using either

- Hewlett Packard Ultra-1 0.32mm x 25m x 0.5μ fused silica WCOT capillary column or
- J&W DB-5 0.32mm x 20m x 1.0μ fused silica WCOT capillary column

Chromatographic peaks were recorded and integrated by Hewlett Packard 3380A

integrator. Hydrogen gas was used as the carrier gas. Oxidized products were quantified by internal standard method.

2.2.5 Gas Chromatography - Mass Spectrometic Analysis

Oxidized products were identified by GC-MS on a Hewlett Packard 5972 series mass selective detector interfaced to a Hewlett Packard 5890 series II gas chromatograph. Chromatographic separation was effected by fused silica capillary column (J&W, DB-5, 0.25mm x 20m x 1.0μ). Argon (high purity) was used as carrier gas.

2.3 Conditions for Oxidation of Olefins

2.3.1 Stoichiometric Oxidation

All stoichiometric reactions were carried out under a nitrogen atmosphere. In a typical run, a solution of olefin (10μL) in CH_2Cl_2 (2mL) was degassed by 3 freeze-thaw cycles in a 10mL round-bottomed flask. The reaction vessel was filled with nitrogen gas. Metal complexes (5mg) were added. The reaction mixture was well stirred for 3 hours. After the addition of an internal standard, an aliquot was taken for GC, ^{1}H-NMR or GC-MS analysis. A control, which did not have any catalyst, subjected to the same condition was conducted to monitor for any oxidized products under this condition.

2.3.2 Catalytic Aerobic Oxidation

i) Atmospheric Pressure

In a typical run, catalyst, olefin and solvent were added into a glass vial. The vial was loosely capped to allow gas exchange with the atmosphere. The vial was kept at constant temperature by immersion in an thermostated oil bath and was well stirred. Aliquot were taken out for analysis at suitable time intervals. A control containing no catalyst was carried out to monitor for any oxidized product obtained.

ii) High Oxygen Pressure

After the addition of suitable amount of catalyst, olefin and solvent, the loosely capped vial was put into a high-pressure reactor. The reactor was pressurized by oxygen supplied from an external compressed oxygen cylinder. The whole reaction vessel was kept at constant temperature and was well stirred. Aliquot were taken out for analysis at suitable time intervals. A control, which did not have any catalyst, subjected to the same condition was conducted to monitor for any oxidized products under elevated oxygen pressure and temperature.

2.3.3 UV-Visible Monitoring of Epoxidation of Olefins Catalyzed by Ru Porphyrins

Ru porphyrin ($1x10^{-5}$ moles) was added to a quartz cell containing 10 μL of olefin in 3 ml of CH_2Cl_2. The progress of the reaction was then monitored by a UV-Visible spectrophotometer at 20 minutes time intervals. The resultant spectral data were recorded. Pseudo-first order plot of the disappearance of the Ru(VI)-dioxo species were obtained by monitoring the absorbance at their respective soret band.

2.3.4 Data Reduction Method

The rate of disappearance of $Ru^{VI}(P)O_2$ was measured by monitoring the decrease in absorbance of the Soret band of the $Ru^{VI}(P)O_2$ at around 420 nm. The reactions were carried out under pseudo-first order conditions with olefin concentration (1 to 100 mM) much higher than that of $Ru^{VI}(P)O_2$ (1 μM). Kinetic data were collected for at least 4 half-lives, the first-order rate coefficient was obtained from a non-linear least square fit of the photometric readings to the integral form of the first-order rate equation:

$$A_t = (A_o - A_\infty)e^{-K_{obs}t} + A_\infty$$

Where A_t = absorbance at time t

A_o = initial absorbance at time, t=0

A_∞ = final absorbance at completion of reaction

K_{obs} = observed first order rate coefficient

The non-linear least square fittings were done with a commercial computer package and

the values of A_o, A_∞ and K_{obs} were evaluated from the best fit.

2.3.5 Reaction of Catalysts with *cis*-Stilbene in the Presence of 1-Methylimidazole

Two sets of reaction were carried out under the same condition. One set of reaction contained catalyst, *cis*-stilbene (10μL), 1-methylimidazole (10μL) in 2 mL CH_2Cl_2. The other set contained catalyst and *cis*-stilbene in 2 mL CH_2Cl_2. These two reaction vessels were put into a high-pressure oxygen reactor and well stirred for 3 hours. Aliquots were taken out from each reaction mixture and analyzed by ^{1}H-NMR, after the required time of reaction.

2.3.6 Competitive Epoxidation of *para*-Substituted Styrenes

The competitive reaction between substituted styrenes and styrene was carried out by adding the catalysts to a mixture of styrene (10 μL) and one of the *para*-substituted styrene (10 μL) in 2 mL CH_2Cl_2. The reaction vessel was then put into a high-pressure oxygen reactor and pressurized with dioxygen. The reaction mixture was well stirred for 1 hour. Aliquots taken during the reaction were analyzed by GC-MS and/ or GC-FID.

The relative reactivities were determined by using,

$$\mathbf{K_{rel} = (\log (X_f / X_i)) / (\log(Y_f / Y_i))}$$

where X_i and X_f are the initial and final concentration of the para-substituted styrenes, and Y_i and Y_f are the initial and final concentration of styrene.

2.3.7 General Procedure for Gas Chromatographic Analysis

About 200μL of the reaction mixture was withdrawn and added to 5.0mL of hexane containing a known amount of internal standard (commonly one of C-6 to C-12 n-alkane). The catalyst was precipitated out and filtered off. Then, about 1 to 2μL of the clear aliquot was injected to the column at ambient temperature. This method was used to separate the low boiling solvent from the high boiling analytes and minimize any tailing of the solvent peak. The oven temperature was elevated and the chromatogram was recorded with an electronic integrator. Quantitative measurement was done by comparing the area ratio of the analytes to that of the internal standard.

2.3.8 Quantitative Measurement of Stilbene Oxidation Products by NMR Spectroscopy

cis-Stilbene and *cis*-stilbene oxide are thermally unstable, they undergo isomerization readily to *trans*-stilbene or *trans*-stilbene oxide in the hot GC injector. Therefore, ^{1}H-NMR analysis was employed to monitor the yield of the oxidized products from the oxidation of stilbene. General procedure is the same as described in Section 2.3 with the exception that $CDCl_3$ was used instead of CH_2Cl_2. At the end of the reaction, 300μL of the reaction mixture was transferred into a 5mm NMR tube containing known amount of standard. The amount of oxidized products present was calculated from the peak area ratio of the analytes to the internal standard. The following NMR peaks were used for measuring the amount of substrates presence.

Substance	Chemical Shift/ ppm and relative number of H	Assignment
cis-Stilbene oxide	4.34(s), 2H	Epoxide, H
trans-Stilbene oxide	3.85(s),2H	Epoxide, H
Diphenylacetaldehyde	4.86(d),1H; 9.92(d),1H	O=C-**H** $(C_6H_5)_2C$-**H**

Chapter 3 Synthesis, Characterization and Spectroscopic Properties of Ruthenium-Constituted Porphyrins

3.1 Experimental

3.1.1 Materials

2,6-Dichlorobenzaldehyde (ALDRICH, ACROS), mesitaldehyde (ALDRICH, ACROS), n-propionic acid (ACROS), N-methyl-2-pyrrolidinone, NMP (ALDRICH), 2,3-dichloro-5,6-dicyanobenzoquinone, DDQ (MERCK), triruthenium dodecacarbonyl, Ru_3CO_{12} (ALDRICH, STREM) were used as received. Pyrrole (MERCK) was distilled from CaH_2(s) under vacuum immediately before use. Anhydrous zinc acetate was prepared by heating the dihydrate salt (ALDRICH) at 350°C for 5 hours. All solvents for synthesis were of analytical grade and used as received. Neutral silica gel (Silica gel 60, MERCK 7753) and activated alumina (γ-Al_2O_3, BROCKMANN activity II, BDH 15001) were used in column chromatography. TDCP, TMP were prepared by literature methods with modification.

3.1.2 Synthesis of Free Base Porphyrins

(A) 5,10,15,20-Tetrakis(2,6-dichlorophenyl)-21H,23H-porphyrin, H_2TDCP

This porphyrin was synthesized by a modified Rothemund method[58] with N-methyl-2-pyrrolidinone in place of pyridine or 2,4,6-collidine. A mixture of 2,6-dichlorobenzaldehyde (0.1 moles), freshly distilled pyrrole (0.1 mole), anhydrous zinc acetate (0.03 mole) and N-methyl-2-pyrrolidinone (30 mL) was filled into a thick glass ampoule and sealed. The sealed ampoule was then kept at 200°C for 72 hours. The resulting mixture was diluted with acetone (L.R.) and then filtered. Purple crystalline zinc porphyrin was obtained. The solid was dissolved in chloroform and then demetallated by washing with conc. HCl(aq.). The solution was then neutralized by sodium hydrogen carbonate. The chlorin impurity in the crude porphyrin products was converted to the porphyrin by treatment with DDQ in chloroform under reflux.[59] The resultant reaction mixture was loaded onto a dry neutral Al_2O_3 column. The free porphyrin was eluted with CH_2Cl_2 while DDQ and other reduced products were retained. Further recrystallization from chloroform/methanol gave pure H_2TDCP (yield 30%).

(B) 5,10,15,20-*meso*-tetramesityl-21H, 23H-porphyrin, H_2TMP

Lindsey's method[60] was employed to synthesize this porphyrin. To a 2 L 3-neck round-bottomed flask fitted with a septum, reflux condenser, and N_2 inlet was charged with CH_2Cl_2 (1 L), mesitaldehyde (1475 μL) and freshly distilled pyrrole (694 μL). The

mixture was purged with N_2 for 10 to 20 minutes in a well-stirred manner. BF_3/methanol (200 μL) was added via syringe. The resultant mixture was stirred for 45 minutes at room temperature and then maintained at 40°C while DDQ (800 mg) was added. The solution was then refluxed for further 1 hour without N_2 supply. The resultant solution was evaporated to dryness and the residue was redissolved in the minimum amount of CH_2Cl_2. The solution was then chromatographed twice on Al_2O_3 columns. The first pink band from the second column was collected, concentrated and recrystallized from CH_2Cl_2/MeOH to gives H_2TMP (yield 20 - 30%). When using Rothemund method, we found that the yield of H_2TMP is comparatively lower (10-15%).

3.1.3 Synthesis of Ruthenium Porphyrins

(A) (Carbonyl)(Methanol)Ruthenium(II) Porphyrin, [Ru^{II}(P)(CO)(MeOH)]

P = [TDCP] or [TMP]

The ruthenium(II) porphyrins were prepared by modification of the literature method.[61] A mixture of $Ru_3(CO)_{12}$ (1.0 g), H_2P (1.0 g) and mesitylene(30 mL) was placed into a round-bottomed flask and heated with stirring at 140°C for 24 hours. The end of the reaction was detected by the disappearance of red spot due to the free base porphyrin in TLC using CH_2Cl_2 as the mobile phase. The mixture was cooled and filtered to remove any undissolved residue. The solution was then loaded onto a dry alumina column. The unreacted $Ru_3(CO)_{12}$ and free base porphyrin were eluted with toluene. The ruthenium porphyrin was eluted with CH_2Cl_2. The solution containing the ruthenium porphyrin

was concentrated and chromatographed again on a silica gel column using CH_2Cl_2 as eluent. The product was recrystallized from CH_2Cl_2/MeOH (yield 50 - 60%).

(B) *trans*-dioxoruthenium(VI) porphyrins, $Ru^{VI}(P)O_2$

P = [TDCP] or [TMP]

$Ru^{II}(P)(CO)(MeOH)$ (100 mg) was dissolved in CH_2Cl_2 (20 mL). Solid m-chloroperoxybenzoic acid, mCPBA (100 mg) was added to the solution.[62] The mixture was well stirred for 2 - 3 minutes. The resultant solution was loaded onto a dry alumina Al_2O_3 column and eluted with CH_2Cl_2. The product solution was concentrated and recrystallized from CH_2Cl_2/n-hexane. The solid $Ru^{VI}(P)O_2$ was filtered off and kept in refrigerator (50 - 80%).

Table 3.1: Position of selected IR absorption peaks of ruthenium tetraphenylporphyrins. Measurements were made with KBr pressed discs.

Compound	Peak position /cm^{-1}		
	"oxidation marker"*	V_{CO}	$V_{as}(RuO_2)$
Ru^{II}(TDCP)(CO)(MeOH)	1007	1946	
Ru^{II}(TMP)(CO)(MeOH)	1008	1940	
Ru^{VI}(TDCP)O_2	1017		824
Ru^{VI}(TMP)O_2	1020		820

*: The strong absorption bands near 1000 cm^{-1}, which were assigned to C-H rocking vibration of the pyrrole ring, appears to be a characteristic vibration of tetraphenylporphyrins.[63] The frequency of the band varies with the nature and the oxidation state of the central metal ion.

Table 3.2: UV-Visible spectral data of ruthenium tetraphenylporphyrins. Measurements were made with solutions in dichloromethane.

Compound	λ_{max} /nm	Log ε
Ru^{II}(TDCP)(CO)(MeOH)	410	5.40
	530	4.31
	558 (sh)	3.66
Ru^{II}(TMP)(CO)(MeOH)	412	5.42
	526	4.38
Ru^{VI}(TDCP)O_2	420	5.49
	510	4.16
	566 (sh)	3.60
Ru^{VI}(TMP)O_2	422	5.44
	526	4.18

Table 3.3: ^{1}H-NMR spectral data of ruthenium tetraphenylporphyrins. Measurements were made with solution in $CDCl_3$ with TMS as internal standard except as indicated.

