ปฏิกิริยาพร้อมการสกัดสำหรับปฏิกิริยาอีปอกซิเดชันของไซโคลเฮกซีนไปเป็นไซโคลเฮกซีนออกไซด์โดยใช้ไดออกไซเรนในระบบคีโตน/โอโซน

นางสาว ปิยะนุช คชาสกุล

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิศวกรรมศาสตรมหาบัณฑิต
สาขาวิชาวิศวกรรมเคมี ภาควิชาวิศวกรรมเคมี
คณะวิศวกรรมศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2543

ISBN 974-13-0136-7

EXTRACTIVE REACTION FOR EPOXIDATION OF CYCLOHEXENE TO CYCLOHEXENE OXIDE USING DIOXIRANES IN THE KETONE/OXONE SYSTEM

Miss Piyanuch Kachasakul

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Engineering in Chemical Engineering
Department of Chemical Engineering
Faculty of Engineering
Chulalongkorn University
Academic Year 2000

ISBN 974-13-0136-7

Thesis Title	Extractive Reaction for Epoxidation of Cyclohexene to Cyclohexene Oxide Using Dioxiranes in the Ketone/Oxone System
By	Miss Piyanuch Kachasakul
Field of study	Chemical Engineering
Thesis advisor	Assistant Professor Suttichai Assabumrungrat, Ph.D.
Thesis co-advisor	Professor Piyasan Praserthdam, Dr.Ing.

Accepted by the Faculty of Engineering, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree.

…………………………………………..…Dean of Faculty of Engineering
(Professor Somsak Panyakeow, Dr.Eng.)

Thesis Committee

…………………………………………..…Chairman
(Associate Professor Ura Pancharoen, Dr.Eng.Sc.)

…………………………………………..…Thesis Advisor
(Assistant Professor Suttichai Assabumrungrat, Ph.D.)

…………………………………………..…Thesis Co-advisor
(Professor Piyasan Praserthdam, Dr.Ing.)

…………………………………………..…Member
(Assistant Professor Seeroong Prichanont, Ph.D.)

…………………………………………..…Member
(Suphot Phatanasri, Dr. Eng.)

ปิยะนุช คชาสกุล : ปฏิกิริยาพร้อมการสกัดสำหรับปฏิกิริยาอีปอกซิเดชันของไซโคลเฮกซีนไปเป็นไซโคลเฮกซีนออกไซด์โดยใช้ไดออกไซเรนในระบบคีโตน/โอโซน (EXTRACTIVE REACTION FOR EPOXIDATION OF CYCLOHEXENE TO CYCLOHEXENE OXIDE USING DIOXIRANES IN THE KETONE/OXONE SYSTEM) อ. ที่ปรึกษา : ผ.ศ. ดร. สุทธิชัย อัสสะบำรุงรัตน์, อ. ที่ปรึกษาร่วม : ศ. ดร. ปิยะสาร ประเสริฐธรรม ; 74 หน้า. ISBN 974-13-0136-7

การศึกษาปฏิกิริยาพร้อมการสกัดสำหรับปฏิกิริยาอีปอกซิเดชันของไซโคลเฮกซีนไปเป็นไซโคลเฮกซีน ออกไซด์โดยใช้ไดออกไซเรนแบ่งเป็น 2 ส่วนคือ การศึกษาเปรียบเทียบการเตรียมไซโคลเฮกซีน-ออกไซด์ด้วยวิธีต่างๆ และ การศึกษาถึงผลกระทบของสภาวะการทดลองที่มีต่อประสิทธิผลของระบบ เช่น อัตราเร็วในการกวน ชนิดของตัวทำละลาย อัตราส่วนเริ่มต้นของตัวทำละลายต่อน้ำ อุณหภูมิ ค่าความเป็นกรดด่าง และ ปริมาณของตัวเร่งปฏิกิริยา จากการศึกษาพบว่าระบบมีประสิทธิผลสูงสุดเมื่อทำการเตรียมไซโคลเฮกซีนออกไซด์โดยการอีปอกซิไดซ์ไซโคลเฮกซีนด้วยไดออกไซเรนโดยใช้การเกิดปฏิกิริยาพร้อมการสกัดและใช้ตัวเร่งปฏิกิริยาย้ายเฟส นอกจากนี้ยังพบว่าระบบที่มีการเกิดปฏิกิริยาพร้อมการสกัดจะมีประสิทธิภาพในการเปลี่ยนไซโคลเฮกซีนไปเป็นไซโคลเฮกซีนออกไซด์ได้ดีกว่าระบบหนึ่งเฟส เนื่องจากการสกัดสารผลิตภัณฑ์พร้อมๆกับการเกิดปฏิกิริยาจะไปช่วยรบกวนสมดุลของปฏิกิริยาและป้องกันไม่ให้สารผลิตภัณฑ์เกิดปฏิกิริยาต่อไปเป็นผลิตภัณฑ์อื่นที่ไม่ต้องการ สำหรับตัวเร่งปฏิกิริยาย้ายเฟสถูกเติมลงไปในระบบเพื่อเพิ่มอัตราเร็วในการเกิดได-ออกไซเรน จากการทดลองพบว่า ค่าผลได้ของไซโคลเฮกซีนออกไซด์สูงขึ้นเมื่ออัตราเร็วในการกวนและปริมาณตัวเร่งปฏิกิริยามากขึ้น ค่าประสิทธิผลที่ดีที่สุดสำหรับกรณีใช้เวลาทำปฏิกิริยานาน 60 นาที คือ อัตราส่วนเริ่มต้นของตัวทำละลายต่อน้ำเท่ากับ 0.83 อุณหภูมิเท่ากับ 25 องศาเซลเซียส ค่าความเป็นกรดด่างเท่ากับ 7.5 และอัตราการกวนเท่ากับ 2040 รอบต่อนาที ค่าผลได้ของไซโคลเฮกซีนออกไซด์ที่สภาวะที่ดีที่สุดของการทดลองมีค่าเท่ากับ 97.5 เปอร์เซ็นต์

ภาควิชา วิศวกรรมเคมี
สาขาวิชา วิศวกรรมเคมี
ปีการศึกษา 2543

ลายมือชื่อนิสิต......................................
ลายมือชื่ออาจารย์ที่ปรึกษา.......................
ลายมือชื่ออาจารย์ที่ปรึกษา.......................

#4270426521: MAJOR CHEMICAL ENGINEERING

KEY WORD: EXTRACTIVE REACTION / EPOXIDATION / DIOXIRANE

PIYANUCH KACHASAKUL: EXTRACTIVE REACTION FOR EPOXIDATION OF CYCLOHEXENE TO CYCLOHEXENE OXIDE USING DIOXIRANES IN THE KETONE/OXONE SYSTEM. THESIS ADVISOR: ASSISTANT PROF. SUTTICHAI ASSABUMRUNGRAT, Ph.D. THESIS COADVISOR: PROF. PIYASAN PRASERTHDAM, Dr. Ing. 74 pp. ISBN 974-13-0136-7.

Extractive reaction for the epoxidation of cyclohexene to cyclohexene oxide using dioxirane was studied. The study was divided into 2 main parts: namely comparison of different preparation methods and effect of operating conditions such as stirring rate, type of solvent, initial solvent/aqueous ratio, temperature, pH and amount of catalyst on the performance of the system. The study showed that the best performance was obtained when cyclohexene was epoxidized with dioxirane in an extractive reaction system with the presence of the phase transfer catalyst. The extractive reaction process was found to be more efficient in term of cyclohexene oxide yield than the single-phase process because it bypassed the equilibrium limitation and prevented further reactions of the desired product. It was found that the rate of dioxirane formation increased with the presence of phase transfer catalyst. The yield of cyclohexene oxide increased with increasing stirring rate and amount of acetone. Dichloromethane was the best solvent for this system in this study. The optimum performance for the reaction time of 60 minutes was achieved when using the initial solvent/aqueous ratio of 0.83, temperature of 25 ^{O}C, pH of 7.5 and stirring rate 2040 rpm. The maximum yield of 97.5% was obtained in this study.

Department	Chemical engineering	Student 's signature
Field of study	Chemical engineering	Advisor's signature
Academic year	2543	Co-advisor 's signature

ACKNOWLEDGEMENT

The author would like to express her highest gratitude to Assistant Prof. Suttichai Assabumrungrat and Prof. Piyasarn Praserthdam for their inspiration, advice, guidance, and supervision throughout this research. In addition, she is also grateful to Associate Professor Ura Pancharoen, as the chairman, Dr. Suphot Phatanasri and Assistant Prof. Seeroong Prichanont, the members of the thesis committees.

Thank for the financial support from the Thailand Research Fund, TJTTP-OECF. and Graduate school, Chulalongkorn University.

Most of all, the author would like to express her highest gratitude to her parents who have always been the source of her support and encouragement.

Finally, grateful thanks to membrane group members who have encouraged her over the years of her study.

CONTENTS

PAGE

ABSTRACT (IN THAI) iv
ABSTRACT (IN ENGLISH) v
ACKNOWLEDGEMENT vi
LIST OF TABLES ix
LIST OF FIGURES x
NOMENCLATURE xii

CHAPTERS

- I INTRODUCTION 1
- II LITERATURE REVIEWS 4
  - 2.1 Extractive reaction 4
  - 2.2 Epoxidation 10
  - 2.3 Phase transfer catalysis 15
- III THEORY 19
  - 3.1 Liquid-liquid extraction 19
  - 3.2 Extractive reaction 23
    - 3.2.1 Examples of liquid-liquid phase diagrams with reactions 23
    - 3.2.2 Processes for improvement in yield 26
  - 3.3 Epoxidation 27
    - 3.3.1 Direct oxidation with stoichiometric oxidants 27
    - 3.3.2 Epoxidation alkenes with dioxiranes 32
    - 3.3.3 Metal-catalyzed epoxidation 33
  - 3.4 Phase transfer catalysis 37
- IV EXPERIMENT 39
  - 4.1 Experimental procedure 39

PAGE

4.2 Analytical method 40
V RESULTS AND DISCUSSION.. 41
5.1 Comparison of different preparation methods........................ 41
Case 1: Epoxidation with $KHSO_5$ 41
Case 2: Epoxidation with $KHSO_5$ and acetone........................ 43
Case 3: Epoxidation with $KHSO_5$, acetone and solvent...... 45
Case 4: Epoxidation with $KHSO_5$, acetone, solvent and phase transfer catalyst.. 47
5.2 Effect of operating conditions on the yield of cyclohexene oxide 49
5.2.1 Effect of stirring rate 49
5.2.2 Effect of type of solvent 50
5.2.3 Effect of initial solvent/aqueous ratio 51
5.2.4 Effect of temperature 52
5.2.5 Effect of pH 52
5.2.6 Effect of amount of catalyst.. 54
5.2.7 Effect of amount of phase transfer catalyst........... 54
VI CONCLUSIONS AND RECOMMENDATION........................ 56
REFERENCES.. 58
APPENDICES
A GAS CHROMATROGRAPHY.. 64
B EXPERIMENTAL DATA 69
VITA.. 74

LIST OF TABLES

TABLE PAGE

5.1 Effect of the acetone amount on the yields of cyclohexene oxide.......... 54
5.2 Effect of the amount of phase transfer catalyst on the yields of cyclohexene oxide.......... 55
B-1 Data of Figure 5.1.......... 69
B-2 Data of Figure 5.3.......... 69
B-3 Data of Figure 5.5.......... 70
B-4 Data of Figure 5.6.......... 70
B-5 Data of Figure 5.7.......... 71
B-6 Data of Figure 5.8.......... 71
B-7 Data of Figure 5.9.......... 72
B-8 Data of Figure 5.10.......... 72
B-9 Data of Figure 5.11.......... 73

LIST OF FIGURES

FIGURE **PAGE**

1.1 Cataytic cycle of the ketone/oxone system 2
3.1 Schematics of liquid-liquid extractors.................................. 20
3.2 Types of ternary liquid-liquid equilibria 28
3.3 Liquid-Liquid equilibrium for a ternary system.............................. 22
3.4 Phase diagrams for $A \longleftrightarrow B$ (K=1.0) in the presence of an inert C...... 24
3.5 Phase diagrams for $A \longleftrightarrow B$ (K=0.35) in the presence of an inert C 25
3.6 Phase diagram for $A+B \longleftrightarrow C$ (K=10.0)................................... 25
4.1 Schematic diagram of the experimental set up 39
5.1 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time in Case 1.. 42
5.2 The scheme for the synthesis of cyclohexene oxide in Case 1.............. 43
5.3 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time in Case 2.. 43
5.4 The scheme for the synthesis of cyclohexene oxide in Case 2.............. 45
5.5 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time in Case 3.. 45
5.6 The scheme for the synthesis of cyclohexene oxide in Case 3.............. 46
5.7 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time in Case 4.. 47
5.8 The scheme for the synthesis of cyclohexene oxide in Case 2.............. 48
5.9 Effect of stirring rate on the yields of cyclohexene oxide.................. 49
5.10 The conversion of cyclohexene oxide as a function of time in biphasic system using different solvent as extractant.................................. 50
5.11 Effect of initial solvent/aqueous ratio on the yields of cyclohexene oxide at various stirring rates.. 51
5.12 Effect of temperature on the cyclohexene oxide yield....................... 53

FIGURE **PAGE**

5.13 Effect of pH on the cyclohexene oxide yield 53
A-1 The calibration curve of cyclohexene in dichloromethane.................. 65
A-2 The calibration curve of cyclohexene oxide in dichloromethane........... 66
A-3 The calibration curve of cyclohexene in toluene............................ 66
A-4 The calibration curve of cyclohexene oxide in toluene..................... 67
A-5 The calibration curve of cyclohexene in benzene............................ 67
A-6 The calibration curve of cyclohexene oxide in benzene..................... 68

Nomenclature

E	Extract
F	Feed stream
K	Equilibrium constant
PTC	Phase transfer catalysis
R	Raffinate
rpm	round per minute
S	Solvent

CHAPTER I

INTRODUCTION

In recent year, single units that combine reaction and separation operations have received considerable attention. The reduction in the number of equipment units leads to investment savings, and simultaneous reaction and separation provides the possibility of bypassing the equilibrium limitation imposed by reversible reaction. The use of reactive distillation in the production of mythyl acetate and methyl *tert*-butyl ether clearly demonstrates the benefits (DeGarmo *et al*., 1992; Doherty and Bazad, 1992). Similar advantages have been realized with simultaneous reaction and adsorption in a chromatographic reactor (Coca *et al*., 1993; Tonkovich and Carr, 1994), permeation in a membrane reactor (Tsotsis *et al*., 1993), and extraction in a liquid-liquid two-phase reactor (Sharma, 1988). The precipitator is another type of reactive separator in which the product precipitates out of solution, thus eliminating a crystallizer from the process flow sheet (Mersmann and Kind, 1988).

In an extractive reaction, a reaction and extraction occur simultaneously. A second liquid phase containing a solvent can be deliberately imposed on the system. Frequently, the solvent selectively extracts an intermediate or a product, thereby preventing its further reaction and resulting in a higher yield and selectivity.

At present, an extractive reaction is used in biochemical processes involving the use of enzyme in most cases. For chemical engineering processes, there is a little research on extractive reaction. A few reactions using an extractive reaction have been studied. Because of these reasons, this work pays attention to investigate the extractive reaction process. Epoxidation, a reaction used to generate epoxide from alkene, is chosen to study the extractive reaction process in this work.

Epoxides are important industrial organic intermediates due to their highly reactive moiety. Generally, epoxides are formed in an initial step and react further to provide industrially important products, such as pharmaceuticals, surfactants, detergents, antistatic agents, corrosion protection agents, additives for laundry detergents, lubricating oils, textiles, and cosmetics.

Generally, oxidizing agents frequently used for epoxidation of alkene are organic peracids and peroxy acids. Dioxiranes are new oxidizing agents. They are the smallest cyclic peroxide systems known as reactive and efficient oxidizing agents, usually prepared in solutions of the parent ketone. The preparation method that has received the most attention is that containing a ketone and a peracid, namely potassium peroxymonosulphate ($KHSO_5$) that can commercially available as oxone^{R}, i.e. $2KHSO_5.KHSO_4.K_2SO_4$. The catalytic cycle usually drawn for dioxiranes, as shown in Figure 1.1, indicates that $KHSO_5$ is the oxidizing agent and the ketone acts as a catalyst.

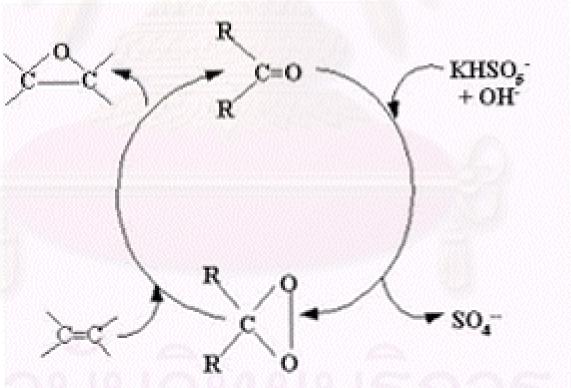


Figure 1.1 Cataytic cycle of the ketone/oxone system.

However, the problems encountered in this reaction system are low conversion and yield so this work will use an extractive reaction to improve conversion and yield of the reaction system.

In this work, to study an extractive reaction, the epoxidation of cyclohexene to cyclohexene oxide by dioxiranes generated in-situ with oxone^R as the oxidant is used as a test reaction. Acetone is used as catalyst. The experiments are only performed in lab-scale level and carried out in a batch reactor. The objectives of the study are to investigate

1. The performance of epoxidation of cyclohexene in an extractive reaction process.
2. The effect of operating parameters on the yield of cyclohexene oxide such as type of solvent, stirring rate, initial solvent/aqueous ratio, temperature, pH and amount of catalyst.

CHAPTER II

LITERATURE REVIEWS

In modern technology, extractive reaction processes receive considerable attention when separation during reaction enhances the reaction efficiency. These devices combine reaction and separation in a single unit operation. They also make it possible to achieve significant enhancement over equilibrium conversion, by continuous removal of an intermediate or a product of reaction through the extraction during the reaction.

These literature reviews will provide information on extractive reaction researches, development of epoxidation of alkene and development of phase-transfer-catalysis.

2.1 Extractive reaction

The deliberate imposition of a second liquid phase has many unique features associated with an improvement in conversion, yield, use of cheaper reagents and the ease of heat removal (Brandstrom, 1983). The use of two liquid phases, in principle, should allow higher conversions from a thermodynamic standpoint compared to that which can be realized in either of the two phase alone (Semenov *et al.,* 1987). It can be shown, by a simple analysis, that for certain values of distribution coefficient, the two-phase system gives higher values of the equilibrium constant and this may be 10^4 times that encountered in the homogeneous phase.

The concept of the extractive reaction has been found applicable in both biochemical and chemical reaction engineering. However, most of the pioneer works were devoted to biochemical processes especially catalysted by enzymes. The following sections provide the literature reviews on the extractive reaction process for enzymatic reactions and extractive reaction process for chemical reactions.

2.1.1 Extractive reaction process for enzymatic reactions

In most cases, simultaneous operation of enzymatic reaction and product separation by liquid extraction was developed for continuous synthesis of peptides with high efficiency by using free enzyme. An organic solvent containing substrates was continuously fed into a bioreactor where the enzyme was freely dissolved in a retained aqueous solution. The substrates were extracted from the organic phase to the aqueous phase, where peptide was enzymatically synthesized, and then the peptide was extracted into the organic phase from the aqueous phase at the same time as it was synthesized. Only the organic solvent containing the product peptide was recovered from the bioreactor.

The precursor of a synthetic sweetener, aspartame, was continuously synthesized from Z-L-aspartic acid and L-phenylalanine methyl ester with thermoase in a stirred tank by the novel method of extractive reaction. The yield of aspartame increased with the residence time of organic solvent and the stirring rotation rate increased, and an almost complete yield was achieved at 10 hours of residence time and 450 rpm of the stirring rate (Hirata *et al*., 1997).

Continuous enzymatic synthesis of aspartame precursor at low pH using an extractive reaction was investigated by Murakami and Harata (1997). The enzymatic synthesis of peptides at low pH has many advantages from the viewpoint of an industrial-scale production, such as, suppression of nonenzymatic decomposition of amino acid ester substrates and a lower requirement of NaOH for pH adjustment. An extractive synthesis of peptides in an aqueous/organic biphasic system at low pH was developed and applied to the protease-catalyzed synthesis of N-(benzyloxycarbonyl)-L-aspartyl-L-phenylalanine methyl ester (Z-APM), the precursor of an artificial sweetener, aspartame. The Z-APM yield in a pure aqueous monophasic system was less than 10%, however, it was over 96% at low pH using extractive synthesis in an aqueous/organic biphasic system although the enzyme activity was very low.

N-Formyl-L-aspartyl-L-phenylalanine methyl ester (N-formyl aspartame, F-AspPheOMe) was synthesized enzymatically utilizing an extractive reaction in an aqueous/organic biphasic system. The N-formyl aspartame yield in a pure aqueous monophasic system was 3% but it was over 80% in a water/1-butanal biphasic system using a simultaneously extractive operation of an enzymatic reaction in an aqueous phase and a product separation from an aqueous to an organic phase. (Murakami *et al*., 1998).

Later, Murakami *et al* (1999) developed a pulsed column reactor as a novel of tool for continuous enzymatic synthesis of peptide in an aqueous/organic biphasic medium. N-Formyl-L-aspartyl-L-phenylalanine methyl ester was enzymatically synthesized continuously. With this extractive method using a pulsed column reactor, it can synthesize peptides with a stable performance even if a peptide (or a peptide-amino acid complex) was precipitated due to its high hydrophobicity.

Lysosomotropic detergents (cytotoxic compounds designed as anticancer agents) acylated with Z-GlyPhe (N-benzyloxycarbonyl-L-glycyl-L-phenlylalanine), masking into cells, were facilitated entry into the target cells, thereby continuous enzymatic synthesis of peptide precursor masking introduction into cells utilizing extractive reaction was studied (Murakami et al., 1999). The precursor of Z-GlyPhe, namely Z-GlyPheOMe (N-benzyloxycarbonyl -L-glycyl-L-phenlylalanine methyl ester), was enzymatically synthesized continuously. The yield of Z-GlyPheOMe was usually 10 % in aqueous medium due to the unfavorable shift of the chemical equilibrium towards a peptide bond hydrolysis. Since this peptide precursor was non-ionic, the precursor was distributed to an organic phase in an aqueous/organic biphasic system. Z-GlyPheOMe was selectively extracted into the organic phase simultaneously with an enzymatic synthesis in an aqueous enzyme solution in an aqueous/organic biphasic system, and 100 % yield of Z-GlyPheOMe was achieved.

2.1.2 Extractive reaction process for chemical reactions

For chemical reactions, extractive reaction process was studied in some reactions such as Hoffman reaction, epoxidation of olefinic compounds, extractive hydrolysis over acid and hydroformylation reaction of propylene which the literature reviews are as follows.

The use of carefully selected second liquid phase may be particularly important when the desired intermediate is capable of undergoing further facile, undesirable reactions. Consider the conversion of $HO(CH_2)_6OH$ to $HO(CH_2)_6Br$ with aqueous HBr. By using a hydrocarbon solvent, the desired product is obtained in high yields and the dibromo-product formation is reduced or eliminated.

Consider the example of making isocyanates from the corresponding amides (e.g. 2-ethylhexanoic acid amide to the corresponding isocyanate). The Hofmann reaction, which converts $RCONH_2$ to RNH_2 with aqueous sodium hypochlorite, is well known. This process involves the use of haloamide as an intermediate and rearrangement of the group R from C=O to N to give the isocyanate RNCO. The water is added to give carbamic acid, and alkaline conditions leads to its decarboxylation to RNH_2. However, by using a second liquid phase, the intermediate isocyanate RNCO, which shows high distribution coefficient into the selected second liquid phase, can be obtained in high yields. Thus, a variety of isocyanates required in fine chemicals manufacture can be made by a safe process obviating the use of hazardous phosgene (Wang *et al.,* 1984). A criterion for realizing high selectivity can be derived.

The epoxidation of olefinic compounds with metachloroperbenzoic acid provides yet another interesting example as the product metachlorobenzoic acid, which is highly soluble in organic solvents, is capable of undergoing undesirable reaction with the epoxy compound thereby lowering the yield and making separation difficult in some cases. Here, by using an aqueous buffered medium at pH 7 and dichloromethane as a solvent, more than 99% of the metachlorobenzoic acid can be taken out in the aqueous phase (Brandstrom, 1983). In this case, the large difference in the pK_a of the metachlorobenzoic acid and the peroxy acid (3.82 and 7.3 respectively) has been exploited like in dissociation extraction (Gaikar and Sharma, 1987). The distribution coefficient of the peroxy acid with respect to the organic phase is also more favourable (633.1 for the peroxy acid compared to 15.8 for the metachlorobenzoic acid).

The superiority of extractive hydrolysis over acid hydrolysis with respect to productivity, yield, raw materials and waste streams, for the transformation of drug intermediates (e.g. for Primaxin) in formate ester form to the corresponding alcohol, has been effectively brought out by King *et al.* (1985). They carried out the hydrolysis of the relevant formate ester with simultaneous extraction of the desired product from the undesired impurities by two-phase reaction/extraction with base.