Compound	Chemical shifts /ppm & relative number of 1H	Assignment
Ru^{II}(TDCP)(CO)(MeOH)	8.44 (s), 8H	Pyrrolic, β-H
	7.73 (m), 12H	Phenyl, *p*- & *m*-H
	0.93 (s, broad), 3H	CH_3OH
Ru^{II}(TMP)(CO)(MeOH)	8.40 (s), 8H	Pyrrolic, β-H
	7.25 (s), 8H	Phenyl, *m*-H
	2.60 (s), 12H	*p*-methyl-H
	1.95 (s), 12H	*o*-methyl-H
	1.82 (s), 12H	*o*-methyl-H
Ru^{VI}(TDCP)O_2	8.88 (s), 8H	Pyrrolic, β-H
	7.81 (m), 12H	Phenyl, *p*- and *m*-H
Ru^{VI}(TMP)O_2	8.81 (s), 8H	Pyrrolic, β-H
	7.31 (s), 8H	Phenyl, *m*-H
	2.65 (s), 12H	*p*-methyl-H
	1.91 (s), 24H	*o*-methyl-H

Note: $Ru^{VI}(P)O_2$ complexes are diamagnetic solids and display well-resolved ^{1}H-NMR spectra. The simple and symmetric NMR spectra indicate a D_{4h} symmetry. Therefore, only 1 set of o-methyl proton signal was observed for $Ru^{VI}(TMP)O_2$. Ru^{II}(TMP)(CO)(MeOH) is not a symmetrical molecule because the Ru metal center is displaced to one side, as a result, the NMR spectra of Ru^{II}(TMP)(CO)(MeOH) shown 2 sets of o-methyl proton.

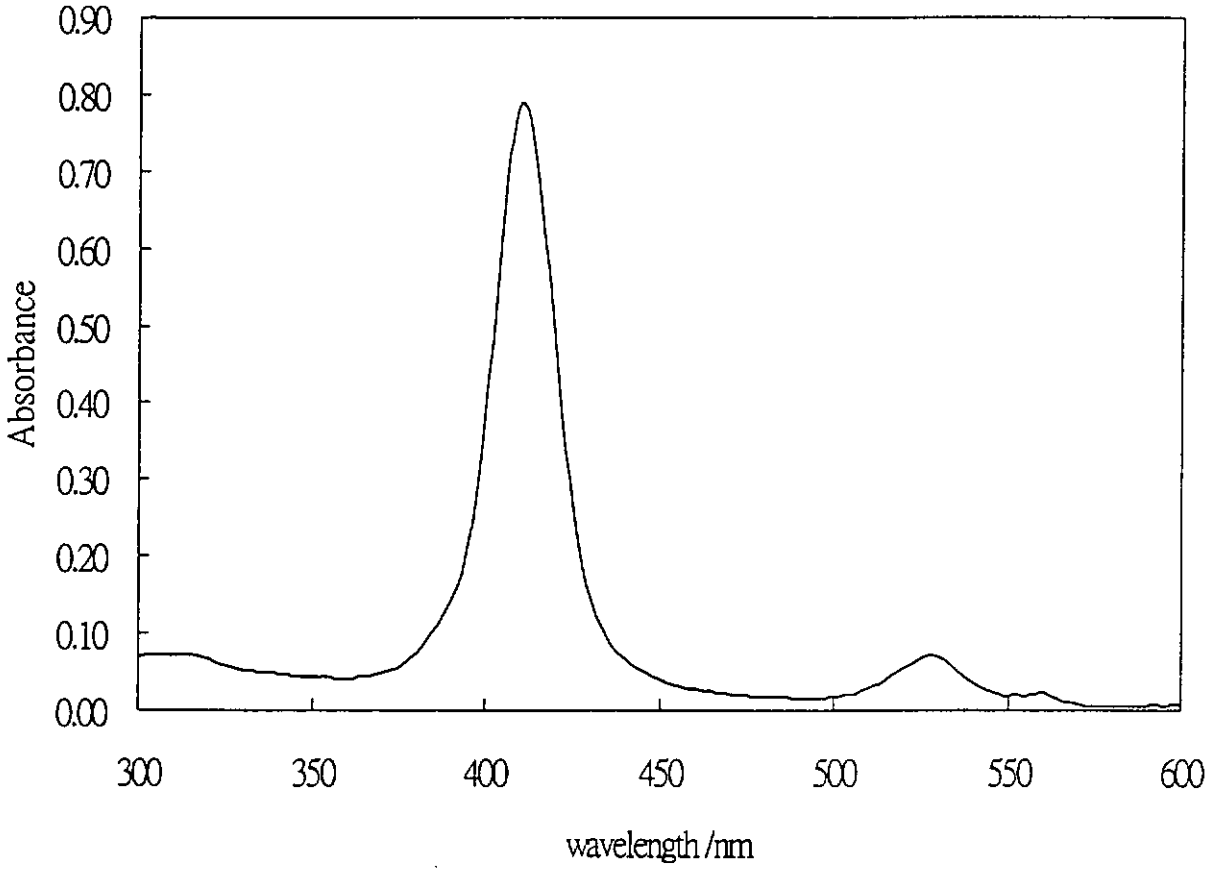


Fig 3.1: UV-Visible spectra of Ru^{II}(TDCP)(MeOH)CO in CH_2Cl_2.

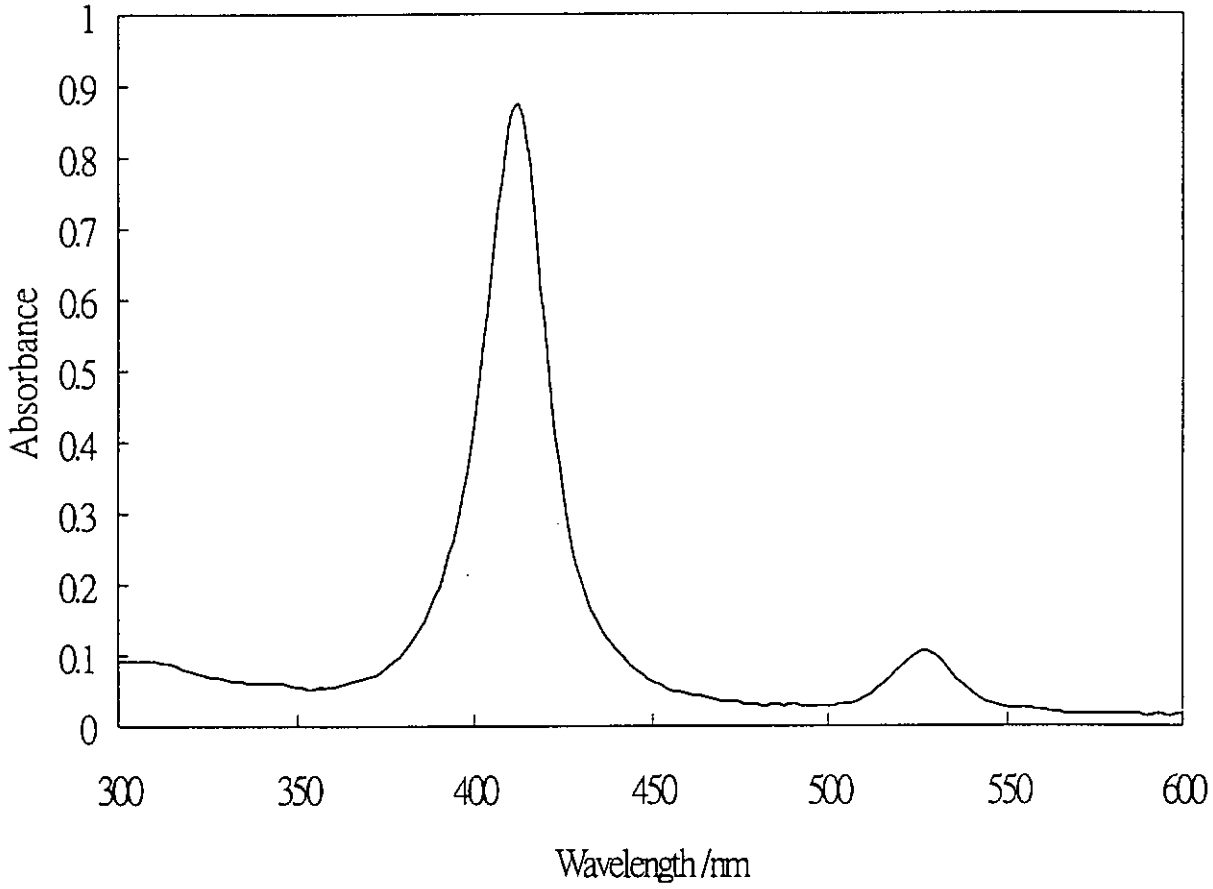


Fig 3.2: UV-Visible spectra of Ru^{II}(TMP)(MeOH)CO in CH_2Cl_2.

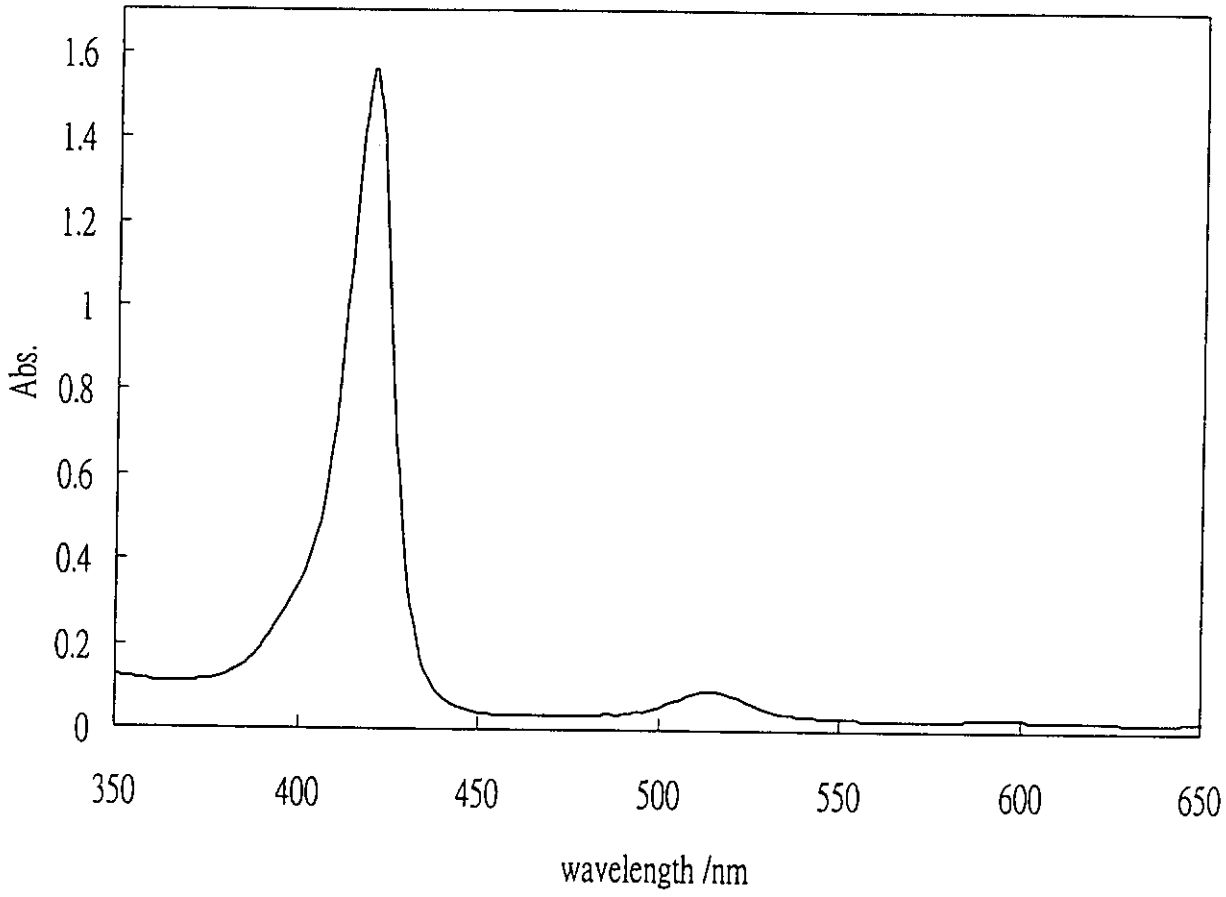


Fig. 3.3: UV-Visible spectra of Ru^{VI}(TDCP) O_2 in CH_2Cl_2.

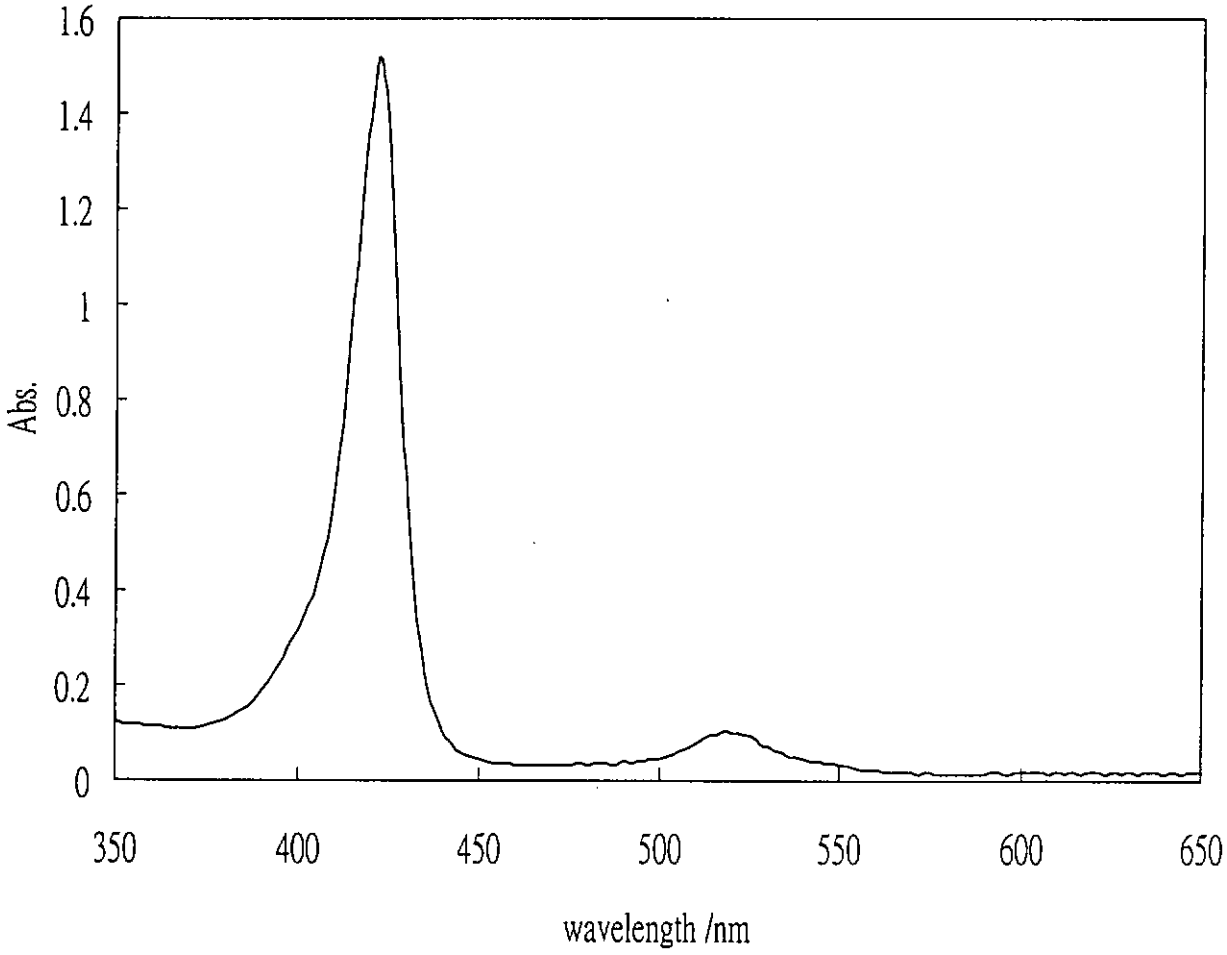


Fig 3.4: UV-Visible spectra of $Ru^{VI}(TMP)O_2$ in CH_2Cl_2.