The adoption of a second liquid phase proved useful in hydroformylation reaction of propylene where Rh based water soluble catalyst based on phosphine (m-sulphophenyl) was used. This complex is water soluble and extractable at $-1 < pH < 0$; the sodium salt is not extractable. This is a good example to bring out the importance of making a homogeneously catalyzed reaction heterogeneous. The separation of products is easy and energy consumption is relatively low; the heat of reaction may be used to generate steam. A variety of fine chemicals are made via the hydroformylation reaction and this strategy should prove useful. In case when the olefinic compound has extremely low solubility in the aqueous phase, a phase transfer catalyst can be employed to transfer the catalyst to the organic phase and yet the problems of the recovery of the catalyst can be made tractable.

In recent year, a synthetic method presented to synthesize extractive reaction processes was studied by Samant and Ng (1998). The objective of the study was to develop liquid-phase processes involving simultaneous reaction and separation by extraction to achieve improved yield, selectivity to a desired product, and separation of byproducts. The method was based on the equilibrium thermodynamic analysis of multicomponent reactive systems with multiple liquid phases. Using transformed coordinates systems with three of fewer degrees of freedom can be conveniently analyzed regardless of the number of components in the system. Key features of the reactive phase diagrams relevant to achieving the process objectives were identified. The method was illustrated with several model examples to demonstrate the advantages of extractive reaction over conventional single-phase processes.

Samant and Ng (1998) also studied the effect of chemical kinetics and mass transfer on extractive reaction processes by deriving a genetic model. Activity-based models were used to describe nonideal liquid-liquid phase equilibrium and reaction kinetics. Maxwell-Stefan formulation and the film model were used to describe multicomponent mass transfer. The effects of kinetics and mass transfer were described in terms of Damkohler number matrices for reaction and for mass transfer, respectively. The elements of these matrices measure the rates of reactions and mass transfer relative to product removal. These effects were demonstrated using examples of systems with inherent phase separation and systems with solvent-induced phase separation. The results showed that it may not always be beneficial to operate extractive reaction processes near the equilibrium thermodynamic limit. Damkohler numbers needed to be chosen carefully to obtain the desired performance. The use of the model in evaluting performance trade-offs and in making judicious choices about reactor attributes is demonstrated.

Furthermore, Samant and Ng (1998) studied the design of multistage extractive reaction (MSER) processes. A general and efficient design procedure for stand-alone counter current MSER cascades and process flowsheets presented in this study determined the range of feasible operation for the MSER process, the number of stages in the MSER cascade, compositions and molar flow rates at each stage and the yield of product distribution of the reaction system. It was based on the geometric properties of the phase and reaction equilibrium surfaces and the composition profiles of the MSER cascade. First, a key design variable was identified and the fired points or pinches of the composition profiles are tracked as a function of this variable by using are-length continuation, without performing stage-to-stage calculations. The location of the fixed points gave the upper or lower bound on the window of the MSER operation. The other bound was determined by the equilibrium behavior of the system. Within the window of operation MSER profiles were guaranteed to be feasible. Then, stage-to-stage calculations were performed as an initial-value problem to complete the design. The results of these calculations provided a comprehensive picture of the trade-offs in the design of MSER processes and can be used as a basis for screening flowsheet alternatives.

The reactions of glyoxylic acid with different aliphatic alcohols using cationic exchange resins as catalysts were studied by Mahajani (2000). The alcohol reacted with both acid and aldehyde groups of glyoxylic acid to form ester and the acetal of the ester, respectively. The simultaneous removal of water during the course of the reaction helped increase the conversion level. An increase in temperature leaded to better selectivity towards the acetal of the ester. The kinetics of the extractive reactions (solid-liquid-liquid mode) of aqueous solution of glyoxylic acid with 2-ethyl hexanol was studied and a significant level of conversion was obtained even with dilute (5% w/w) solution.

2.2 Epoxidation

Generally, epoxides are produced from the epoxidation of alkenes with peracids such as m-chloroperbenzoic acid (m-CPBA), trifluoroperacetic acid and 3,5-dinitroperbenzoic acid. Because peracids are easy to prepare, they are often used as reagents for epoxidation. However, these systems provide low yields and give by-products, e.g. meta-chlorobenzoic acid, that are necessary to separate from a main product. Peroxy acids such as percarboxylic acids are usually used as oxidizing agents. A solvent is often employed to moderate the reaction and to facilitate subsequent recovery of the epoxide in high yield. For example, Kuo and Chou (1987) studied the epoxidation of oleic acid with oxygen in the presence of benzaldehyde to produce epoxidized oleic acid using Co^{3+} as the catalyst. The results indicated that the epoxidized oleic acid was formed by a series of free-radical reactions. The experimental results showed that at 75% conversion of oleic acid, 66% yield of total theoretical epoxidized oleic acid was obtained, illustrating the high selectivity (88%). Roy *et al.* (1991) also considered the epoxidation using peroxy acid. They studied the effect of performic acid concentration and other reaction parameters on epoxidation of natural rubber latex. The product distribution and optimum acid concentration were determined from experimental data. It was found that, at 28 ^{O}C and acid concentration of 2.3 mol/dm^3, epoxide yields up to 70% was achieved and with increasing acid concentration initially the overall rate constant increased, reached a maximum, and then sharply decreased. The maximum epoxidation level decreased with increased acid concentration.

Another way to enhance yield of epoxide is addition of a solvent that selectively extracts an intermediate or a product from the reaction system. Thus, it bypasses the equilibrium limitation imposed by the reversible reaction and prevents the further reaction of required product. Anderson and Veysoglu (1973) studied the epoxidation of acid-sensitive olefinic compounds with m-chloroperbenzoic acid in an alkaline biphasic solvent system. During the course of their research, they found the solid buffer-single solvent procedure to be unsuited for certain acid-sensitive compounds. They wished to report a mild and simple epoxidation procedure using a two-phase system which proved superior to the single solvent method for the epoxidation of acid-sensitive compounds. Furthermore, the yields of epoxides were comparable to those obtained by a single solvent procedure. For instance, the epoxide product derived from 6-methylhept-5-en-2-one undergoed facile rearrangement to an undesirable by-product 1,3,3-trimethyl-2,7-dioxabicyclo[2.2.1]heptane. When the series reaction was carried out in the presence of dichloromethane, the product was extracted into the hydrocarbon phase and a higher selectivity to the epoxide product is obtained (83-85% yield). For epoxidation of cyclohexene, 71% yield was obtained with using the olefin-peracid ratio of 1:1 and the reaction time of 4 hours.

Few epoxidation processes are carried out in aqueous solution, and most of them include the use of catalysts and phase-transfer agents. From preceeding researches, direct epoxidation of olefin by hydrogen peroxide can be achieved only by means of suitable catalysts which are based mainly on group 5A,B and 6A,B metal oxides (e.g. Payne *et al.,* 1959; Reich *et al.,* 1978; Hori *et al*., 1978). To date, however, valuable results in the case of simple, monosubstituted olefins have been obtained only by working under virtually anhydrous condition. Later, Carlo *et al.* (1983) found that the two-component association consisting of tungstate and phosphate (or arsenate) ions, under acidic conditions, represents a valuable catalytic system for epoxidation of these olefins by very dilute hydrogen peroxide (<10%) according to the technique of phase-transfer catalysis. High selectivities to epoxide (80-90%) on both hydrogen peroxide and olefin at a substantially complete conversion of hydrogen peroxide are usually attained after relatively short reaction times and under mild conditions. It should be pointed out that the unusual reactivity of hydrogen peroxide toward terminal alkenes and, in general, isolated alkenes obtainable by this method is reached only when both tungstate and phosphate ions are present. On the contrary, when used one by one, they show poor or no catalytic activity, respectively. This catalytic association is formed in situ in the reaction mixture by simply introducing a suitable source of its two components. Water-soluble alkaline tungstates, on the one hand, and phosphoric (arsenic) acid or its alkaline salts or mixtures of both, on the other, preferably used in a 1:2 molar ratio, are particularly appropriate for the purpose. The effectiveness of the method here reported appears to be a function of the pH of the aqueous phase. It increases as the pH decreases, and to the extent permitted by stability to hydrolysis of the epoxide formed, low pH values are those of choice.

Afterwards, the epoxidation of alkenes by potassium peroxymonosulphate ($KHSO_5$) in biphasic mixtures of water, a ketone (usually acetone), dichloromethane, and a phase-transfer catalyst have been investigated. The active oxidant in this system is a dioxirane generated by reaction of $KHSO_5$ with the ketone. Without the ketone, low epoxidation occurred. Curci *et al.,* (1980) studied the epoxidation of alkenes by dioxirane intermediates generated in the reaction of potassium peroxymonosulphate with ketones. They found that the $KHSO_5$-acetone system can be employed to epoxidize olefins which are insoluble in aqueous media by using a dichloromethane-buffered water biphasic system under conditions of phase-transfer catalysis. In a typical procedure, a solution of $KHSO_5$ in water is added dropwise to a well-stirred biphasic mixture of dichloromethane and buffered (pH 7.5) water at 6 ^{O}C containing acetone, the alkene, and catalytic amounts of 18-crown-6 or tetrabutylammonium hydrogen sulphate ($Bu_4N^+HSO_4^-$) as phase-transfer catalyst. Reaction time depends upon alkene structure and the amount of the phase-transfer catalyst used. This method provides 80% yields and 97% alkenes conversion when cyclohexene was epoxidized by using $Bu_4N^+HSO_4^-$ as a phase-transfer catalyst. Cicala *et al.* (1982) also considered this system but they studied on stereo- and regioselectivities in the epoxidation of some allylic alcohols by the dioxirane. Since stereo- and regioselectivities epoxidation of allylic alcohols often represent a key step in synthetic routes to naturally occurring substances, they deemed it useful to determine the attainable selectivity in the oxidation of such substrates by using the $KHSO_5$-acetone reagent. Later, Corey and Ward (1986) alse studied the epoxidation of α,β-unsaturated acids using this system.

For direct (background) reaction between $KHSO_5$ and cyclohexene (without ketone) in the dichloromethane/water system, Curci and colleagues (1988,1989) reported that a yield of <0.1% was received after 6 hours. One of the factors causing a very low yield was the stirring rate. Curci and colleagues did not specified the stirring method used in their procedure. A slow stirring rate might explain why their background reaction showed so little product formation after 6 hours. Because the dichloromethane/water system is biphasic, stirring is very important to ensure sufficient contact between the two phases.

A method using aqueous potassium peroxymonosulphate solution to oxidize alkenes into epoxide and diols without phase-transfer catalyst was investigated by Zhu and Ford (1991). Their research screened the epoxidation of several alkenes. They found that cyclohexene cyclooctane and β-methylstyrene can be oxidized into epoxides in high yield and if stirring rate increases, a higher yield will be obtained. However, few kinetic data were provided for two-phase epoxidation reaction. Baumstark *et al.* (1988) reported a second-order rate constants for the epoxidation of di- and monosubstitued alkenes by dioxirane in dried acetone at 23 ^{O}C.

Apart from using ketone as the catalyst for epoxidizing alkenes with $KHSO_5$, other catalysts such as manganese porphyrins and platinum complexes have been investigated. From the reports, using manganese porphyrins and platinum complexes as catalysts in this system is impractical because organometallic complexes decompose rapidly during the epoxidation (e.g. Poorter and Meunier, 1985; Meunier *et al.,* 1987; strukul *et al.,* 1989). Afterwards, Campaci and Campestrini (1999) studied the epoxidation of cyclooctane to cyclooctane epoxide by oxone^R ($2KHSO_5.KHSO_4.K_2SO_4$) for evaluating the catalytic activity of a few manganese hemiporphyrazines. The oxidations were carried out in an anhydrous two-phase system (solid oxone^R/ solid catalyst/ 1,2-dichloroethane solution). The experimental results showed that, at 25 ^{0}C, epoxide yield up to 86% was obtained but the very long reaction time; 211 hours, was required.

In recent year, Connell *et al.* (1996) studied the epoxidation of cyclohexene by dioxiranes over ketone catalyst. The catalytic activity of acetone, butan-2-one and pentan-2-one presented as homogeneous catalysts or supported on inorganic and polymer materials (heterogeneous catalysts) was investigated. They found that using homogeneous catalysts provided yield, turnover frequency and initial rate higher than using supported catalysts.

In addition, Connell *et al.,* (1998) studied the epoxidation of cyclohexene to cyclohexene oxide by dioxiranes in the ketone/oxone system. A monophasic system (tetrahydrofuran/water) was compared with a biphasic system (dichloromethane/ water). The experimental results showed that the yield of cyclohexene oxide for the direct reaction (without ketone) in the tetrahydrofuran/water system was 46.5% after 60 min. This was very high compared with the dichloromethane/water system (8.4% after 60 min). In addition, it showed that the cyclohexene was in better contact with $KHSO_5$ in the tetrahydrofuran/water system than dichloromethane/water system. In contrast, when using ketone as the catalyst, the yield of cyclohexene oxide in the biphasic system was higher than in the monophasic system. Because in the biphasic system, the product is extracted into the second liquid phase, the equilibrium limitation is overcome and a higher selectivity to the epoxide product is obtained. Moreover, it was found that the rate of cyclohexene oxide formation increased in proportion to increasing ketone concentration using 1,1,1-trifluoroacetone, acetone and butan-2-one. The greater the solubility of a ketone in water the greater its catalytic activity. In dichloromethane/water system, the yield of cyclohexene oxide was 91% after 60 min at 25 ^{0}C, using acetone 27 mmol as catalyst, while in the same condition, the yield of cyclohexe oxide in the tetrahydrofuran/water system was only 67%.

2.3 Phase Transfer Catalysis (PTC)

PTC has brought in a major change in the processes for the manufacture of fine chemicals (Freeman, 1986; Starks, 1987). For instance, use of scrupulously moisture free conditions and catalysis by sodium alkoxide has been replaced by allowing 40-50% NaOH to be used thereby bringing considerable ease of conducting reactions and reducing cost of chemicals. Many reactions which are not possible or take an unusually long time have been made possible through PTC; even steric hindrance has been overcome (e.g. methylation of 2-*tert*-butyl phenol/2,6-di-*tert*-butyl phenol). Here, quaternary ammonium compounds like trioctylmethylammonium chloride, benzyltriethyammonium chloride, tetrabutylammonium hydrogen sulphate, etc. or the corresponding phosphonium compounds, are used which allow ionic species to be transferred from aqueous to the organic phase where the reaction occurs neatly and quantitatively. Multisite catalysts have also been developed. Higher selectivity, easier processing, use of inexpensive solvents, use of cheaper chemicals and ease of heat removal have been realised through PTC. It appears that no catalytic method has made such an impact as PTC on the manufacture of fine chemicals. Indeed, in the manufacture of synthetic pyrethroids like fenvalreate, cypermethrin etc., PTC is used very extensively. Some speciality polymers are made through the use of PTC (Starks, 1987).

Most of the applications have been for relatively slow reactions. However, Sharma and co-workers have shown that for a number of reaction, such as alkaline hydrolysis of sparingly soluble esters, reaction of $POCl_3$/RCOCl with substituted phenols, where mass transfer is accompanied by a fast reaction in the diffusion film, PTC can be advantageously employed (Lele *et al*., 1983; Krishnakumar and Sharma, 1983). In the case of triarylphosphates, an elegant, room temperature process has been developed using cheap solvents like toluene; it is desirable to use the organic phase as the continuous phase as it becomes very viscous. Recently, Talley and Berman (1987) utilized the above strategy of Krishnakumar and Sharma to make the corresponding phosphorothionates based on the reaction of $PSCl_3$. Here, the conventional process based on the reaction of $PSCl_3$ with the corresponding phenolic substance at higher temperature did not work. The kinetics of reaction between $POCl_3$ and sodium salt of phenolic substances to make triarylphosphates show some interesting features of mass transfer with chemical reaction (Krishnakumar and Sharma, 1985). Lele *et al.* (1983) and Krishnakumar and Sharma (1984, 1985) discussed some quantitative aspects of fast reactions occuring in the diffusion film.

The transfer of species other than anions, such as metal ions, diazonium ions, NO_2^+ and formally non-charged species like H_2O_2, N_2H_4 has been successfully accomplished. In addition, Friedel-Cracts reactions have been catalysted. Even metal atoms as crown complexes can be transferred with crown ethers or with anthrancene. The interesting applications have been in epoxidation of difficult olefin compounds (including hexafluoropropene) with NaOCl, side chain chlorination of substituted toluenes, diazotization of pentafluoroaniline, polymerization with free radicals, etc.

Catalytic hydrogenations, oxidations and carbonylations, with H_2, O_2 and CO, respectively, of a variety of substances, in gas-liquid-liquid systems, have been successfully realised through PTC (Starks, 1987).

PTC has been found to be very useful in solid-liquid reactions, including the classical case of the reaction between benzyl chloride and sodium acetate/bezoate, and here the kinetics of the reaction may become sensitive to small amounts of water that may be present in the system (Yadav and Sharma, 1981). In the recent years, the existence of a new phase arising out of the addition of a small amount of water, referred to as omega phase, which can make considerable difference to the rates of reaction, has been stressed.

PTC may well provide a way of recovering valuable chemicals from the waste streams of fine chemicals plants. Krishnakumar and Sharma (1984) have shown how phenolic substances from aqueous alkaline streams can be recovered as useful, saleable substances and their content brought down to below 5 ppm in the waste streams. Even penicillin from waste liquors discharged from fermentation plants can be recovered (Linblom and Elander, 1980).

Chiral PTC has been used effectively for making intermediates for drugs. Dolling and co-workers have used 8-R, 9-S, N-(P-trifluoromethylbenzyl) cinchonium bromide to carry out and important asymmetric alkylation, giving 95% ee (Starks, 1987). We can expect further bread-throughs in this important area of organic synthesis for fine chemicals. Freeman (1986) has given many examples of relevance.

Lindblom and Elander (1980) have given a number of examples of relevance in the pharmaceutical industry which include C-alkylations and N-alkylations. The C-alkylations of phenylacetonitrile (mono- and di-), alkylation of benzylpenicillin with α-chlorodiethyl carbonate (where the acid part and the halide part in the esterification would have degraded quickly under normal conditions adopted for the reaction), N-alkylation of purines and adenine, etc. are discussed at some length and the supremacy of PTC is clearly shown.

One of the limiting factors has been the lack of stability of phase transfer catalysts at high temperatures, particularly under highly basic conditions. For this purpose, relatively cheap polyethylene glycols (of molecular weights 400 and 600) have proved very useful in some cases. These are stable at much higher temperatures upto 200 ^{O}C or so. A catalyst, Trident, TDA-N(CH_2CH_2O-$CH_2CH_2OCH_3$)$_3$ has been commercially introduced which is effective for aromatic substitutions upto 130 ^{O}C and also give a synergestic effect in the Ullmann reaction of haloaromatics with phenols in the presence of copper catalysts. The dimethyl-aminopyridinium quaternaries have also been introduced which are good for aromatic nucleophilic displacements and are 100 times more effective than tetrabutylammonium bromide and can function upto 200 ^{O}C (Starks, 1987). The utility of this type of catalyst has been tested for speciality engineering plastics like polysulphones. PTC is already used in making polycarbonates; even sterically hindered bisphenol-2,2-bis(4-hydroxy-3, 5-dimethylphenyl) propane has been successfully converted to polycarbonates.

The problem of recovering catalysts merits further attention. The strategy of using solid supported PTC did not so far, seem to be commercially successful, either due to reduced activity and/or due to poor life. It would be useful to examine solubility of catalysts in different solvents for recovering them through extraction; the possibilities of manipulating variations in solubility with temperature should also be explored. In the case of catalysts like PEG and reactions involving 40-50% NaOH, three liquid phases may be encountered and this should facilitate the recovery of catalysts; kinetics of such reaction systems deserve to be studied.

Fife and Xin (1987) have brought out the role of inverse PTC where substances like 4-dimethylaminopyridine, 4-pyrrolidinopyridine, etc. are used and an organic reactant like RCOCl is transferred to the aqueous phase. This subject merits further attention. Particularly due to possibilities of realizing higher selectivity.

There is a lot of scope, apart from designing new, cheap and stable high temperature resistant, benign catalysts, for bringing out the role of PTC in slow and fast reactions, a rational basis for selection of solvents, predicting equilibria, assessing rate constants in the organic phase, etc. The manipulation of selectivity also merits attention. The use of PTC in chiral synthesis is expected to expand.

CHAPTER III

THEORY

This chapter provides some useful theories which are essential for understanding the extractive reaction process. The chapter is divided into 4 sections; i.e. liquid-liquid extraction, extractive reaction, epoxidation reaction and phase transfer catalysis. Details are as follows.

3.1 Liquid-Liquid Extraction (Alders, 1955)

In liquid-liquid extraction, a liquid feed of two or more components to be separated is contacted with a second liquid phase, called solvent, which is immiscible or only partly miscible with one or more components of the liquid feed and completely or partially miscible with one or more of the other components of the liquid feed. Thus, the solvent, which is a single chemical species or a mixture, partially dissolves certain components of the liquid feed, affecting at least a partial separation of the feed. Liquid-liquid extraction is sometimes called extraction. Solvent extraction, or liquid extraction.

Liquid-liquid extraction may be presented by a three-component system forming two liquid phases. The solvent and the feed are two essentially immiscible liquids with possible mutual solubility. The extract component, to be extracted from the feed by the solvent, is soluble in both phases.

The basic extraction process is presented in Figure 3.1. The extract is the solvent-rich phase that gets enriched in the extract component and the raffinate is the feed phase that gets depleted in the extract component. If the solvent is lighter than the feed, it must be introduced at the column bottom.

Unlike absorption or stripping, extraction does not involve vaporization or condensation or the heat that accompanies these processes. For this reason extraction is nearly an isothermal process although some temperature variation could occur as a result of heat of solution.

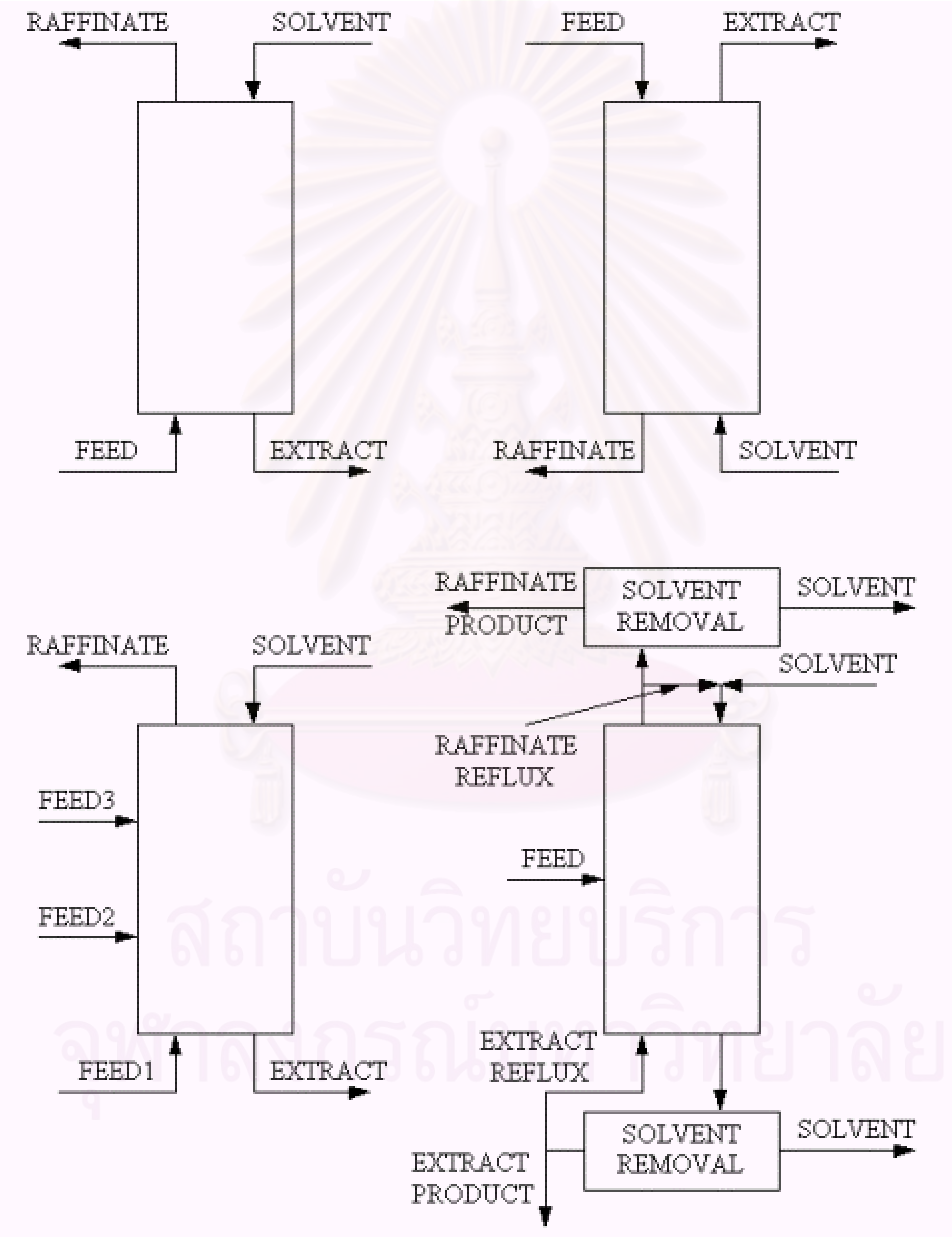


Figure 3.1 Schematics of liquid-liquid extractors.

The simplest liquid-liquid extraction involves only a ternary system. The liquid-liquid equilibrium relationships are best represented graphically on a triangular diagram. Various types of ternary liquid-liquid phase diagram were shown in Figure 3.2.