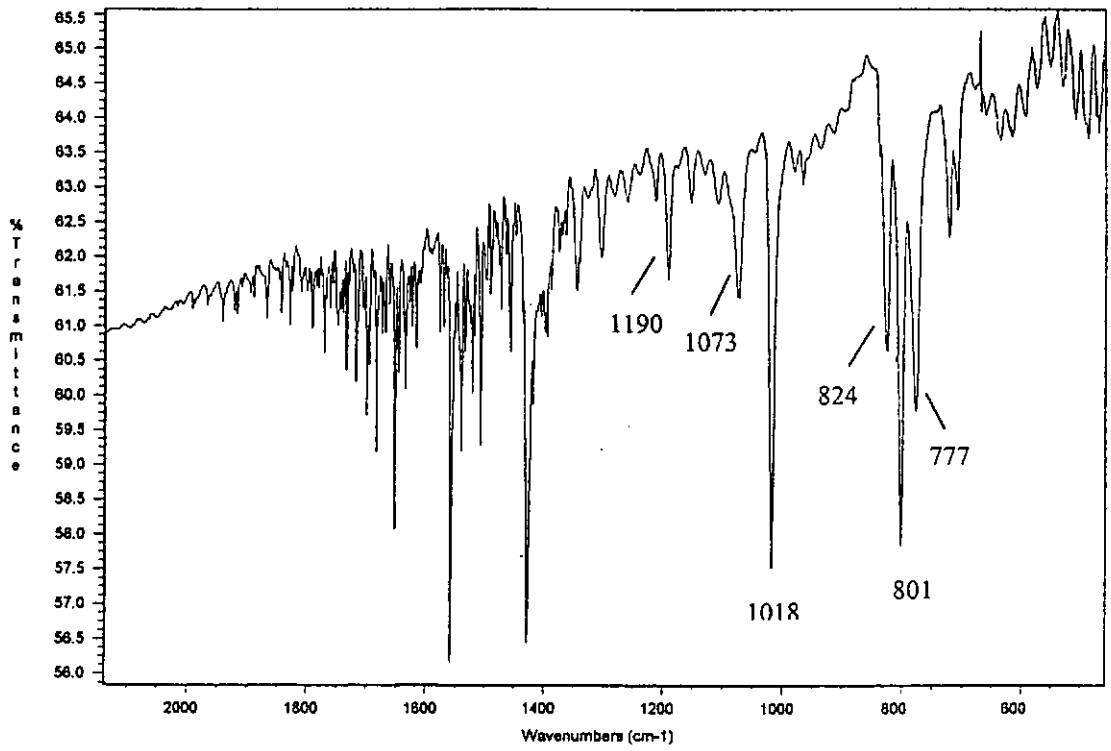


Fig 3.5: FT-IR spectrum of $Ru^{VI}(TDCP)O_2$ in KBr pressed disc.

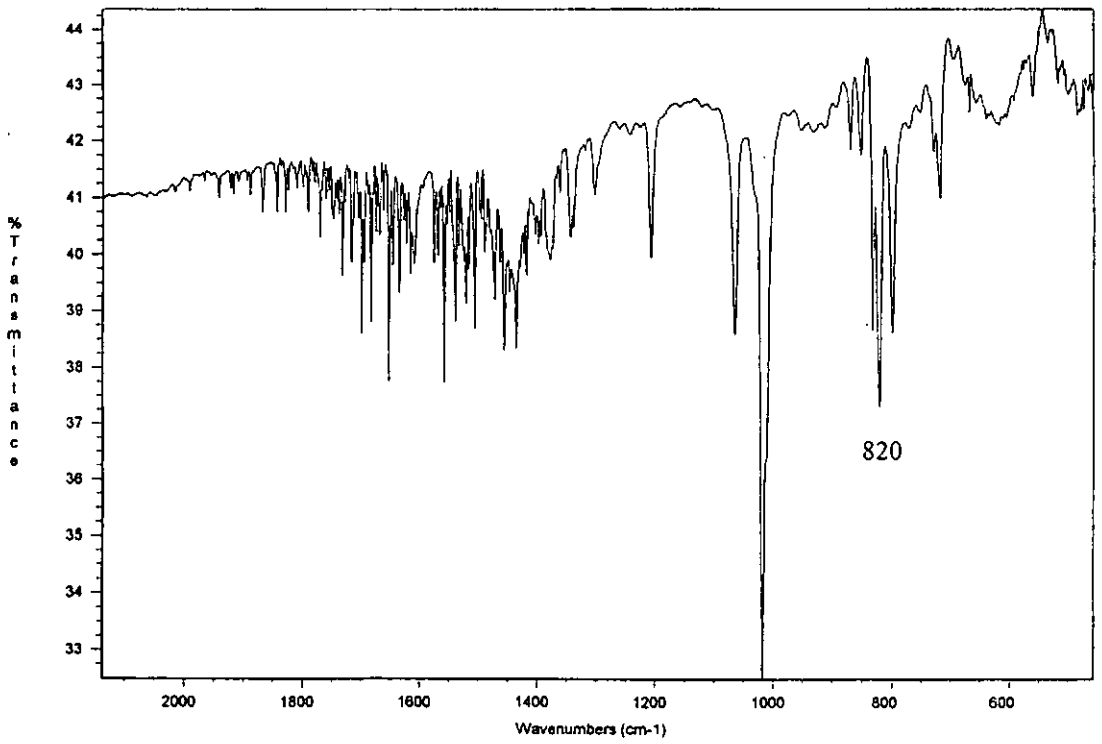


Fig 3.6: FT-IR spectrum of $Ru^{VI}(TMP)O_2$ in KBr pressed disc.

Chapter 4 Results and Discussion

4.1 Yield of Epoxides

Most of the synthetic metalloporphyrins characterized in the past decades, were found to be ineffective catalysts toward epoxidation reactions. TPP, TTP, 3,4,5-$(MeO)_3$TPP and 2,4,6-$(MeO)_3$TPP are good examples. Our studies showed that they were incapable of catalyzing aerobic epoxidation reaction of olefins. The formation of μ–oxo dimer - which is an inactive species - prevented the uptake of oxygen atom from external oxidants and insertion of oxygen atom to the double bonds of olefins.

Various para-substituted styrenes have been epoxidized by $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ into the corresponding epoxides under aerobic conditions and anaerobic condition for stoichiometric measurements(Table 4.1). Products formed by oxidative cleavage of C=C bond, e.g. benzaldehyde and phenylacetaldehyde, were detected in the oxidation of styrene. Small amount of phenylacetaldehyde was formed in the epoxidation of *p*-chlororstyrene and *p*-fluorostyrene.

Oxidation of *cis*-stilbene gave stereoretentive product, *cis*-stilbene oxide, in majority. Change in O_2 pressure changed the ratio of *cis*- to *trans*- epoxide in the epoxidation of *cis*-stilbene. In $Ru^{VI}(TMP)O_2$ catalyzed epoxidation of *cis*-stilbene, *cis*- to *trans*- epoxide ratio changed from 2.4 for 10 bar O_2 to 0.4 for anaerobic system. Similar observation was found in $Ru^{VI}(TDCP)O_2$ catalyzed reaction, the *cis*- to *trans*-

epoxide ratio changed from 3.6 for 10 bar O_2 to 1.9 for anaerobic condition.

Table 4.1: Yield of various substrates epoxidized by A) $Ru^{VI}(TDCP)O_2$ and B) $Ru^{VI}(TMP)O_2$.

(A)

Entry	Substrates	Products	Turnover[a]	
			10 bar	20 bar
1	Styrene	Styrene oxide	3.0	15.2
		Benzaldehyde	Nil	0.8
		Phenylacetaldehyde	Nil	1.6
2	*p*-Chlorostyrene	*p*-Chlorostyrene oxide	3.0	4.0
		p-Chlorophenylacetaldehyde	0.7	0.9
3	*p*-Fluorostyrene	*p*-Fluorostyrene oxide	2.9	3.7
		p-Fluorophenylacetaldehyde	0.8	0.9
4	*cis*-Stilbene	*cis*-Stilbene oxide	2.7	Nil
		trans-Stilbene oxide	1.1	Nil
5	Norbornylene	Norbornylene oxide	7.7	Nil
6	*trans*-β-Methylstyrene	*trans*-β-Methylstyrene oxide	0.7	Nil
7	*trans*-Stilbene	Nil	Nil	Nil

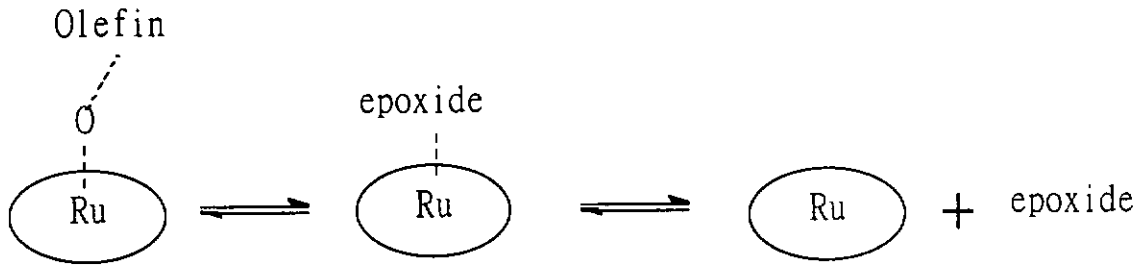
(B)

Entry	Substrates	Products	Turnover	
			10 bar	20 bar
1	Styrene	Styrene oxide	11.5	20.7
2	*p*-Chlorostyrene	*p*-Chlorostyrene oxide	13.6	13.6
3	*p*-Fluorostyrene	*p*-Fluorostyrene oxide	11.4	19.8
4	*cis*-Stilbene	*cis*-Stilbene oxide	6.9	12.9
		trans-Stilbene oxide	1.9	1.8
5	Norbornylene	Norbornylene oxide	17.9	9.9
6	*trans*-β-Methylstyrene	*trans*-β-Methylstyrene oxide	2.7	
7	*trans*-Stilbene	Nil	Nil	Nil

Reaction condition: refer to experimental section.

[a] Turnover is based on total amount of products obtained per amount of catalysts used,

The change in *cis-/trans-* oxide ratio can be explained by the difference in the rate of formation of catalyst-olefin complex and the rate of oxygen rebinding to the catalyst. Formation of epoxide involves the binding of olefin to the active center of the catalyst, Ru=O, and then the formation of Ru-O-olefin complex (scheme 1).

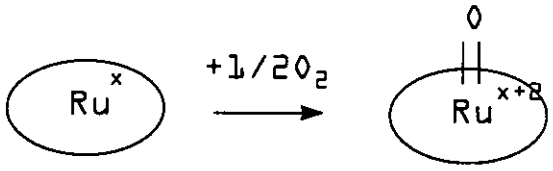


Scheme 1

After the departure of the formed epoxide, the complex then take up an oxygen atom from dixoygen dissolved in the reaction mixture.

The electronic properties of the metal complex and the concentration of the oxygen control the rate of the oxygen uptake. The results in the epoxidation reaction of *cis*-stilbene shown that product distribution are oxygen concentration dependent. Since then, we speculate that there is a dynamic interaction between the epoxide and Ru-O-olefin complex(Scheme 1).

After the departure of the formed epoxide molecules, oxygen will compete with the epoxide for the vacant site on the Ru center (Scheme 2)



Scheme 2

Therefore in the presence of oxygen molecule, the oxygen atom will soon occupy the vacant site on the active center of the catalyst. And we believe that Ru-O-olefin is the origin of the rearrangement products.

Overall speaking, $Ru^{VI}(TDCP)O_2$ has a lower turnover rate in catalytic epoxidation reactions than $Ru^{VI}(TMP)O_2$. It is related to the electronic properties of the Ru-O active center and the C=C double bond of the substrates (detailed discussion will be given later).

The variation of oxygen pressure, which is the same as varying the external oxidant concentration, only have significant effect in the total yield of the epoxidation of styrene and p-fluorostyrene. These can be explained by the steric environment casted by the substrates and the catalysts. As p-fluorostyrene and styrene are less bulky than the other substrates, less hindered approach of the substrates to the catalyst plane is suggested. For the other substrates, the olefins to the Ru=O center was hindered and limited the reaction rate.

Table 4.2: Stoichiometric epoxidation of olefin by $Ru^{VI}(TMP)O_2$ and $Ru^{VI}(TDCP)O_2$. Reaction condition please refer to Section 2.3.1.