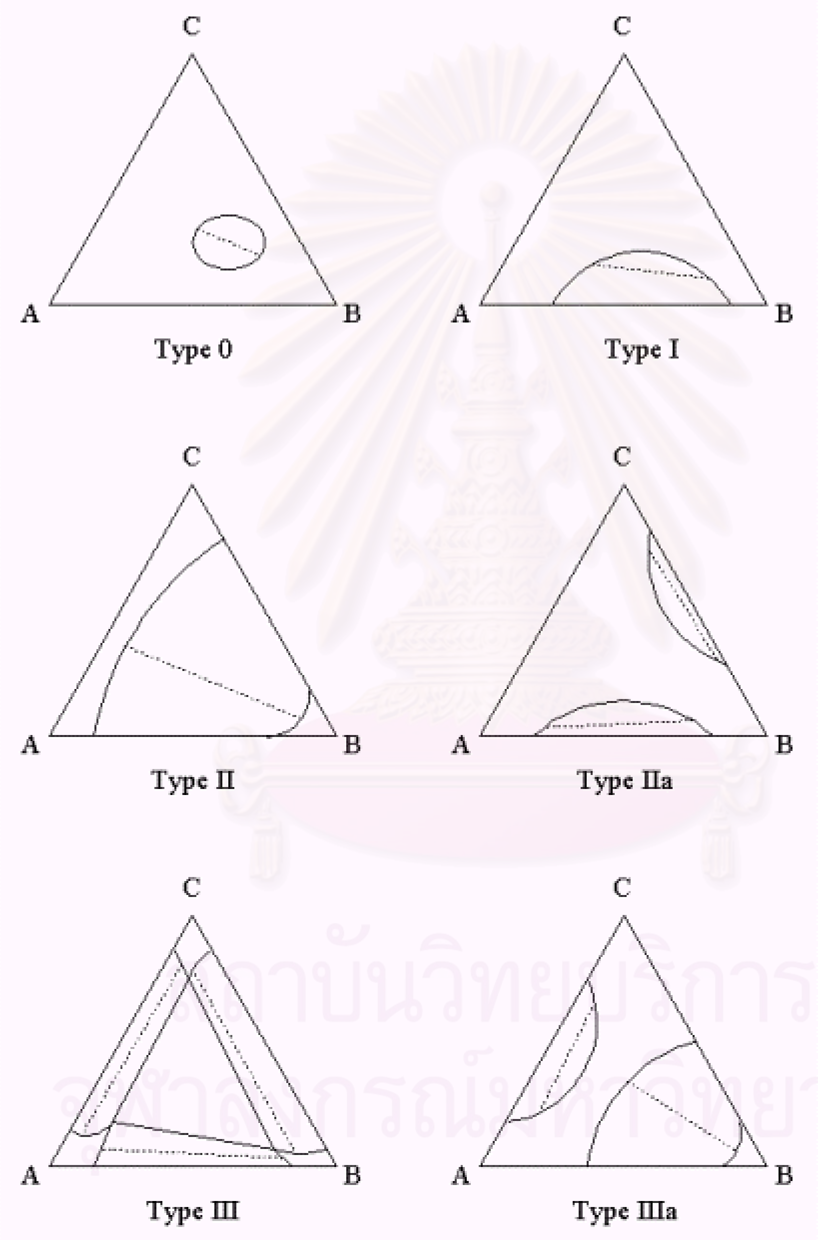


Figure 3.2 Types of ternary liquid-liquid equilibria.

The general shape of the equilibrium curve or curves depends on the mutual solubilities of the components in the ternary. In many extraction processes, there is total miscibility between the extract component and each of the other components and partial miscibility between the solvent and the raffinate. A ternary having these characteristics is represented on an equilateral triangle in Figure 3.3, where E is the extract component, R the raffinate, and S the solvent. Each of binaries, ER and ES, forms a single liquid phase at all compositions while binary RS forms two liquid phases between compositions represented by points A and B and a single phase outside this composition range. The ternary mixture forms two liquid phases under curve APB and a single liquid phase outside the curve.

The tie lines shown in Figure 3.3 represent liquid compositions at equilibrium with each other. Thus, point M represents the combined composition of a mixture that separates in to two liquid phases at equilibrium with compositions represented by points L and Q. The compositions of the two phases approach each other as the tie lines become shorter. At point P, the plait point, the tie line vanishes and the liquid compositions become identical, forming a single phase.

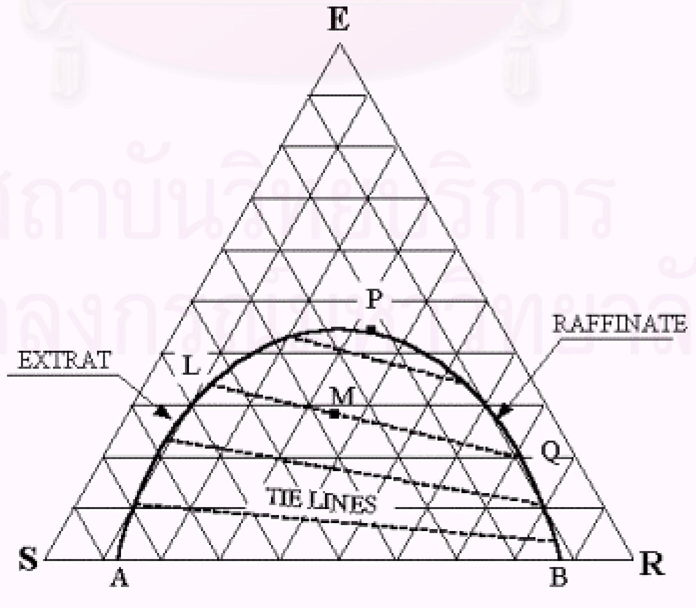


Figure 3.3 Liquid-Liquid equilibrium for a ternary system.

3.2 Extractive Reaction (Samant and Ng 1998).

In an extractive reaction, a reaction and extraction occur simultaneously. A second liquid phase containing a solvent can be deliberately imposed on the system. Frequently, the solvent selectively extracts an intermediate or a product, thereby preventing its further reaction and resulting in a higher yield.

This section presents a systematic procedure based on equilibrium thermodynamic analysis for the synthesis of extractive reaction processes such as the liquid-liquid phase diagrams for the examples involving liquid-liquid phase separation and chemical reaction. Several examples of extractive reaction processes for improvement in yield, selectivity to a desired product and separation of impurities are presented. These examples demonstrate the advantages of extractive reaction processes over conventional single-phase processes.

3.2.1 Examples of liquid-liquid phase diagrams with reaction

Type I System with One Reaction. Consider a system that is composed of components *A*, *B*, and *C* with the following reaction:

$$A \longleftrightarrow B \tag{3.1}$$

Where *C* is partially miscible with *A*. Figure 3.4 shows the phase diagram for this system with *K*=1.0. Curve *aPb* is the phase envelope, point *P* being the plait point. Point *b* lies extremely close to pure component vertex *C*. Curve *cC* is the reaction equilibrium curve. The dashes are the tie lies and the arrows are the lines of constant stoichiometry. For *K*=1.0, the reaction equilibrium curve and the phase envelope do not intersect. Thus, the system is always in single phase at equilibrium. Given an initial composition, the equilibrium composition of the system corresponds to the point of intersection of the stoichiometric line through the initial composition and the curve *cC*.

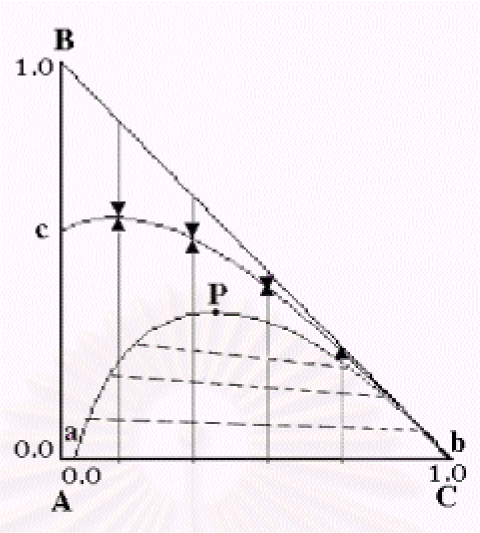


Figure 3.4 Phase diagrams for A↔B (K=1.0) in the presence of an inert C.

Figure 3.5 is the phase diagram for the same system with *K*=0.35. In this case, the reaction equilibrium curve *cC* and the phase envelope *aPb* intersect at point *d* and *e*. The shaded region bounded by the stoichiometric lines through point *d* and *e* forms the two-phase region of the phase diagram. If the initial composition of the system lies in this region, at equilibrium the system would split into two phases with compositions corresponding to points *d* and *e*. Line de is the unique reactive tie line for the system. Outside the shaded region, the system is always in single phase and the equilibrium compositions lie on sections *cd* and *eC* of the curve *cC*.

Type II System with One Reaction. Consider a system of components *A, B,* and *C* with the following reaction:

$$A + B \longleftrightarrow C \tag{3.2}$$

Where *C* is partially miscible with both *A* and *B*. Figure 3.6 is the phase diagram for this system with *K*=10.0. Curve *ab* and *cd* are the phase-equilibrium curves and curve *BefhgA* is the reaction-equilibrium curve. The dashes are the tie lines and the arrows are the stoichiometric lines. Points *e, f, h*, and *g* are the points of intersection of the phase and reaction equilibrium curves. Thus, it has two reactive tie lines *ef* and *gh*.

Stoichiometric lines through the end points of these tie lines form two separate two-phase regions (shaded) for this system. Within these regions, the system splits into two phases corresponding to the end point of the reactive tie line in that region. Out side these regions, the system is always in single phase and the equilibrium compositions would lie on sections *Be, fh,* or *gA* of the equilibrium curve.

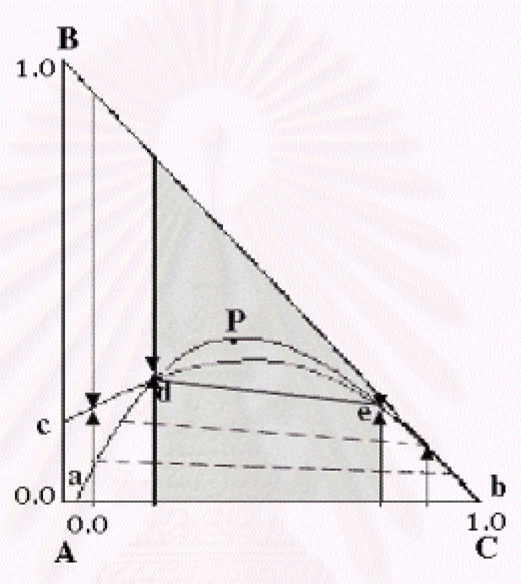


Figure 3.5 Phase diagrams for $A \leftrightarrow B$ (K=0.35) in the presence of an inert C.

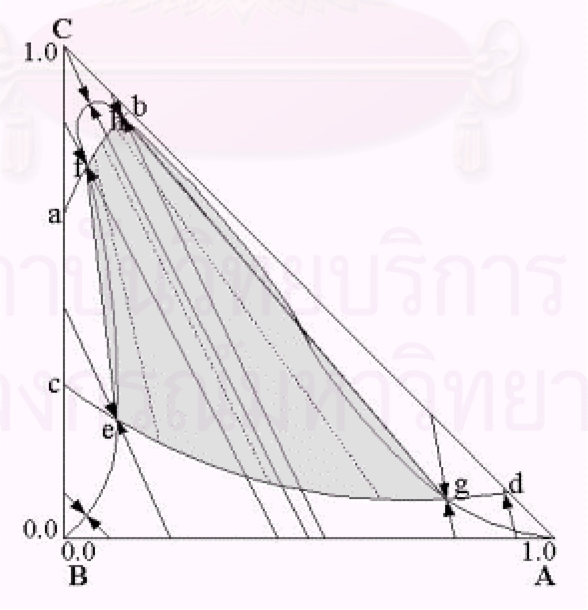


Figure 3.6 Phase diagram for $A+B \leftrightarrow C$ (K=10.0).

3.2.2 Processes for improvement in yield

Extractive reaction process can be synthesized for improving the yield of a desired product, defined as

$$\text{Yield} = \frac{\text{Amount of desired product produced}}{\text{Amount of reactant fed to the reactor}}\quad , \qquad (3.3)$$

The yield as defined here is the per-pass yield. The overall yield from both the single-phase and the extractive reaction processes will always be 100% if all the unconverted reactants are recycled without any loss. Low per-pass yield from a single-phase process implies large loads on the separation system and large recycle flows. Using an extractive reaction we increase the per-pass yield considerably, thus decreasing the recycle of unconverted reactants. But extractive reaction processes also involve recovery and recycle of an inert solvent. However, a judicious choice of solvent can keep this recycle flow low, Improvement in per-pass yield becomes especially significant when reactants are loss through purge or waste streams, as is usually the case with many industrial processes.