Substrates	Products	Turnovers	
		$Ru^{VI}(TMP)O_2$	$Ru^{VI}(TDCP)O_2$
cis-Stilbene	*cis*-Stilbene oxide	2.0	0.2
	trans-Stilbene oxide	1.0	0.5

Apart from the effect of oxygen pressure on the rate of reaction, product stereo-selectivity was also affected by oxygen pressure. In the epoxidation of *cis*-stilbene by TMP, *cis-/trans-* ratio of the formed epoxides changed from 2.0 (Table 4.2) to 7.1 (Table 4.1) in anaerobic and 20 bar O_2 conditions. Similar result was observed for TDCP catalyzed epoxidation of *cis*-stilbene. The *cis-/trans-* ratios of the epoxides were 0.4 (Table 4.2) and 2.4 (Table 4.1) in anaerobic and 10 bar O_2 condition. These can be explained by the difference in the rate of the epoxide formation, which includes the formation of a catalyst-olefin intermediate, followed by the departure of the epoxide molecule, and the rate of oxygen molecule binding to the ruthenium center. In anaerobic condition, the rate of oxygen binding to the ruthenium center can be neglected, and the interaction time of the olefin molecule and the catalyst is relatively longer. Thus rearrangement reaction during the intermediate step is more likely to occur. On the other hand, in aerobic condition the rate of oxygen binding become competitive leading to a shorter interaction-time for the olefin-catalyst intermediate stage and the degree of

rearrangement process is comparatively lower.

Our results showed that in the epoxidation of olefins, epoxides were the predominant products with only minor amounts of aldehydes. In the epoxidation of styrene, *cis*-stilbene and *trans*-β-methylstyrene, the corresponding stereospecific epoxides (table 4.1) were formed. Although the turnover is relatively low, only little amount of rearranged or C-C cleavage products are obtained, confirming that the catalysts are selective.

4.2 Reactivity of $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$

In all the epoxidation, epoxides were the predominant products with the exception of small amount of oxidative cleavage products in some of the reactions. *cis*-Stilbene oxide were formed as the major product in the epoxidation of *cis*-stilbene. No epoxide was obtained in the epoxidation of *trans*-stilbene. TMP was found to be a better catalyst than TDCP, this was clearly shown in the time-course study of the styrene epoxidation (Fig 4.3).

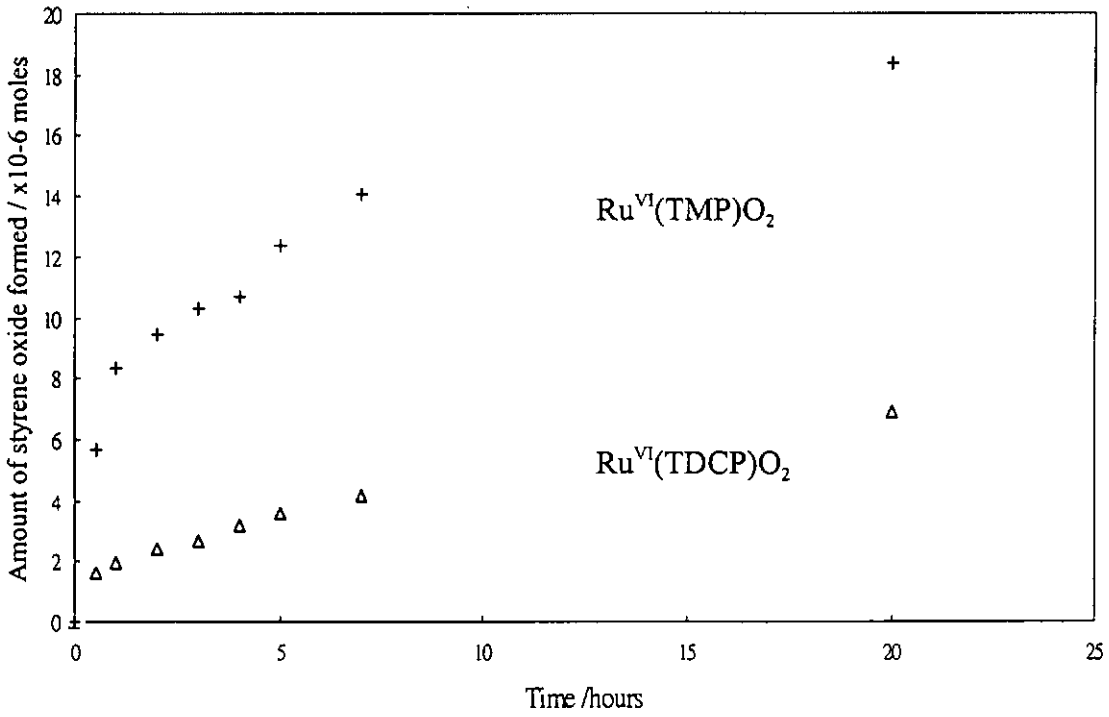


Fig. 4.1: Time dependence formation of styrene oxide catalyzed by $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ at 5 bar O_2.

(A) Effect of Electron-donating and Electron-withdrawing Substitutents on Phenyl Ring of Ruthenium Tetraphenylporphyrins

The difference in the rate for epoxidation of $Ru^{VI}(TMP)O_2$ and $Ru^{VI}(TDCP)O_2$ can be explained by the difference in the rate of heterolytic O-O bond cleavage of (Por)Ru-O-O species. Watanabe et al.[64] showed that the rate of heterolytic O-O bond cleavage of Ru-O-O species depends on the substitutents on the *meso*-phenyl groups of the porphyrin molecules. It was found that the introduction of an electron-donating group, like $-CH_3$ in TMP, on the phenyl groups on the porphyrin macrocycles enhances the rate of the cleavage reaction by "pushing" electrons into the σ^* orbital of the Ru-O-O. On the contrary, an introduction of an electron-withdrawing group retards the O-O bond cleavage reaction. Therefore, the concentration of the $Ru^{VI}(TDCP)O_2$ was lower than $Ru^{VI}(TMP)O_2$ with the reaction mixture, and the rate of epoxidation was slower. That is to say that, $Ru^{VI}(TDCP)O_2$ is a less active oxidant than $Ru^{VI}(TMP)O_2$ because of the slower rate in O-O bond cleavage.

(B) Ease of Oxidative Degradation

Abhik Ghosh et al.[65] has showed that electron-withdrawing substitutents at the *ortho-* position on the phenyl groups offers limiting effect on the ionization potential of the porphyrin core. In Ghosh's studies of the ionization potentials of H_2TDCP and H_2TPP, [64] the ionization potential of H_2TDCP was found to be higher than H_2TPP by

0.05eV. Although the presence of electron-withdrawing substitutent on the porphyrin help little in preventing degradation, the presence of *ortho-* electron-withdrawing substitutents provides steric protection to the macrocycle against oxidative degradation. In fact, $Ru^{VI}(TDCP)O_2$ is more resistance to oxidative degradation than $Ru^{VI}(TMP)O_2$ because of the *ortho*-chloro substitutent which is illustrated in the time-course UV-Visible spectroscopic study of various olefins epoxidation catalyzed by the 2 catalysts (Fig. 4.2 and 4.3). Results showed that the rate of disappearance of $Ru^{VI}(TDCP)O_2$ is slower than $Ru^{VI}(TMP)O_2$ in the epoxidation reactions (Table 4.3).

Nonetheless, various olefins give similar rate of degradation of catalyst, these suggested that nature of substrates does not have significant effect in the stability of the catalysts. To conclude, the difference in the rate of epoxidation is controlled by the electronic and steric effect simultaneous.

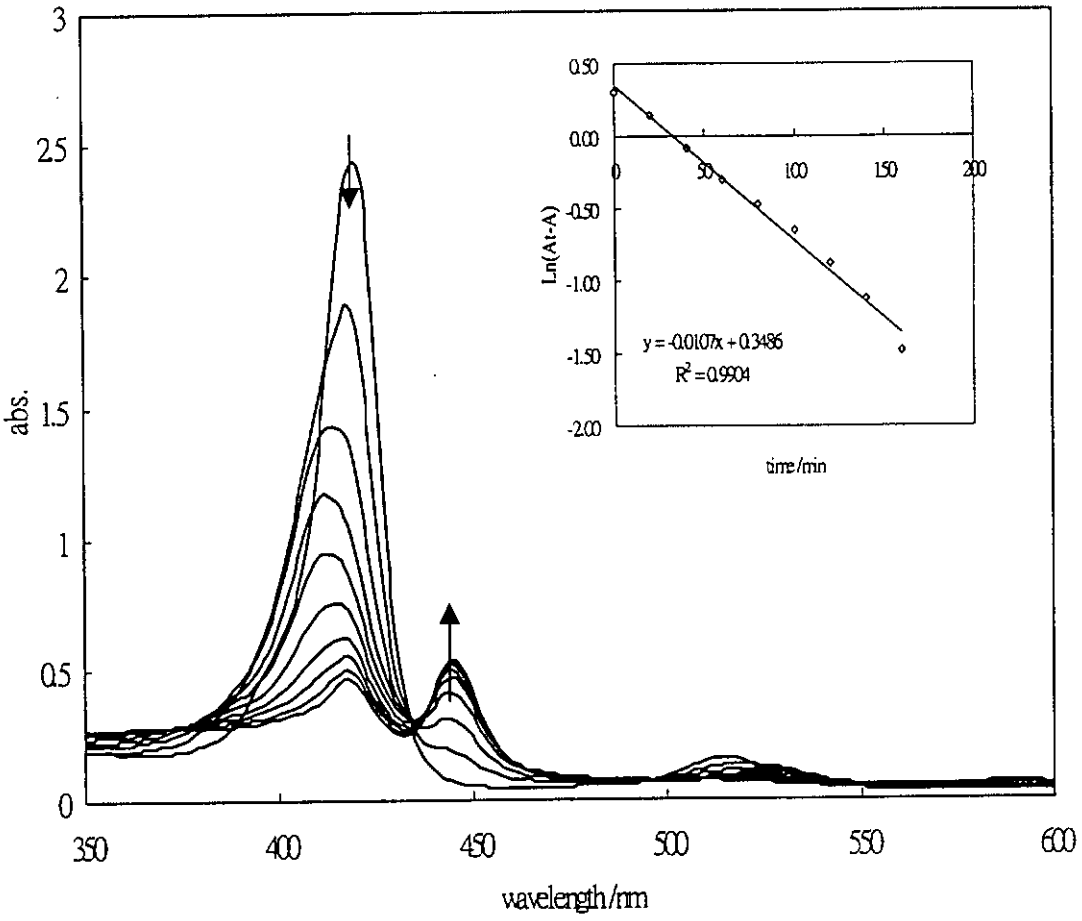


Fig. 4.2: UV-Visible spectral change observed for the reaction of $Ru^{VI}(TDCP)O_2$ with norbornylene in CH_2Cl_2 at 25°C under atmospheric oxygen pressure. Time interval between each trace is 20 mins. Inset: Pseudo-first order plot for the disappearance of $Ru^{VI}(TDCP)O_2$ monitored at 424nm. Reaction condition please refers to Section 2.3.4.

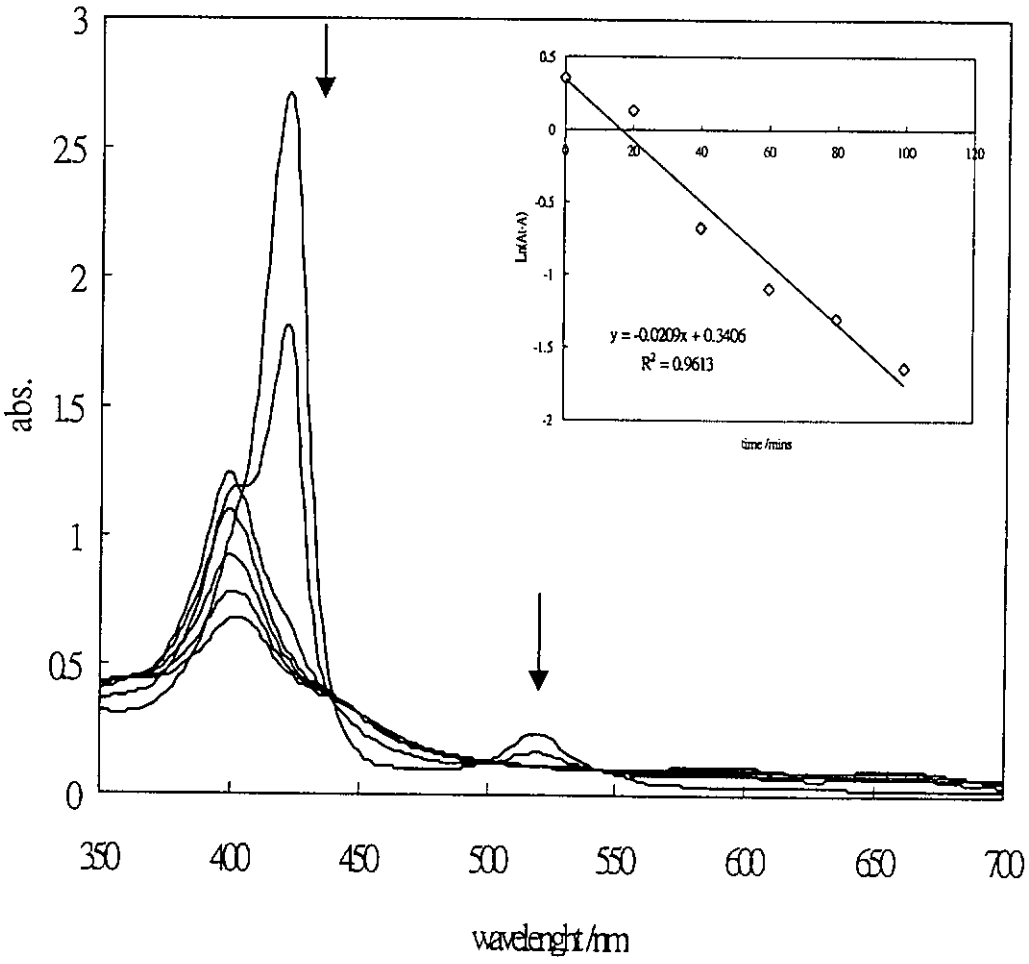


Fig. 4.3: UV-Visible spectral change observed for the reaction of $Ru^{VI}(TMP)O_2$ with norbornylene in CH_2Cl_2 at 25°C under atmospheric oxygen pressure. Time interval between each trace is 20 mins. Inset: Pseudo-first order plot for the disappearance of $Ru^{VI}(TMP)O_2$ monitored at 420 nm. Reaction condition please refers to Section 2.3.4.