Example 1: Use of Solvent to Extract the Desired Product. Consider a system with reaction:

$$A \longleftrightarrow B \qquad (3.4)$$

Solvent *S* is completely miscible with *B* but partially miscible with *A*. Yield of the desired product can be substantially improved by employing a solvent that is completely miscible with it and partially miscible with other reactants and products. In this case, extraction of the desired product into the solvent-rich phase pushes the reaction equilibrium to the right, thus increasing the yield.

Example II: Use of Solvent Miscible with Reactants and Products. Consider the following system where *B* is the desired product:

$$A \longleftrightarrow B \qquad (3.5)$$

Reactant *A* and product *B* are partially miscible. Solvent *S* is completely miscible with *A* and *B*. When phase separation already exists in the reaction mixture, at appropriate temperature and equilibrium constant value, yield of a desired product can be improved by the addition of a solvent completely miscible with the reactants and product.

Example III: Use of Solvent partially Miscible with the Desired Product. Consider a reaction:

$$A \longleftrightarrow B + C \qquad (3.6)$$

Solvent *S* is completely miscible with *A* and *C*, but partially miscible with the desired product *B*. For multiproduct reactions, the yield of the desired product can be increased by using solvent partially miscible with it and completely miscible with other reactants and products.

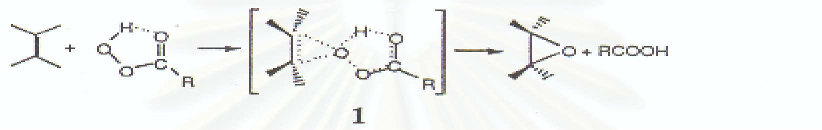
For series reactions, parallel reactions and series-paralled reactions, multiproduct reactions, the yield and product distribution can be improved using solvent partially miscible with desired product and completely miscible with other reactants and product too.

3.3 Epoxidation reaction

3.3.1 Direct Oxidation with Stoichiometric Oxidants (Georgea, 1995)

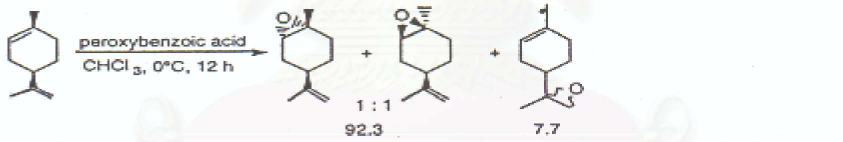
Discovered by Prileshajew in 1990, the typical epoxidation reaction of alkenes is their oxidation with organic peracids. Of the large number of different peroxycarboxylic acids used in epoxidation, commercially available m-chloroperbenzoic acid (m-CPBA) is the most favored, but the water-soluble and more stable magnesium monoperoxyphthalate gained more widespread application recently. Aliphatic peracids (peroxyformic, peroxyacetic, peroxytrifluoroacetic acid) generated mostly in situ are used preferentially in large scale syntheses.

A simple generally accepted mechanism known as the "butterfly" mechanism first suggested by Lynch and Pausacker (1955) involves the nearly nonpolar cyclic transition state **1** [Eq. (3.7)]. It is formed as a result of the nucleophilic attack on the monomeric, intramolecularly hydrogen-bonded peracid by the π electrons of the alkene double bond.



(3.7)

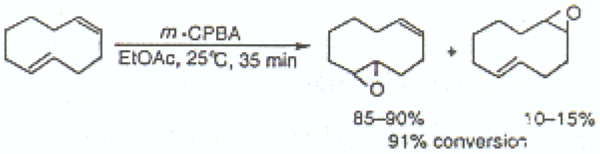
In support of this mechanism are the higher reactivity of peracids possessing electron-withdrawing groups, and that of alkenes with more nucleophilic (more substituted) double bonds permitting regioselective oxidation of dienes [Eq. (3.8)]. Also in accord with the mechanism is the increasing reaction rate with increasing dielectric constant of the solvent and the complete *syn* stereoselectivity.



(3.8)

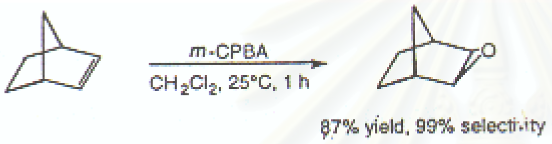
A closely related 1,3-dipolar cycloaddition mechanism with an 1,2-dioxolane intermediate could not be experimentally proven. Further studies concerning details of the mechanism including molecular orbital calculations and solvent effects have been carried out leading, among others, to the suggestion of the formation of a nonsymmetric transition state and an electron donor-acceptor complex.

The more energetic *cis* double in acyclic alkenes is epoxidized faster than the *trans* double bond. In contras, opposite reactivity is observed for the stereoisomers of cycloalkenes, with the *trans* isomers being more reactive as a result of higher ring strain. This was demonstrated in the selective monoepoxidation of *cis,trans*-1,5-cyclodecadiene [Eq.(3.9)]. The lack of formation of transannular addition products was taken as evidence of the single-step formation of a transition state with little or no ionic character.

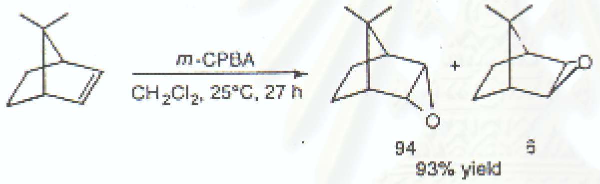


(3.9)

Since peroxy acids have a relatively low steric requirement, steric hindrance arises mainly in the epoxidation of bridged cycloalkenes. Marked difference in *exo/endo* selectivity was observed in the reaction of norbornene and 7,7-dimethylnorbornene with m-CPBA (Brown *et al.,* 1970) [Eq. (3.10) and (3.11)]. In competitive epo-xidation norbornene reacts at a rate approximately 100 times that of and 7,7-dimethylnorbornene.



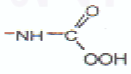
(3.10)



(3.11)

Besides peracids, other carboxylic acid derivatives such as peroxy-carboximidic acids (**2**), peroxycarbamoic acids (**3**), and peroxycarbonic acids (**4**) also gained importance. Usually prepared in situ in the reaction of the corresponding acid derivatives with hydrogen peroxide [Eq. (3.12)], they all the common general formula **5**, and contain the HOO-moiety in conjugation with a double bond. They decompose with ease to transfer oxygen to the double bond. α-Hydroperoxy ethers, amines, ketones, acids, and acid derivatives with the general formula **6** have properties comparable to those of organic peracids.

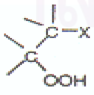
2



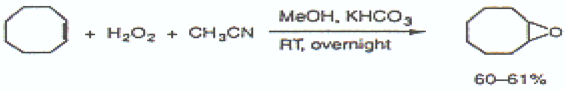
3

4

5



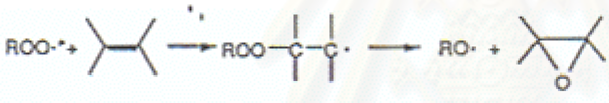
6



(3.12)

Further useful stoichiometric oxidizing agents include metal-peroxo complexes of Mo(VI) and W(VI), and high-valent metal-oxo compounds. $CrO_2(NO_3)_2$ in aprotic solvents with a basic cosolvent may yield epoxides with high selectivity. The actual oxidizing agent was found to be an oxochromium(V) compound formed by one-electron oxidation of solvent. Molybdenum(VI)-oxoperoxo complexes $MoO(O_2)_2L$ are more selective oxidizing agents. Epoxidation with these reagents proceeds via reversible complexation of the metal followed by irreversible oxygen transfer to the alkene or through direct oxygen transfer to the noncoordinated olefin. An analogous W(VI) complex and polymolybdateperxo and polytungstate-peroxo compounds exhibit higher activity.

Direct oxidation of alkenes with molecular oxygen initiated by free radicals to yield epoxides occurs through addition of peroxy radicals to produce the more stable β-peroxy alkyl radicals (7) [Eq.(3.13)]. The latter are known to cyclize rather readily to give epoxides and alkoxy radicals.

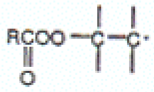


7

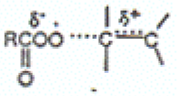
(3.13)

Maximum yield of epoxides can be expected with molecules, first 1,1-dimethylalkenes, which prefer addition to abstraction (allyl hydrogen removal). These oxidations are not stereoselective; mixtures of the isomeric oxiranes are formed in the reaction of isomeric n-octenes. This was interpreted as a additional evidence of the formation of radical intermediate **7** allowing the rotation about the carbon-carbon bond.

In cooxidation of alkenes and aldehydes, and in photosensitized epoxidations, acylperoxy radicals are the epoxidizing agents. The mechanism of the former oxidation, on the basis of kinetic measurements and the nonstereospecificity of the reaction, involves alkylperoxy radicals formed through the σ-bonded radecal **8** as the intermediate.

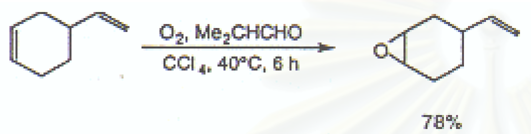


8



9

In contrast to the preceding observations, stereoselecitve epoxidation has been described recently. Internal olefins reacting with a stoichiometric amount of pivalaldehyde yield quantitatively the corresponding epoxides. The higher reactivity of the internal double boud permits selective epoxidation of dienes [Eq(3.14)]. The stereoselective nature of the reaction supports the suggestion that epoxidation in this case does not occur by acylperoxy radicals but rather by peracids generated from autoxidation of aldehydes.



(3.14)

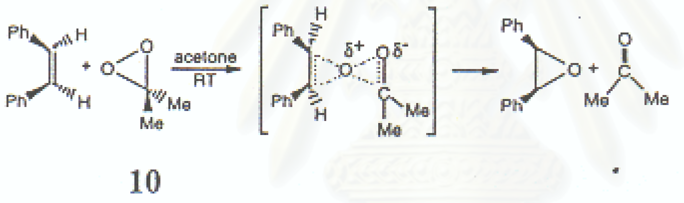
Photoepoxidation of alkenes with oxygen in the presence of photosensitizers can be used as a synthetic method. The complete absence of any nucleophile in the reaction mixture prevents secondary transformations of the fromed oxirane and thus allows the perparation of sensitive epoxides.

The acylperoxy radical was found to epoxidize olefins much faster than peracids also formed under reaction conditions. The result ruled out the role of the latter. The addition of RCO_3* was observed to occur 10^5 faster than that of ROO*. The relative reactivity of alkenes suggests a strongly electrophilic radical forming the polar transition state 9. The rotation about the carbon-carbon bond in intermediate is fast compared to cyclization. As a result isomeric alkenes are transformed to oxirances of the same, predominantly trans stereochemistry. A practical process for the epoxidation of a wide range of alkenes was described in the presence of biacetyl as sensitizer to yield epoxides in about 90% yield.

A recent detailed study on the reaction of 2,3-dimethl-2-butene with ozone revealed that epoxide formation strongly depends on alkene concentration and temperature. Under appropriate reaction conditions (neat alkene, 0 ^{O}C) the corresponding tetramethyloxirane was the main product. Dimetheldioxirane formed from energy-rich acetone oxide (a cleavage product of the alkene) was postulated to be responsible for epoxidation.

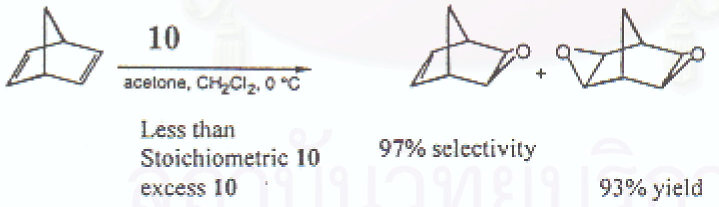
3.3.2 Epoxidation of alkenes with dioxiranes (Curci *et al.,* 1980)

Several new powerful oxidizing agents have recently been discovered and used in alkene epoxidation. Dioxiranes [dimethyldioxirane (**10**), methyl(trifluoromethy)dioxirane] react readily with alkenes to give epoxides in high yields. Compound dimethyldioxirane was first generated in situ from potassium peroxymonosulphate and acetone and was used as such. The rate of oxidation of *cis* dialkylalkenes with dimethyldioxirane was found to be 10 times higher than that of the corresponding *trans* isomers. In contrast, aryl-substituted alkene isomers exhibited similar reactivity. These observations and the exclusive retention of configuration demonstrated for both cis-stilbene [Eq.(3.15)] and trans-stilbene testify an electrophilic O transfer and the butterfly transition state analogous to epoxidation with percids.