Table 4.3: Pseudo-first order rate for $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ in the aerobic epoxidation of various olefins. Reaction condition please refers to Section 2.3.4.

	Rate /x10^{-3}Mmin^{-1}	
Substrates	**$Ru^{VI}(TDCP)O_2$**	**$Ru^{VI}(TMP)O_2$**
Styrene	-10.3(±1.0)	-11.8(±1.0)
Norbornylene	-10.7(±1.0)	-20.9(±2.0)
cis-Stilbene	-8.9(±1.0)	-17.3(±2.0)
Cyclohexene	-9.3(±1.0)	-16.1(±1.5)

4.3 *cis*-Stilbene Epoxidation

cis-Stilbene has been widely used as a mechanistic probe in metalloporphyrin catalyzed epoxidation reaction.[66] The difference in reactivities towards *cis*-stilbene and *trans*-stilbene epoxidation catalyzed by $Ru^{VI}(TMP)O_2$ and $Ru^{VI}(TDCP)O_2$ revealed that steric hindrance around the active metal center posed an important fact in determining the product selectivity. Ostovic et al.[67] found that the steric requirement for the formation of a charge transfer complex should be the origin of the stereo-selectivity of the epoxidation reaction. That is to say, the HOMO of the substrate - the π-orbital of the C=C double bond, and the LUMO of the metal center - the 2 empty Ru-O dπ-pπ anti-bonding orbitals, should be sufficiently close to each other. Ostovic studied the epoxidation of *cis*- and *trans*-stilbene catalyzed by $(Br_8TPP)Cr^{V}(O)(X)$, and found that the calculated distances between the C=C bond of the substrates and the electrophilic oxygen molecules was much longer for *trans*-stilbene(3.88 A) than *cis*-stilbene(2.81 A). The above evidences explained for the lower reactivity of *trans*-stilbene than *cis*-stilbene in TDCP and TMP catalyzed epoxidation.

In our studies, results obtained from TDCP & TMP catalyzed epoxidation of *trans*-stilbene indicated that *trans*-stilbene is comparatively inactive to epoxidation in our system. ^{1}H-NMR monitoring of the reaction mixture using $CDCl_3$ as the solvent indicated that *trans*-stilbene epoxide was not formed even after 1 day. Phenylacetaldehyde and benzaldehyde were not formed too. It showed that *trans*-stilbene can not approach to the Ru=O active centre and hence no reaction occured.

4.4 The Effect of π–Donating Ligand

The catalytic properties of the metalloporphyrins show a surprisingly dependence on the presence of axial π-donating bases. Improvement of chemo- and stereo-selectivity and also the rate of the reactions were found in the metalloporphyrins catalyzed reactions. Montanari et al.[68] first reported the synthesis of "tailed" Mn(III) tetraarylporphyrin which gave the highest olefin epoxidation rate among other metalloporphyrins by using a phase transfer reagent and hypochlorite in the presence of excess amount of pyridine and imidazole. Meunier used Mn-TPP in olefin epoxidation utilizing commercial bleaching reagent but only to find that the yield was too low.[69] Collman et al. reported that an axial ligand can have influence on the selectively of the oxidants towards various substrates, the total rate of reaction and the stability of the catalyst during the reaction.[70] It has been suggested that the π-donating base coordinates to the metal axially in a *trans*- manner to the oxofunctionality. Hansson et al. has found that the presence of an axial ligand had influence on the energy difference between the a_{1u} and a_{2u} orbitals.[71] Studies of 3 different oxomanaganese porphyrins with axial ligands revealed the following observations:[72]

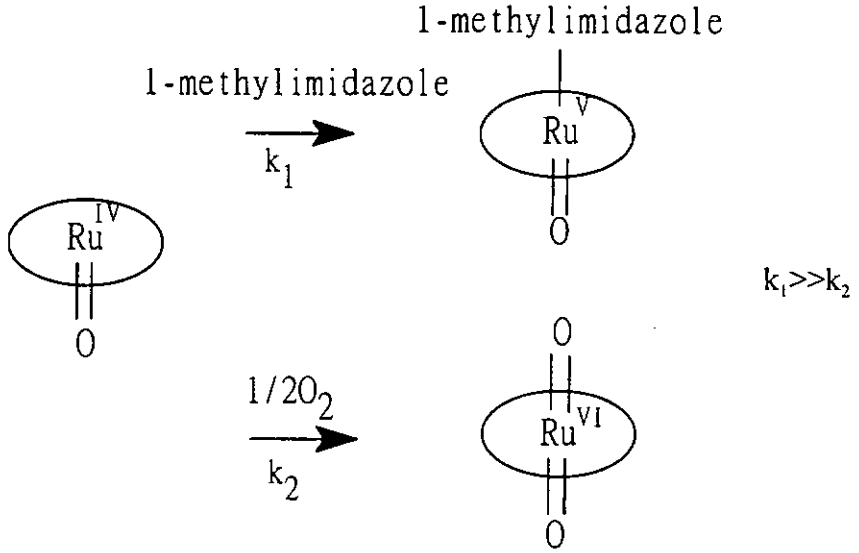
i) The Mn=O bond distance is increased in the presence of axial ligand

ii) the oxygen in the Mn=O fragment becomes more electrophilic, and

iii) lastly, the oxygen becomes a better π-acceptor.

The above can be explained by the interaction of the π-orbital of the donating ligand perpendicular to the bases with the oxomanaganese antibonding π* orbital.[70]

In the study of the effect of π-donating ligand on the rate and product distribution of the epoxidation of *cis*-stilbene catalyzed by TMP and TDCP, 1-methylimidazole was chosen to act as an electron-rich π-donating ligand. Suprisingly a higher yield of epoxide is observed for the reaction without 1-methylimidzaole than the reaction with 1-methylimidazole added (see table 4.4 and 4.5). The results can be explained by the competitive binding of the π-donating ligand to the vacant site on the catalysts leading to one site less available for oxygen binding which in turn decrease the reactivities as illustrated in the simplified equation:



The interaction between 1-methylimidazole and the Ru centre, suggested from the strong affinity of nitrogen to ruthenium centre, may be so strong that no further epoxidation occurred (table 4.4 and 4.5).

An improvement in the epoxide yield after the introduction of 1-methylimidazole was not observed. This is probably due to the "blocking" of vacant sites on the ruthenium center. Nonetheless, the presence of a π-donating ligand was found to have

significant effect on the product distribution in TMP catalyzed epoxidation. In TMP catalyzed epoxidation of *cis*-stilbene, the *cis*-/*trans*- ratio is around 1 in the presence of 1-methylimidazole and as high as 230 with no 1-methylimidazole added (Table 4.4 and 4.5). The amount of *cis*-epoxide formed decreased, when 1-methylimidazole was added and an increase in the amount of *trans*-epoxide was observed. Despite the factor of "blocking" of the vacant site on the active center, the oxygen in the Ru=O fragment is more electrophilic in the presence of 1-methylimidazole. As a result, the transition state becomes more positively charged in nature, which result in the formation of rearranged products. Apart from lost of product selectively, the total yield of epoxide decreased by a factor of 20. We proposed that under this situation, the rate of *trans*-epoxide formation dominated and hence a higher ratio of *trans*-/*cis*- epoxide was found.

Table 4.4: Time dependence of formation of *cis*-stilbene oxide in the epoxidation of *cis*-stilbene catalyzed by $Ru^{VI}(TMP)O_2$ under 20 bar O_2. Reaction condition please refers to Section 2.3.5.

	Turnover	
Time /hr	**with 1-methylimidazole**	**without 1-methylimidazole**
0.5	0.44(0.58)[a]	9.20(0.08)
1	0.57(0.72)	11.57(0.08)
2	0.60(0.76)	17.35(0.08)
3	0.65(0.66)	19.47(0.08)

[a] Values in parenthesis are the turnover value of *trans*-stilbene oxide.

For TDCP catalyzed reaction, the total epoxide yield was not affected after the addition of 1-methylimidazole and no *trans*-stilbene oxide was formed (Table 4.5). From the results of TMP and TDCP catalyzed epoxidation of *cis*-stilbene, it was found that the presence of a π-donating ligand has a profound effect in product selectively in TMP catalyzed *cis*-stilbene epoxidation but it is not the case for TDCP system.

Table 4.5: Time dependence of formation of *cis*-stilbene oxide in the epoxidation of *cis*-stilbene catalyzed by $Ru^{VI}(TDCP)O_2$ under 20 bar O_2. Reaction condition please refers to Section 2.3.5.

	Turnover	
Time/hr	**with 1-methylimidazole**	**without 1-methylimidazole**
0.5	0.03	0
1.5	0.07	0.06
2.5	0.21	0.27
4.5	0.22	0.88
24	2.7	3.56

Mole ratio: catalyst: substrate (: 1-methylimidazole) = 1: 20 (: 1)

4.5 Concerted Mechanism for Epoxidation

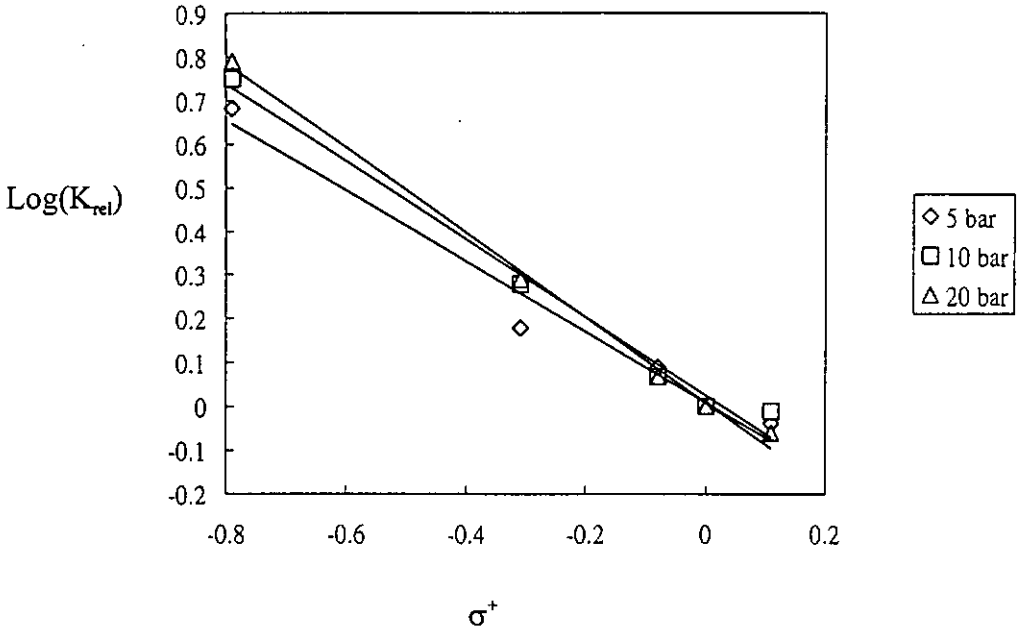
From the results of the control experiment, no epoxide was formed when no catalyst was added to the reaction mixture. In other words, the possible active species during the reaction should be an oxo-ruthenium species.

A Hammett treatment (Table 4.6) of the relative reactivities of various para-substituted styrenes against σ^+ gives p^+ of -0.81, -0.89, -0.98 for TDCP and -0.77, -0.85, -0.92 for TMP for 5 bar, 10 bar and 20 bar O_2 pressure respectively (Fig. 4.4).

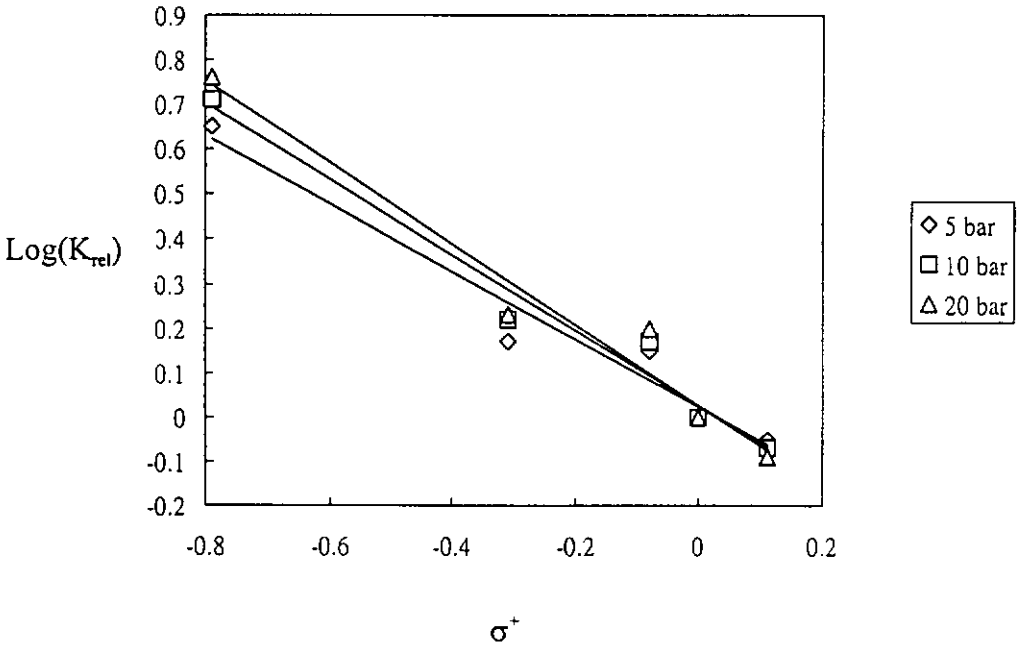
The negative ρ^+ value for TDCP & TMP suggested that there maybe a development of a positive charge on the α-carbon atom of the *para*-substituted styrenes in the transition states.[73] And the slight differences in the values suggested that the modification of the ligands by *ortho*-substituents on the *meso*-phenyl rings doesn't affect the electronic states of the Ru-O bond[74].