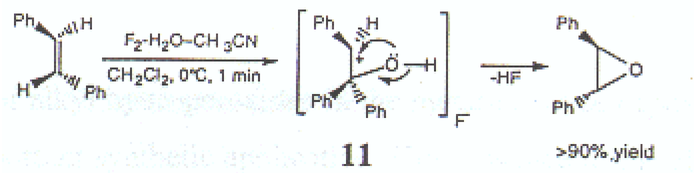
(3.15)

The mild neutral reaction conditions permit the transformation of alkenes to sensitive spiroepoxides and norbornadiene to exo-monoepoxide or exo,exo-diepoxide.



(3.16)

The relatively stable complex HOF.CH_3CN generated in the reaction of F_2 with water and CH_3CN can epoxidize various alkenes quickly and efficiently. Because of the partial positive charge on oxygen generated by the strongly electronegative fluorine, HOF is a strongly electrophilic reagent. This fact and the very high recation rate and the full retention of configuration [Eq. (3.17)] suggest a fast two-step process involving formation of the highly unstable β-oxacarbocation **11**.



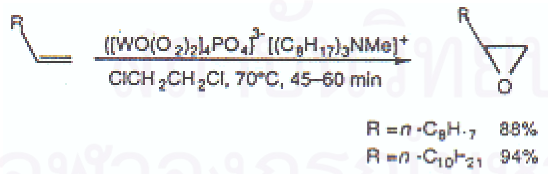
(3.17)

3.3.2 Metal-Catalyzed Epoxidation (Ogata and Sawaki , 1986).

Hydrogen peroxide is able to convert alkenes to epoxides in the presence of metal catalysts. Several metal oxides (MoO_3, WO_3, SeO_2, V_2O_5) are know to catalyze such epoxidations. All these catalysts from stable inorganic peracids, and these peracids are supposedly involved in epoxidation in a process similar to organic peracids.

Tunsten (VI) complexes are among the best transition-metal catalysts for epoxidation with H_2O_2. Pertungstenic acid and pertungstati, which are highly stable in aqueous solution, decompose slowly, permitting selective epoxidation under mild condetions. Epoxidations under phase-transfer conditions were found to give the best results.

The use of heteropoly acids such as $H_3PM_{12}O_{40}$ [M=Mo(VI), W(VI)] with dilute H_2O_2 is of increasing interest in selective synthesis of epoxides. Reactions with phase-transfer catalysis again proved to be efficient and synthetically valuable. Even the least reactive simple terminal alkenes are converted under mild conditions, in short reaction time to epoxides in high yields.



(3.18)

The preceding reactions, however, have the disadvantage that H_2O_2 is usually employed in aqueous solution. It is know that water seriously retards epoxidation, and it may further transform the product epoxides to the corresponding 1,2-diols. This often results in low selectivity, which is the main reason why these reactions do not have the same broad synthetic utility as epoxidations with alkyl hydroperoxides.

The use of alkyl hydroperoxides in the metal-catalyzed epoxidation of alkenes is their most important synthetic application. High-valence d^0 metals such as Mo(VI), W(VI), V(V), and Ti(IV) are the most effective catalysts. Used as soluble complexes or as heterohnized supported catalysts, they can give epoxides in near-quantitative yields.

tert-Butyl hydroperoxide, the most stable, commercially available alkyl hydroperoxide, is used most frequently. A key question to ensure high selectivity in epoxidation with the ROOH-transition-metal systems is to avoid homolytic cleavage of the hydroperoxide since this may lead to nonstereoselective epoxidation and allylic oxidation. Arylalkyl hydroperoxides (ethylbenzene hydroperoxide and cumene hydroperoxide) with increased electrophilicity satisfy this requirement and are used accordingly.

Comparative studies concerning the activity of different metal catalyst in epoxidation of cyclohexene led to the findings that metals in the highest oxidation state with strong Lewis acidity and poor oxidizing ability exhibit good catalytic activity and high selectivity in epoxidation. Mo(VI) and W(VI) meet these requirements best [Eq. (3.19)]. V(V), a better oxidant, exhibits low selectivity in the oxidation of simple nonsubstituted alkene and is used mainly in the epoxidation of unsaturated alcohols, just as Ti(IV).

(3.19)

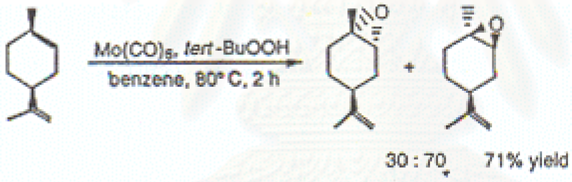
	time (h)	% conversion	% yield
$Mo(CO)_6$	2	98	94
$W(CO)_6$	18	95	89
$VO(acac)_2$	2.5	96	13
Ti(O *n*-Bu)$_4$	20	80	66

The best of these catalysts are soluble molybdenum(VI) complexes, of which $Mo(CO)_6$ and $MoO_2(acac)_2$ are the most frequently used, and most thoroughly tested and characterized. Different molybdenum complexes catalyze the epoxidation of a wide variety of alkenes in nonpolar solvents (benzene, polychlorinated hydrocarbons), at moderate temperature (80-120 °C). Of the simplest alkenes, ethylene can be transformed with *tert*-BuOOH + MoO_2(8-hydroxyquinoline)$_2$ to ethylene oxide in high yield, and propylene oxide is currently manufactured on a large scale by Mo-catalyzed epoxidation . Many different heterogeneous molybdenum catalysts have been used in epoxidations. The ROOH-transition metal reagents display regularities very similar to those in epoxidation with organic allow selective monoepoxidation of dienes.

(3.19)

	time (h)	% conversion	% yield
$Mo(CO)_6$	2	98	94
$W(CO)_6$	18	95	89
$VO(acac)_2$	2.5	96	13
$Ti(O\ n\text{-}Bu)_4$	20	80	66

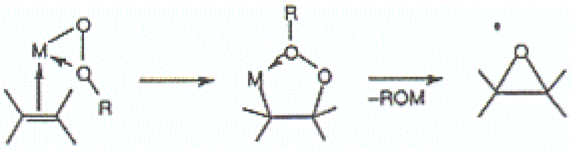
Similar differences in the reactivity of *cis* and *trans* alkenes (higher reactivity of *cis* compounds), and similar regio- and stereoselectivities are observed in both systems, but slight differences may occur [Eq. (3.21)]. One important advantage of the use of ROOH-transition-metal reagents over the traditional organic peracids is that they are particularly useful in the synthesis of acid-sensitive epoxides.



(3.21)

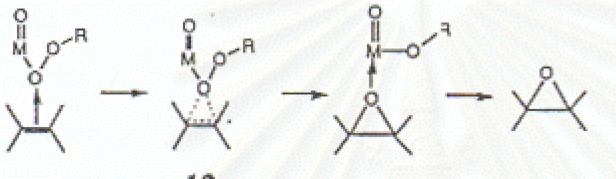
Mechanistic investigations concerning the Mo(VI)-catalyzed epoxidations with alkyl peroxides as oxidants point to the similarities to the V(V)- and Ti(VI)-catalyzed processes. Of the numerous suggestions, two mechanisms are consistent with most experimental observations.

Mimoun (1980) proposed a mechanism that is general for both stoichiometric epoxidations with peroxo complexes and for catalytic systems employing alkyl hydroperoxides. It involves an alkylperoxide species with the alkene complexed through the metal [Eq. (3.22)]. Insertion to the metal-oxygen bond produces a peroxometallacycle, which decomposes to give the product epoxide and metal alkoxide.



(3.22)

According to the other mechanism, the intact alkyl hydroperoxide or alkyl hydroperoxidic species activated by coordination to the metal through the oxygen distal to the alkyl group is involved in the epoxidation step [Eq. (3.23)]. The epoxide is produced via the transition state **12** resembling that suggested for epoxidation by peroxomolybdenum reagents and by organic peroxides. The initially formed epoxide is coordicated to the metal. Complexation of the alkene in different orientations to the metal, followed by coordination to the peroxide oxygen, was suggested on the basis of frontier orbitals.

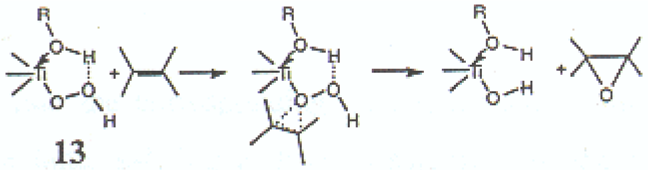


12

(3.23)

Nonstereospecific aerobic epoxidations of alkenes in the presence of aldehydes catalyzed by nickel(II), iron(III), and cobalt(II) complexes, and clay-supported nickel acetylacetonate have recently been reported. A radical mechanism has been postulated. The involvement of active copper species and peracids were suggested in a similar reaction catalyzed by copper salts.

A unique titanium(IV)-silica catalyst prepared by impregnating silica with $TiCl_4$ or organotitanium compounds exhibits excellent properties with selectivities comparable to the best homogeneous molybdenum catalysts. The new zeolite-like catalyst titanium silicalite (TS-1) featuring isomorphous substitution of Si(IV) with Ti(IV) is a very efficient heterogeneous catalyst for selective oxidations with H_2O_2. It exhibits remarkable activities and selectivities in epoxidation of simple olefins. Propylene, for instance, was epoxidized with 97% selectivity at 90% conversion at 40°C. Shape-selective epoxidation of 1- and 2-hexenes was observed with this system that failed to catalyze the transformation of cyclohexene. Surface peroxotitanate is suggested to be the active species. It forms a complex with the alkene to undergo an intramolecular oxygen transfer to the C-C double bond. A different, heterolytic peracid-like mechanism was suggested for protic solvents with the participation of **13** as the active species.



13

(3.24)

3.4 Phase transfer catalysis (Wang, 1997).

The reaction problem of two immiscible reactants was not solved until Jarrous found that the reaction was enhanced by adding a small catalytic quantity of a quaternary salt. The application of a quaternary salt as a phase transfer catalyst in two-phase reactions to synthesize specialty chemicals has since been extensive studied by many chemists. Today, phase transfer catalysis (PTC) is considered to be one of the most effective tools in synthesizing organic chemicals from two immiscible reactants. The greatest advantages of synthesizing organic chemicals by PTC are acceleration of the reaction rate even at a moderate operating temperature, a high conversion of reactant to the product and high selectivity.

Two-phase transfer catalysis mechanism

The most widely accepted two-phase reaction mechanism by phase transfer catalysis is that in which an aqueous reactant reacts with a quaternary salt to produce an organic-soluble quaternary organic salt (called the active catalyst). Then, the quaternary organic salt (active catalyst) further reacts with the organic reactant to form the desired product in the organic phase. The quaternary salt, produced from the organic phase reaction, will then transfer to the aqueous phase to obtain further regeneration. Thus, the complicated nature of the system stems from the two mass-transfer steps and the two reaction steps in the organic and aqueous phases as well as the equilibrium partitions of the catalysts between the two phases.

Example: Synthesis of phenol ether. As applied to the alkylation of phenols, the process can be represented by reaction (3.25) ($Q^+ = R_4N^+$). In practice, the phenol is added to a two-phase system consisting of an aqueous solution of the quaternary ammonium hydroxide and a methylene chloride solution of the alkylating agent. The phenol, which in most cases is partitioned naturally between the two phases, is converted into the corresponding quaternary ammonium phenoxide in the aqueous phase. The latter salt has a discrete solubility in the organic phase; consequently, transport of the phenoxide ion into the organic solvent solution is followed by rapid irreversible alkylation and formation the phenol ether.

CHAPTER IV

EXPERIMENT

The epoxidation of cyclohexene to cyclohexene oxide was carried out in a batch reactor. The pH of the reaction was maintained at a constant value with diviation less than 0.01 pH unit. A Radiometer Copenhagen pH stat fitted with a recorder showed base addition as a function of time. The schematic diagram of the experimental set up was given in Figure 4.1.

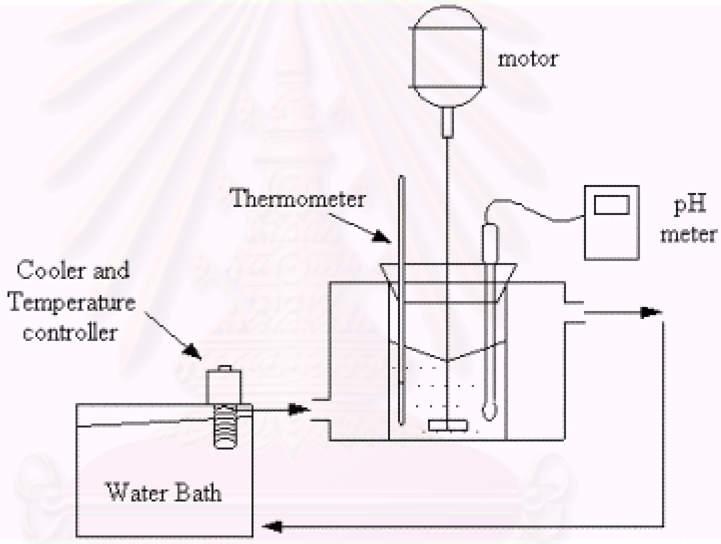


Figure 4.1 Schematic diagram of the experimental set up.