Table 4.6: Competitive epoxidation result of various para-substituted styrenes by $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ at different O_2 pressure. a:5 bar; b: 10 bar; c: 20 bar oxygen. Reaction condition please refers to Section 2.3.6.

			Log(Krel)	
Entry	**Substrates**	**Products**	**$Ru^{VI}(TMP)O_2$**	**$Ru^{VI}(TDCP)O_2$**
1	p-methoxystyrene	epoxide	0.68 [a]	0.65 [a]
			0.75 [b]	0.71 [b]
			0.79 [c]	0.76 [c]
2	p-methylstyrene	epoxide	0.18 [a]	0.17 [a]
			0.28 [b]	0.22 [b]
			0.29 [c]	0.23 [c]
3	p-fluorostyrene	epoxide	0.09 [a]	0.15 [a]
			0.07 [b]	0.17 [b]
			0.07 [c]	0.20 [c]
4	p-chlorostyrene	epoxide	-0.04 [a]	-0.05 [a]
			-0.01 [b]	-0.07 [b]
			-0.06 [c]	-0.09 [c]



(a)



(b)

Fig 4.4: Hammett plot of competitive epoxidation of para-substituted styrenes catalyzed by (a) $Ru^{VI}(TMP)O_2$ and (b) $Ru^{VI}(TDCP)O_2$ at different oxygen pressure.

The formation of small amount of *trans*-stilbene oxide (Table 4.1) during the

epoxidation of *cis*-stilbene indicates the presence of a cationic or a radical intermediate. We then carried out control reactions with a radical inhibitor, hydroquinone, and found that the total yield and the product distribution were not affected (Table 4.7).

Table 4.7: Effect of the addition of hydroquinone on the amount of rearranged products obtained during the reaction of $Ru^{VI}(TDCP)O_2$ and styrene under 5 bar O_2 at 25°C.

	Without hydroquinone		**With hydroquinone**	
Time /hr	**Styrene oxide/ x10^{-6} moles**	**benzaldehyde/ x10^{-6} moles**	**Styrene oxide/ x10^{-6} moles**	**Benzaldehyde/ x10^{-6} moles**
0.5	1.8[a]	0.3[a]	1.3	0.3
3	2.8	0.3	2.9	0.4
6	3.0	0.3	2.8	0.4

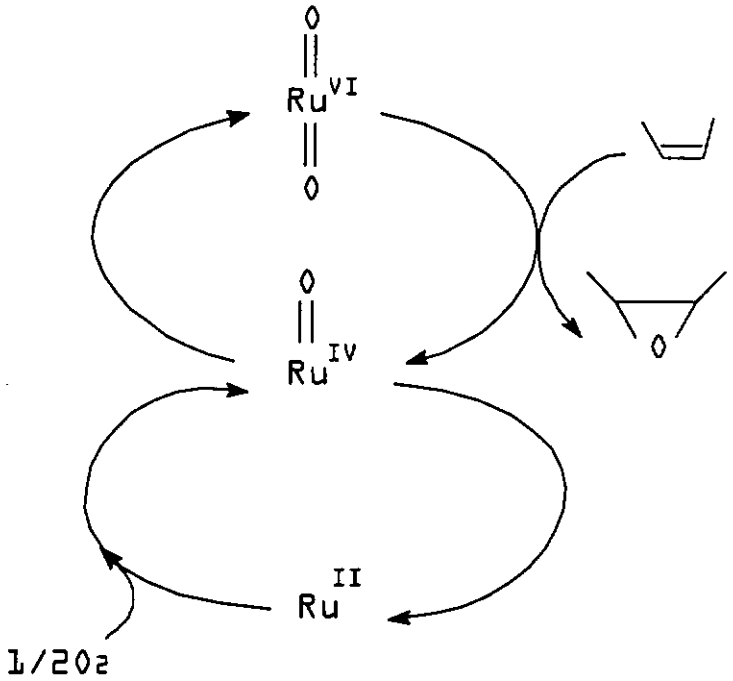
Those evidences suggest that the possible intermediate may be a cationic species. Also, the difference in reactivities of TDCP and TMP towards electron-deficient olefins, e.g. *cis*-stilbene, suggested that the presence of an electron-withdrawing group in the *ortho*-position of the phenyl group on the ligand makes the catalyst itself more electrophilic and thus has lower reactivity towards epoxidation of electron-deficient olefins.

In order to gain an insight on the transition state of the epoxidation reaction, we studied the competitive oxidation of norbornylene and cyclohexene. Sharpless [75] studied the mechanism of epoxidation of olefins by covalent peroxides of molybdenum and was found that a 3-membered transition state corresponded to a mole ratio of cyclohexene oxide: epoxynorbornylene equals to 1-10. The product mole ratio of cyclohexene oxide: epoxynorbornylene were 5.0 for TDCP and 10.3 for TMP. These proved that the possible intermediates may be a 3-membered species.[75]

The negative p^+ values for the TDCP and TMP catalyzed competitive epoxidation of various para-substituted styrenes are similar to the reported p^+ value for known concerted processes[76] such as, carbene insertion to the double bond (p^+=-0.62 to -1.61)[77] or epoxidation with perbenzoic acid (p^+=-1.2).[78] In the latter case, there is a retention of the product configuration (*cis*-olefin gives solely *cis*-epoxide). Base on the results of the competitive epoxidation of para-substituted styrenes and norbornylene with cyclohexene, a concerted insertion of the metal-bound oxygen into the olefin double bond forming epoxide is more convincing.

4.6 Reaction cycle

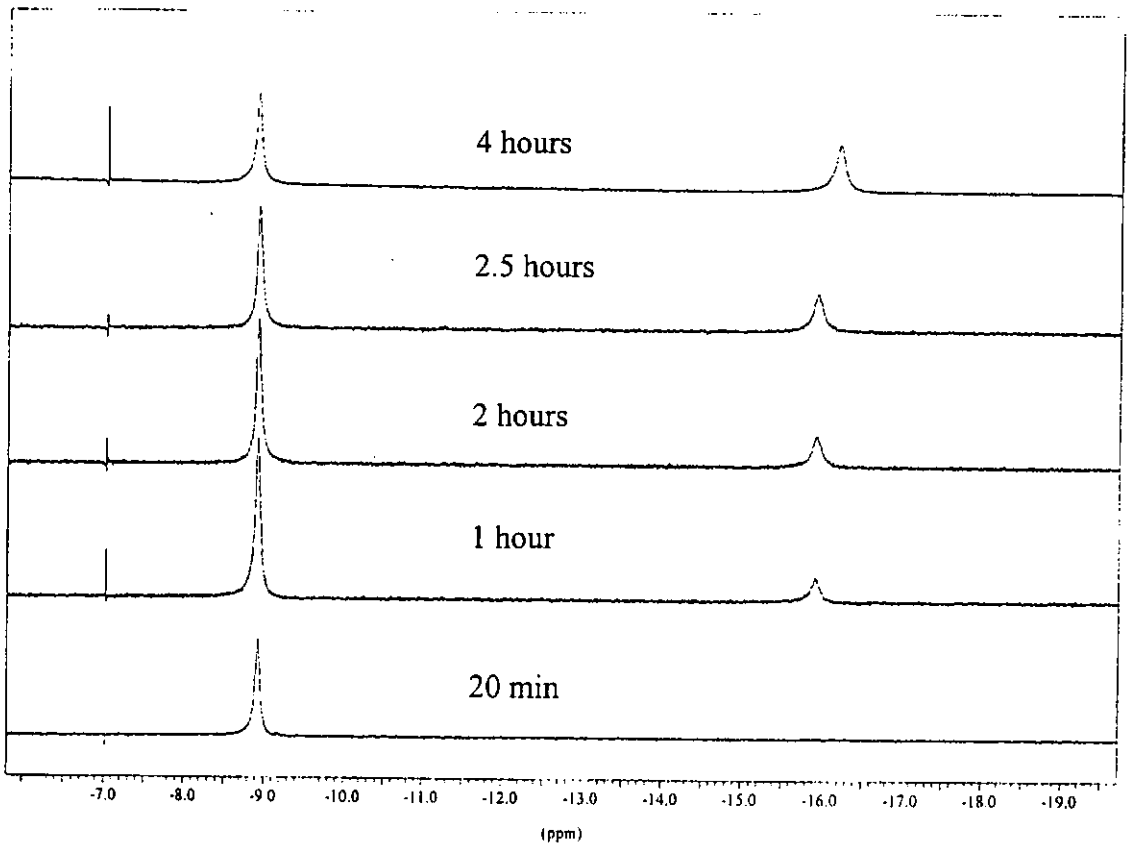
Groves and his co-workers[79] have proposed a disproportionation mechanism for ruthenium porphyrins catalyzed olefin epoxidation. A initially formed $Ru^{IV}(P)O$ complex disproportationates to $Ru^{VI}(P)O_2$ and $Ru^{II}(P)$ (Scheme 4).



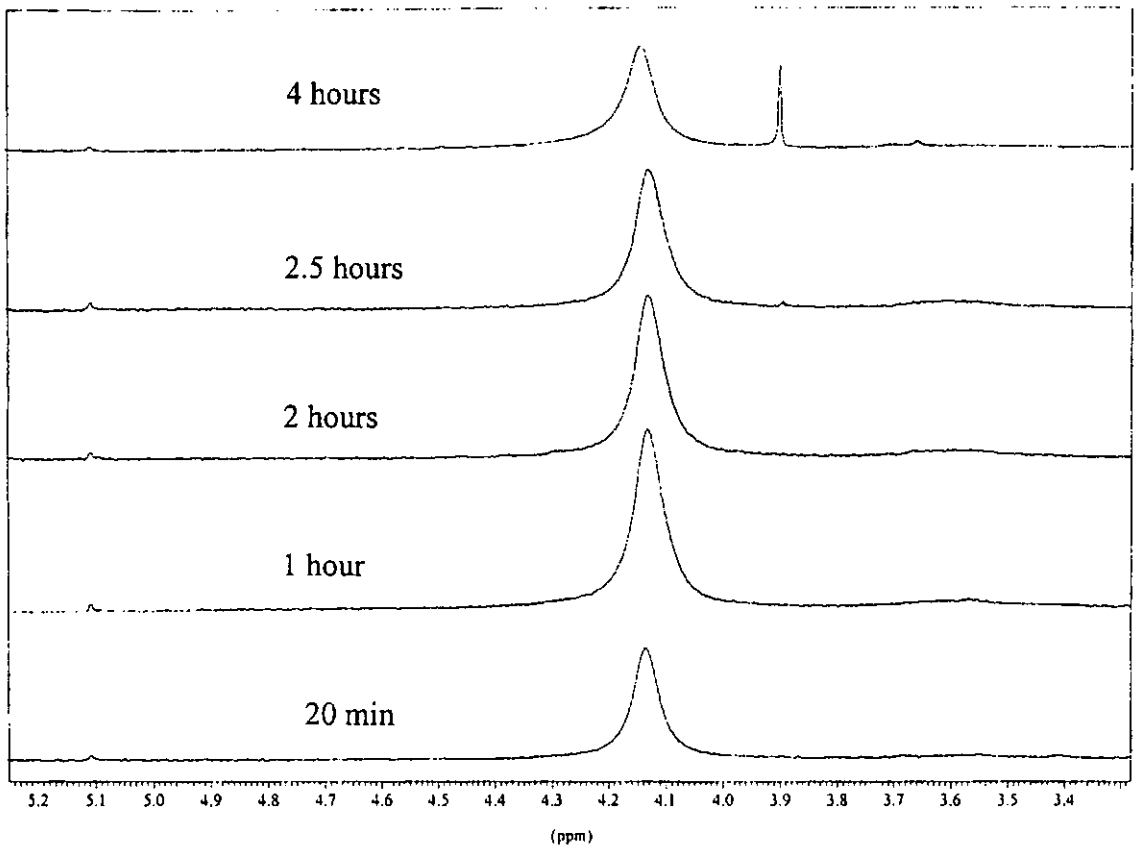
Scheme 4

The little dependence of oxygen pressure in epoxidation rate suggested that oxygen uptake by the complex during the reaction may not be a rate-determining step. And if disproportionation reaction is the case in Ru porphyrins catalyzed epoxidation reactions, then one must expect the existence of Ru(VI), Ru(IV) and Ru(II) species during the reaction. However, we found that during aerobic epoxidation of olefins, the amount of

$Ru^{VI}(P)O_2$ was decreasing together with the increase in amount of Ru(IV)(P)(O) and *cis*-stilbene epoxide (Fig. 4.5). This evidence tells us that $Ru^{IV}(P)O$ can also be a efficient oxidant besides $Ru^{VI}(P)O_2$.



(a)



(b)

Fig 4.5: Time dependence formation of (a) $Ru^{IV}(TMP)O$ (-8.9 ppm) and $Ru^{IV}(TMP)(SO)O$ (-15.8 ppm)(discuss later in this section); and (b) *cis*-stilbene oxide (4.1 ppm) in the aerobic epoxidation of *cis*-stilbene catalyzed by $Ru^{VI}(TMP)O_2$.

In situ ^{1}H-NMR studies of the aerobic epoxidation of olefins by $Ru^{VI}(TDCP)O_2$ and $Ru^{VI}(TMP)O_2$ showed that the catalyst first transfer one of its oxygen atom to the substrate forming epoxide and $Ru^{IV}(P)O$. We believe that $Ru^{IV}(P)O$ was the key active catalyst during the reaction as its appearance kept in pace with the growing yield of the epoxides(Fig 4.6).

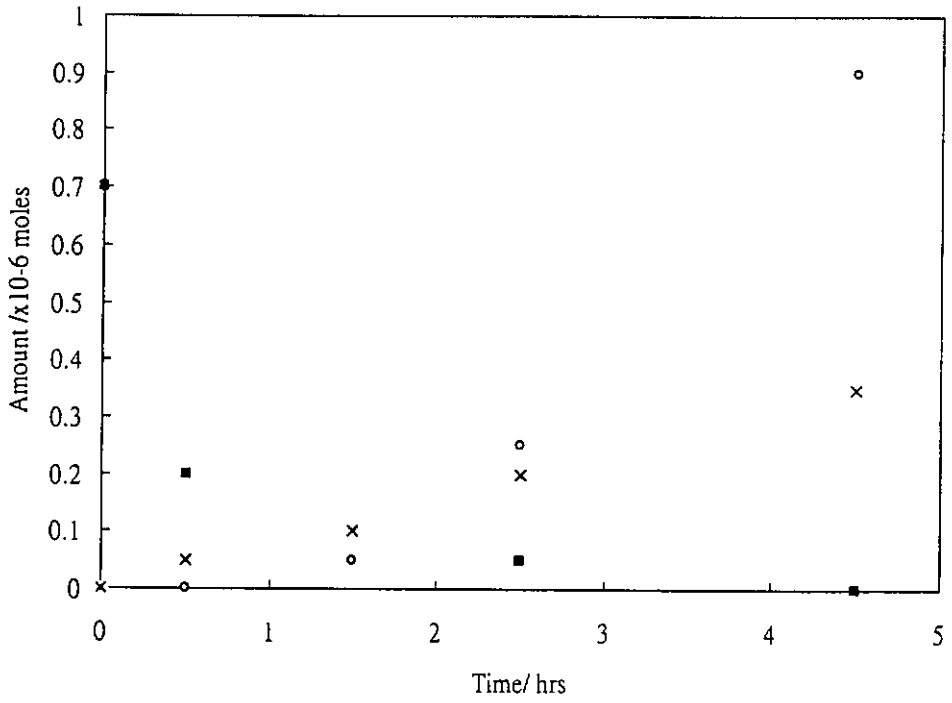
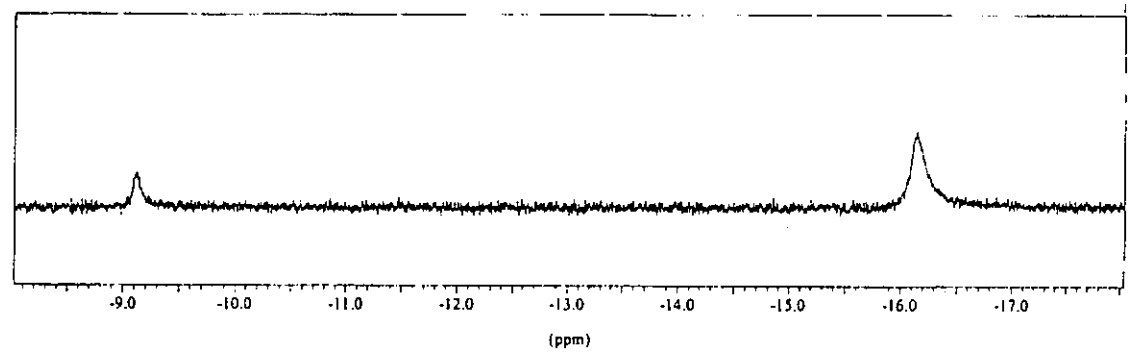


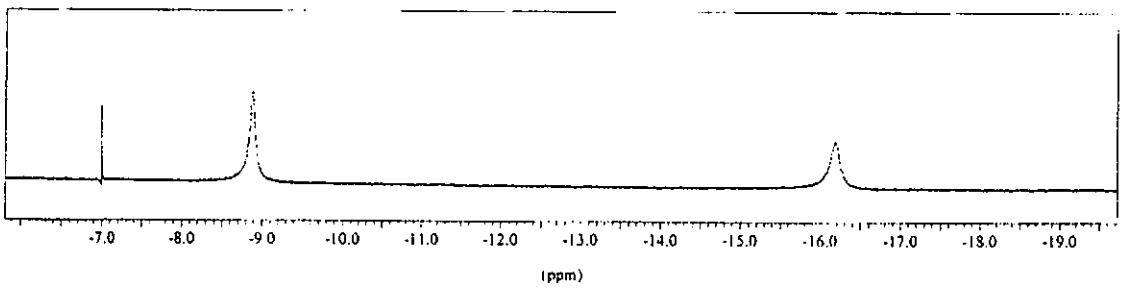
Fig 4.6: Time course study of the formation of *cis*-stilbene oxide (o). The change in concentration of $Ru^{VI}(TDCP)O_2$ (■) and $Ru^{IV}(TDCP)O$ (×) were monitored.

On the other hand, the decrease in concentration of $Ru^{VI}(P)O_2$ showed that $Ru^{IV}(P)O$ was unlikely to disproportionate into $Ru^{VI}(P)O_2$ and $Ru^{II}(P)$.

However, in anaerobic condition both TDCP and TMP generate a third species during the reaction. They exhibit an extra upfield peak at, -15.7 and -16.5 ppm, for TDCP and TMP respectively in ^{1}H-NMR spectra (Fig. 4.7).



(a)



(b)

Fig. 4.7: Intermediates formed during anaerobic epoxidation of *cis*-stilbene catalyzed by (a) $Ru^{VI}(TMP)O_2$; (b) $Ru^{VI}(TDCP)O_2$.

Results from curies plot found that the formed species may be a $Ru^{IV}(P)O(SO)$, whereas SO is the oxidized substrates(Fig. 4.8 and 4.9).[80]

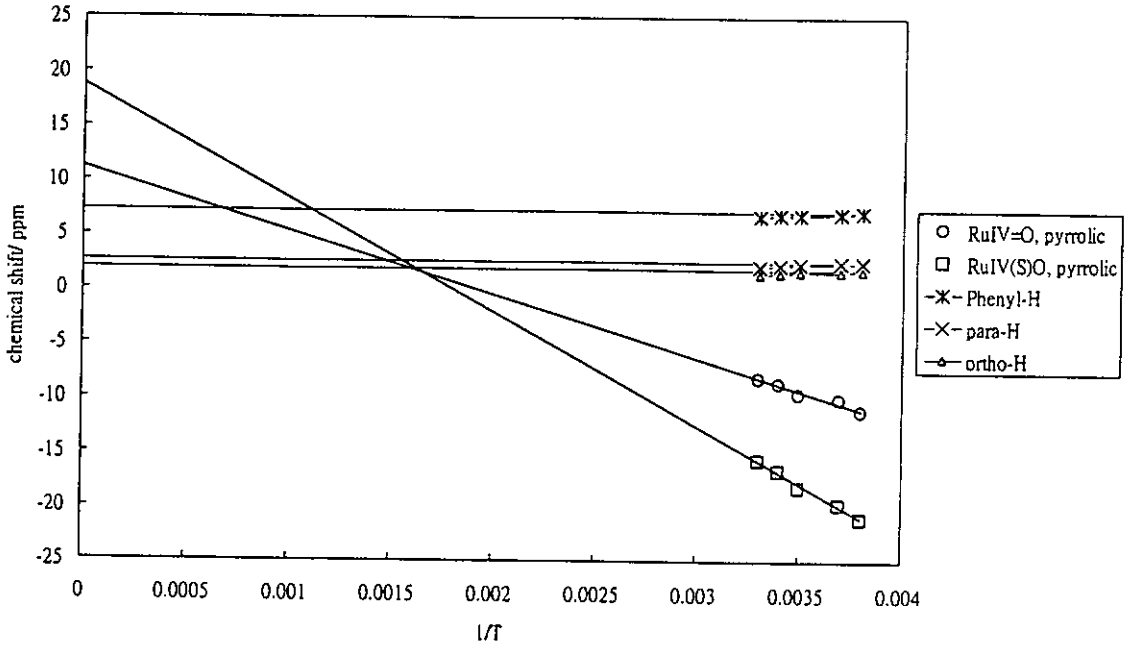


Fig. 4.8: Curie plot of the formed species during the anaerobic epoxidation of *cis*-stilbene catalyzed by $Ru^{VI}(TMP)O_2$.

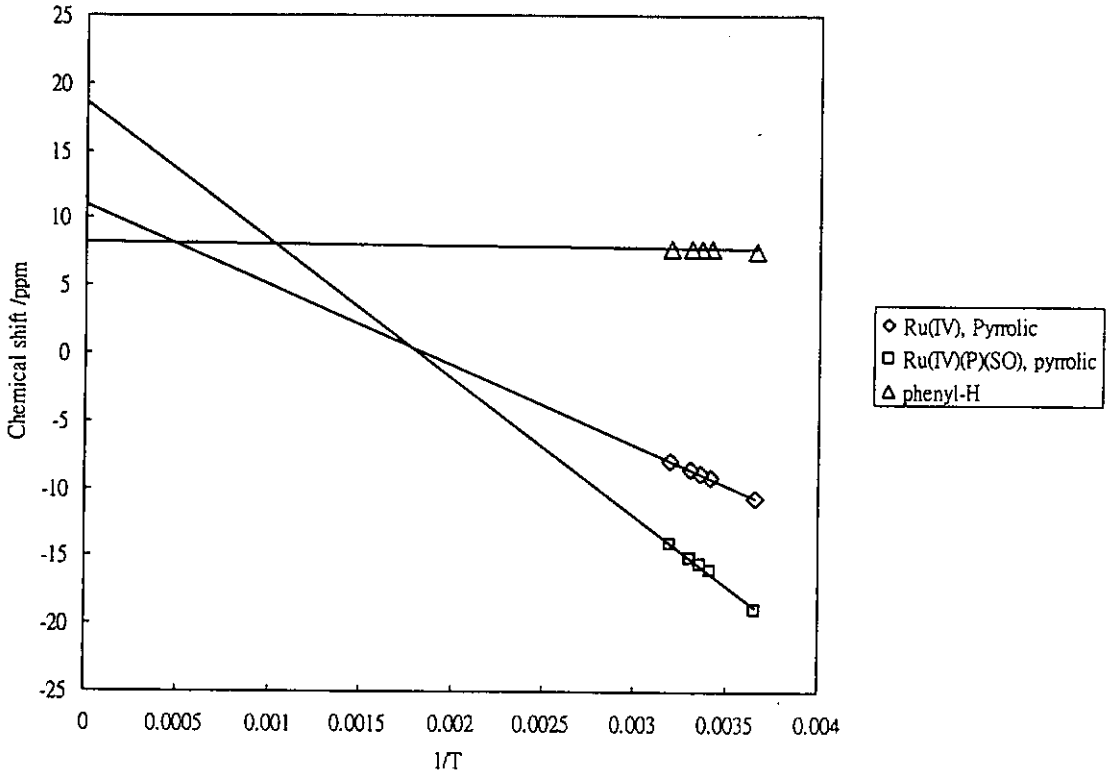
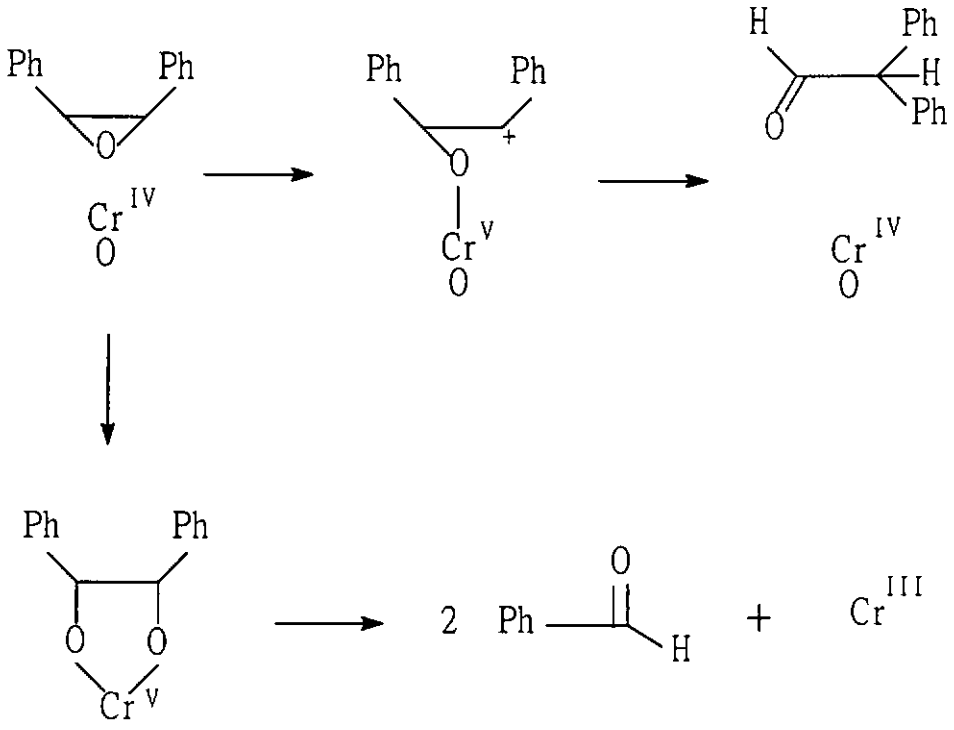


Fig. 4.9: Curie plot of the formed species during the epoxidation of styrene catalyzed by $Ru^{VI}(TDCP)O_2$ under atmospheric O_2 Pressure.

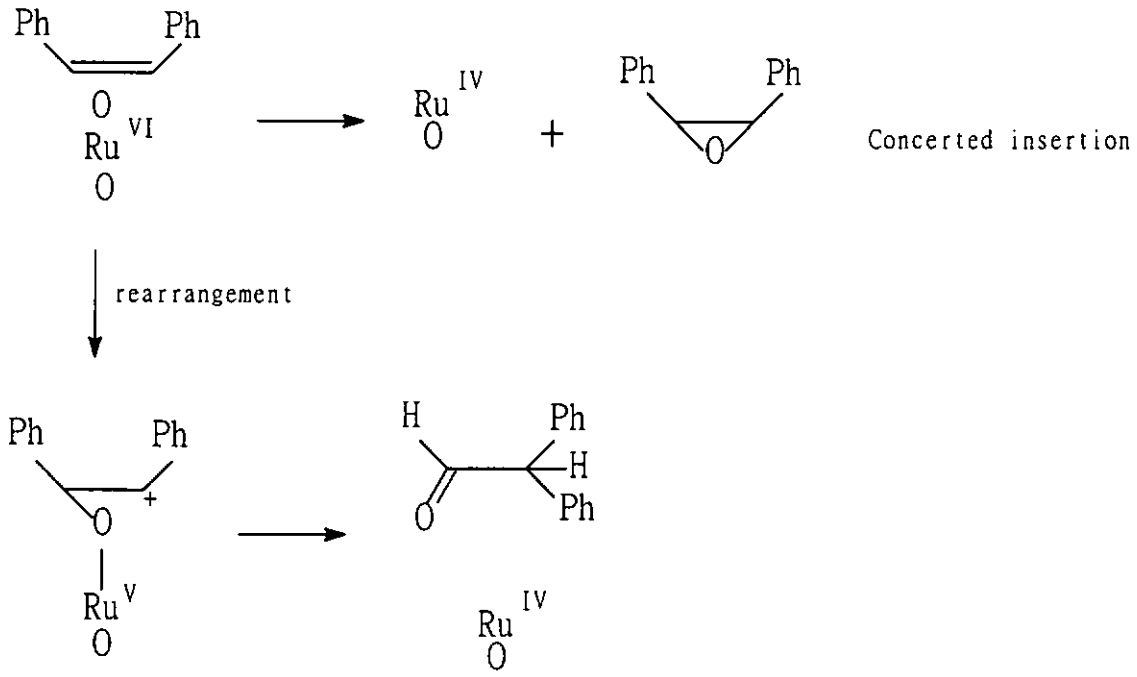
Attempts to obtain crystals of the final product of the catalyst after reaction for X-ray crystallography investigation failed. However, results from FT-IR and UV-Visible spectroscopy studies of the isolated product in the reaction indicated it to be a $Ru^{II}(P)(CO)$ species, oxidation marker : 1007 cm^{-1} for TDCP and 1009 cm^{-1} for TMP. GC-MS analysis of the final oxidized substrates revealed that a mixture of *cis*- and *trans*-stilbene oxide together with diphenylacetaldehyde were formed for TDCP and TMP catalyzed epoxidation. Bruice et al. had proposed a mechanism (Scheme 5) accounting for the formation of the rearranged products during reaction.[81]



Scheme 5 (taken from ref. 78)

We found that the above situation may not hold true for our studies, we have carried out a control experiment, which was done by reacting corresponding epoxide with TDCP and TMP. We found that only trace amount of aldehyde was formed after 2-3 days! In other words, the rearranged products may not come from the direct reaction of catalysts and the generated epoxides.

Speculations of mechanism are as follow (Scheme 6):



Scheme 6

4.6.1 Involvement of Substrates in the Intermediate State

Different olefins gave similar rate of epoxide formation, with the exception of norbornylene and *cis*-stilbene. The difference in the rate of epoxidation of norbornylene and *cis*-stilbene to other olefins can be explained by the steric hinderance induced by the substrates. This was further suported by the low reactivity of *trans*-Stilbene which gave only trace amount of *trans*-stilbene oxide even after reaction for 2 days. As the stereochemistry of the olefins and epoxides were retained during the reactions, therefore, it led us to speculate that the intermediate is not a charge-transfer complex. Since kinetics and competitive reaction data suggested that the reaction proceed via a concerted and 3-membered intermediate state, a direct concerted oxygen insertion mechanism rather than a metallooxetane formation is convincing.

4.6.2 Termination of reaction cycle

(A) N-Alkylporphyrin Formation

Cytochrome P-450, was an effective catalyst for oxidation of hydrocarbons. But, at the end of the reaction the hemin complex was found either destroyed or changed to an inactive species, N-alkylporphyrin, which occurred mostly with terminal olefins.[82] Allyl barbiturates, dihydropyridines and dihydroquinoline, sydnones, alkyl hydrazines, and even 1-alkenes and 1-alkynes were found to be inactivators for cytochrome P-450. Synthetic metalloporphyrins have been used to study the inactivation mechanism of

cytochrome by olefins using oxygen atom donors, e.g. iodosobenzene. Various research groups have successfully characterized N-alkylhemins.[83] From the results of ^{1}H-NMR, UV-Visible spectroscopy and LC-MS analysis of the final products of the reactions, no N-alkyporphyrins were found in our cases suggesting that the reactions were not terminated by self-catalyzed N-alkylation reaction. In fact, the catalysts were found either destroyed after reaction or changed to an inactive $Ru^{II}(P)(CO)$ species.[84]

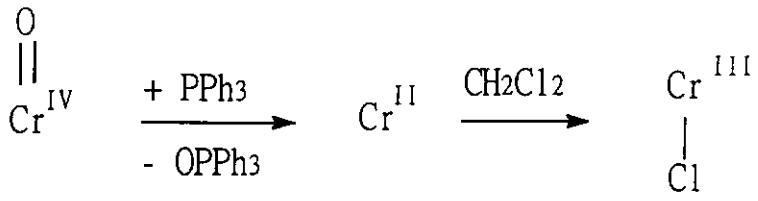
(B) Substitutents on the Phenyl Ring of Porphyrin Moiety

When compared to classical porphyrins, like tetraphenylporphyrins, TDCP and TMP all have substitutents on the meso-phenyl rings. For TMP, the substitutents are methyl groups and are electron-donating in nature. By donating electron density to the ring, the porphyrin will be more susceptible to electrophilic attack, e.g. bimolecular attack of 2 porphyrin molecules. On the other hand, in the case of TDCP the substitutents are Cl atoms which are electron-withdrawing. They will then remove the electron-density from the ring making the ring less susceptible to, when compared to TMP, electrophilic attack and increase the catalyst life-time.

(C) Formation of $Ru^{III}(P)Cl$ Species

From the time dependence studies of the UV-Visible spectrum of the 2 catalysts during reaction, TDCP was found to be more resistance to degradation process (Table 4.3). But, we found that a suspected $Ru^{III}(TDCP)Cl$ species (absorbance at 402 nm) was

formed during the reaction of $Ru^{VI}(TDCP)O_2$ with norbornylene. Similar observation has been reported and respective mechanism was proposed by Groves.[85]



Scheme 6

Only $Ru^{III}(P)Cl$ species was found in TDCP system while TMP gives $Ru^{II}(P)(CO)$ species. Detailed mechanism is not yet clarified. The electronic density of Ru(II) center effected by TDCP ligand may play an important role in determining the ease of the formation of $Ru^{III}(P)Cl$ species.

(D) Deactivation of Ruthenium Porphyrin by CO Binding

The ruthenium(II) porphyrins were well accepted as having very strong affinity for a carbonyl moiety. The -CO group that binded to the resulting "bare" ruthenium(II) porphyrin may came from decarbonylation of aldehyde which was generated during the epoxidation reaction of styrene or stilbene.

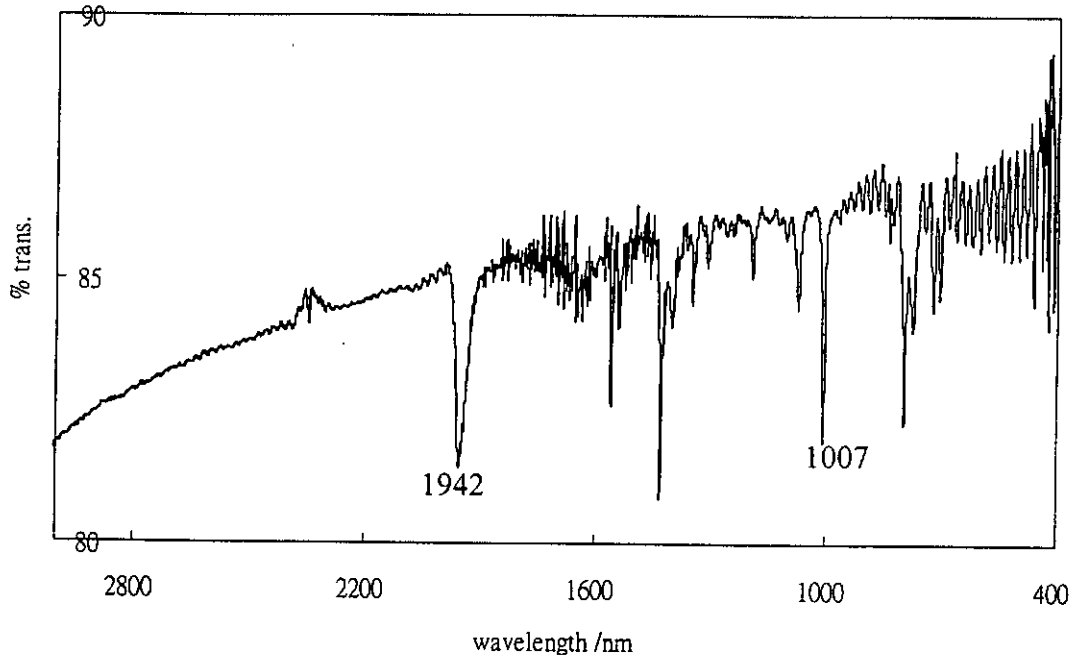


Fig 4.10: FT-IR spectrum of product obtained after epoxidation reaction of styrene catalyzed by $Ru^{VI}(TDCP)O_2$. Absorption at 1942 cm^{-1} was assigned as a Ru-CO bond, and 1007 cm^{-1} was assigned as a Ru(II) species.

The low intensity of the Ru-CO band in the IR spectra shown that only some of the bare Ru(II) porphyrins are bind with CO molecules.

Chapter 5 Conclusion

$Ru^{VI}(TMP)O_2$ and $Ru^{VI}(TDCP)O_2$ are effective catalyst in hydrocarbons oxidation. Various oxidants have been chosen in the reaction studies and many mechanisms have been proposed. However, no detailed studies on the catalytic behaviour of the catalysts when using dioxygen solely as an external oxidant have been reported. Valentine[86] uses dioxygen/aldehyde system to generate ROO· species and argues that the presence of high valent M=O species is necessary in the epoxidation reaction of olefins. The role of the metal complexes in the experiments is to aid in the initiation step for the free radical autooxidation of the added aldehyde and the acylperoxy radicals thus formed are the active epoxidation reagents. However, this system was found to generate many undesired products, e.g. hydroxylation of substrates, aldehyde or ketone formation etc. The lack of stereoretented products would definitely be a disadvantage.

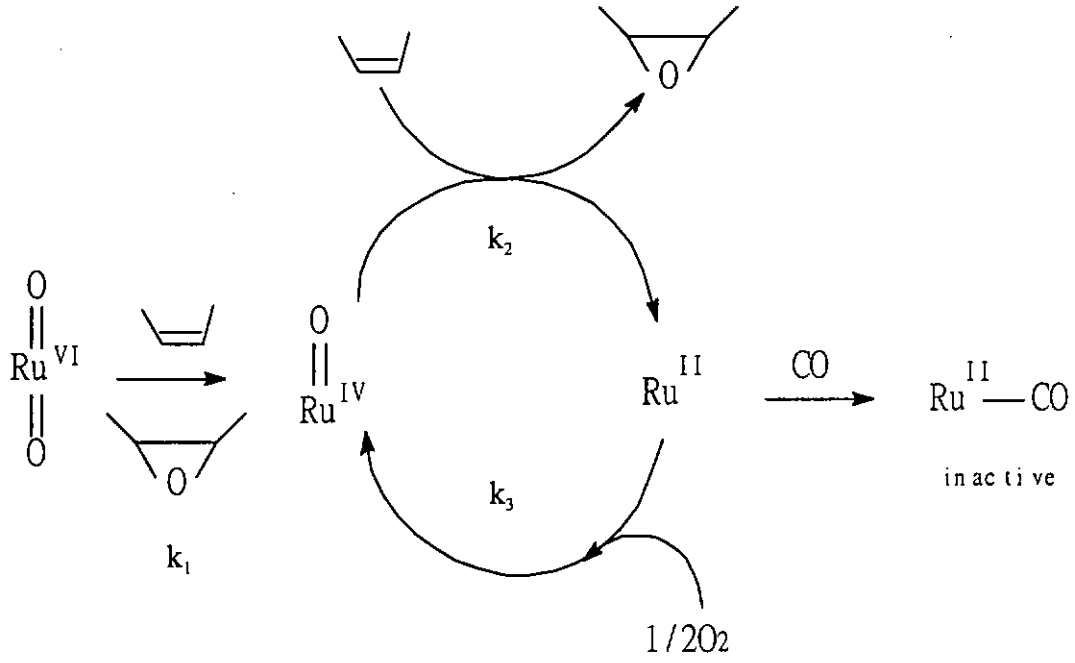
In this work, various substrates have been effectively epoxidized into corresponding epoxides with the retention of its configuration, and small amounts of rearranged products were obtained in the epoxidation of some olefins. The presence of a π–donating ligand, 1-methylimidazole, affects the product distribution in $Ru^{VI}(TMP)O_2$ catalyzed epoxidation of *cis*-stilbene. *trans*-Stilbene epoxide becomes the major oxidation product while $Ru^{VI}(TDCP)O_2$ catalyzed olefin epoxidation showed the same product distribution in the presence of 1-methylimidazole.

From the results of NMR spectroscopy and kinetic studies, the reaction should

proceed through a direct oxygen insertion of the Ru-bound electrophilic oxygen molecule to the electron-rich C=C double bond of the substrates, followed by the formation of a 3-membered intermediate and finally the formation of epoxide. The catalyst then takes up an oxygen molecule from an external oxidant and continues the reaction cycle.

The combination of 2 factors: a) low solubility of dioxygen in reaction mixture and b) higher affinity for CO molecule of bare Ru(II) complex, generates an inactive $Ru^{II}(P)(CO)$ species which terminates the reaction. Despite binding to CO, bare Ru(II) complex can uptake extra oxygen atom from dioxygen dissolved in the mixture and thereby generating a $Ru^{IV}(P)O$ species which is acting as an active oxidant during the reaction. The decrease in the amount of $Ru^{VI}(P)O_2$,while at the same time epoxide is still producing, during the catalytic epoxidation reaction indicated that $Ru^{VI}(P)O_2$ may not be the active oxidant. Disproportionation reaction proposed by Groves was not observed in our studies.

A concerted O_2 insertion mechanism (Scheme 7) is proposed based on our findings.



Scheme 7

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