4.1 Procedure

Oxone, $2KHSO_5.KHSO_4.K_2SO_4$ (3.69 g, 11.18 mmol $KHSO_5$), was placed in the reaction vessel. Na_2EDTA (0.1 g, 0.27 mmol) was added to prevent trace metal-catalysed decomposition of $KHSO_5$ along with the phase transfer catalyst, Bu_4NHSO_4 (0.17 g, 0.5 mmol). Phosphate buffer (10 cm^3, pH 7.5) and distilled water were added to bring the total volume of the solution of 30 cm^3. The mixture was stirred until everything had dissolved and organic solvent was added. The reaction temperature was controlled at a required value. The pH of the reaction mixture at this stage was 1.7; 0.5M KOH was added to bring the pH to the required value for the reaction (pH 7.5 in most cases). Once the desired pH was obtained, the substrate cyclohexene (2.47 mmol, 0.255 cm^3), the internal standard n-octane (0.2 cm^3) and the acetone (as the catalyst) were added. As the reaction proceeded, KOH was added as required to maintain the constant pH. Samples of the reaction mixture were taken at various times for GC analysis.

4.2 Analytical method

Analysis was carried out in a SHIMADZU GC 14B gas chromatography. It was fitted with a capillary column with dimensions of 30 m x 0.248 mm (0.25 μm film thickness) and a flame ionisation detector. Two internal standards were used in this work. The first one was n-octane which was added to the reaction system and used to measure the diluting effect of KOH addition used to maintain the pH constant. The second internal standard was prepared as a 1% (v/v) solution of standard substance in organic solvent and was added prior to GC analysis. A sample of 5 cm^3 was withdrawn from the reaction vessel and added with a few drops of 1 M H_2SO_4 to quench the reaction. This was allowed to settle and a set volume of the organic solvent layer (1 cm^3) was withdrawn and the internal standard (1 cm^3) was added.

More details on operating condition of the GC and calibration curves are given in Appendix A.

CHAPTER V

RESULTS AND DISCUSSION

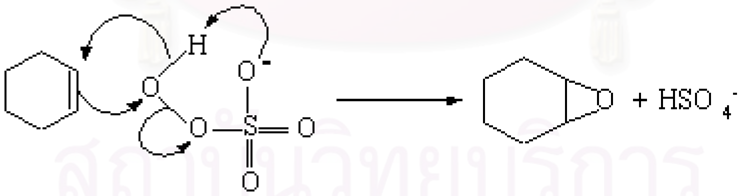
This chapter can be divided into two main sections; i.e. 1) comparison of different preparation methods and 2) effect of operating conditions on the performance of the system.

5.1 Comparison of different preparation methods

In this part, the methods to prepare cyclohexene oxide were divided into four cases; 1) epoxidation with $KHSO_5$ 2) epoxidation with $KHSO_5$ + acetone 3) epoxidation with $KHSO_5$ + acetone using solvent and 4) epoxidation with $KHSO_5$ + acetone using solvent and phase transfer catalyst.

Case 1: Epoxidation with $KHSO_5$ (H_2O + $KHSO_5$ / Cyclohexene)

In this case, cyclohexene was directly epoxidized with $KHSO_5$. The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time are shown in Figure 5.1.



(5.1)

From Figure 5.1 shows the conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time. It was found that very low conversion of cyclohexene with moderate selectivity of cyclohexene oxide of approximately 50% was obtained after a reaction time of 60 minutes. Because two reactants (cyclohexene and KHSO5) are immisible, the reaction takes place at an interphase as illustrated by Figure 5.2. Interfacial mass transfer may be a rate determining step for the reaction system and, consequently, the low conversion was obtained. In addition, it was observed by the same investigators that KHSO5 can further transform the product to its corresponding 1,2-diol. As a result, the moderate selectivity was observed in the system.

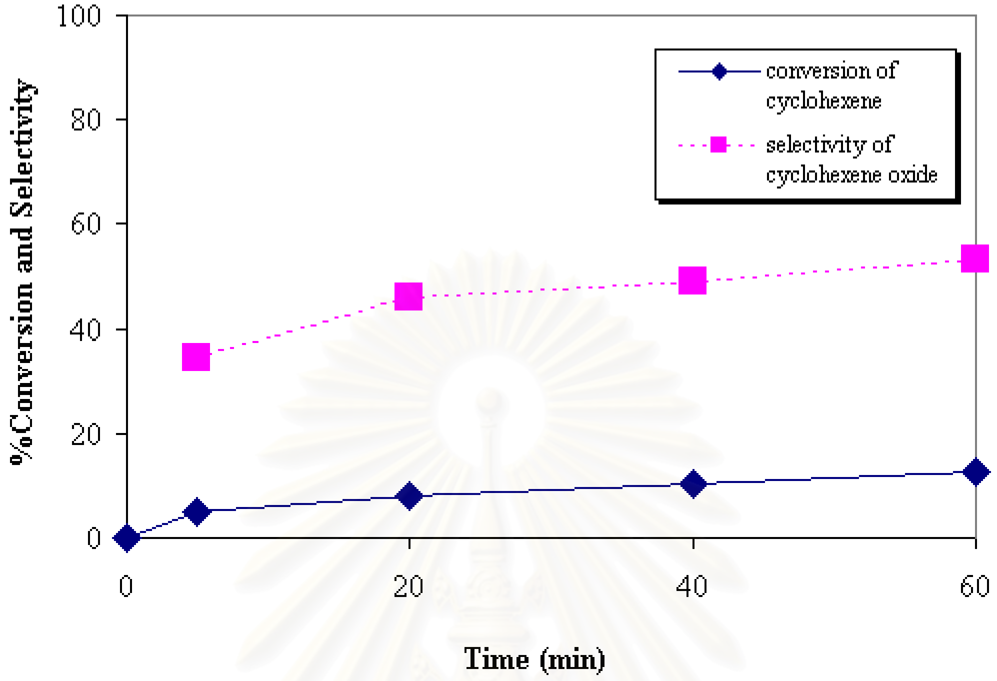


Figure 5.1 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time. (Case 1: Cyclohexene = 9.7 mmol (1 cm^3), oxone = 11.18 mmol (3.69 g), stirring rate = 2040 rpm, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 minutes).

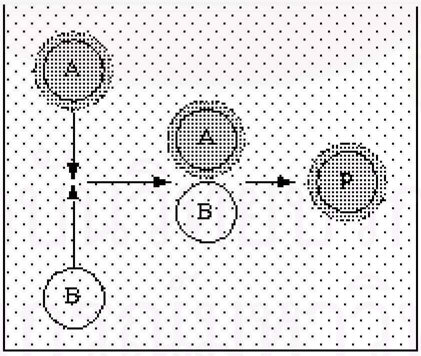


Figure 5.2 The scheme for the synthesis of cyclohexene oxide in Case 1(A: cyclohexene; B: $KHSO_5$; P: cyclohexene oxide; ▩ : organic phase; ⬚ :aqueous phase)

Case 2: Epoxidation with $KHSO_5$ + Acetone

(H_2O + $KHSO_5$ / Cyclohexene + Acetone)

Figure 5.3 shows the conversion of cyclohexene and the selectivity of cyclohexene oxide for this system. It is observed that the addition of acetone to the reaction system in Case 1 can significantly improve both conversion and selectivity; i.e. the conversion increases from 12% to 57% and the selectivity increases from 53% to 99%. This is because a dioxirane, a highly reactive and efficient oxidizing agent, was formed from acetone and $KHSO_5$ and then it selectively reacts with the reactant, cyclohexene, to form cyclohexene oxide and acetone as shown in Eqs. 5.2 and 5.3, respectively. The dioxirane has been successfully utilized to epoxidize other alkenes such as cyclooctane, β-methylstyrene and pyridine (Murray and Jeyaraman, 1985).

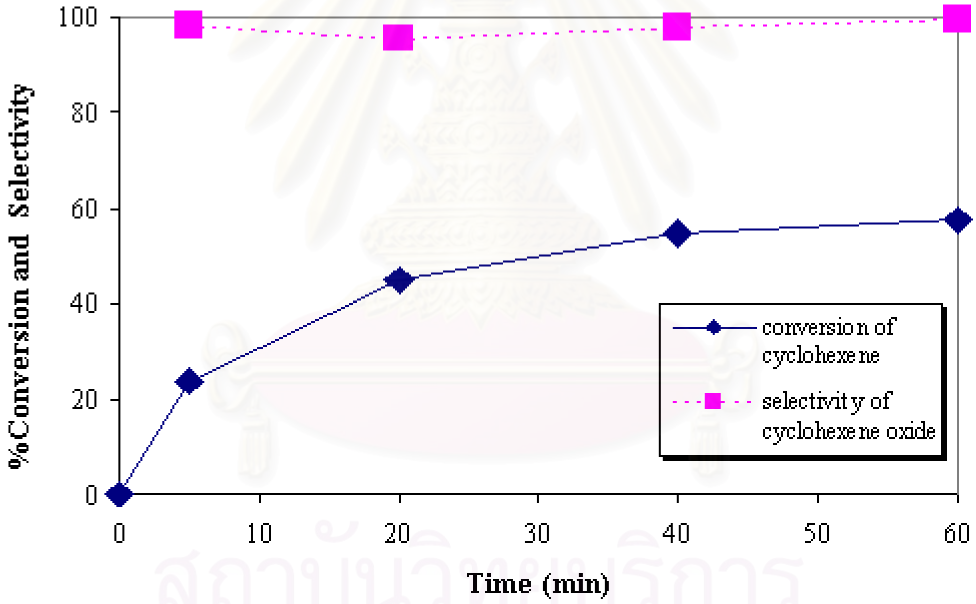
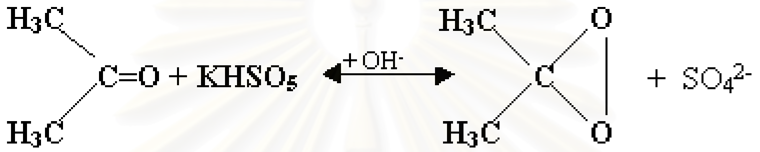


Figure 5.3 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time. (Case 2: Cyclohexene = 9.7 mmol (1 cm^3), oxone = 11.18 mmol (3.69 g), acetone = 27 mmol, stirring rate = 2040 rpm, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time 60 = minutes).

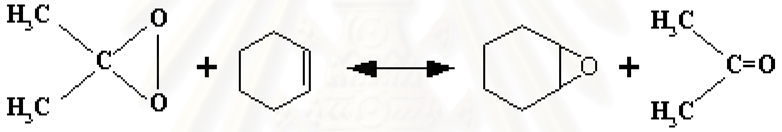
From Figure 5.4 shows the schematic diagram of the synthesis of cyclohexene oxide. Since the dioxirane produced from acetone and KHSO5 is miscible with the reactant, cyclohexene, the reaction can also take place readily in the organic phase together with at the interface. This should also be another reason for the improved conversion compared to Case 1. In addition, it should be noted that acetone is considered to be a catalyst in this system since it is consumed to form the dioxirane but it is subsequently generated as a co-product in the cyclohexene oxide production.

step 1: Formation of dioxirane (at an interphase).



(5.2)

step 2: Epoxidation of cyclohexene using dioxirane (in the organic phase).



(5.3)

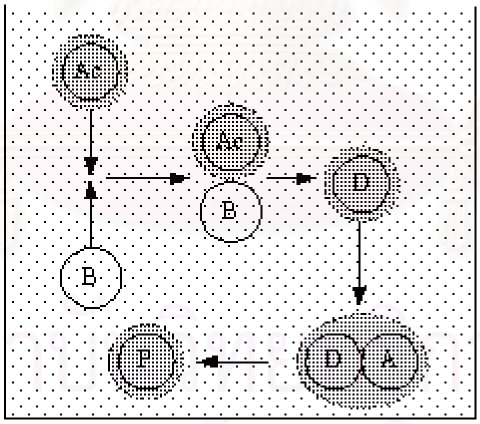


Figure 5.4 The scheme for synthesis of cyclohexene oxide in Case 2(A: cyclohexene; B: $KHSO_5$; Ac: acetone; D: dioxirane; P: cyclohexene oxide; ▦: organic phase; ⬚: aqueous phase)

Case 3: Epoxidation with $KHSO_5$ + actone using solvent

(H_2O + $KHSO_5$ / Cyclohexene + Acetone + Solvent)

This system represents an extractive reaction process. The operating condition was the same as Case 2 except that dichloromethane as a solvent was added. The results of conversion and selectivity as a function of reaction time are shown in Figure 5.5. Comparison between the cases with and without dichloromethane reveals that both systems offered very high selectivity of almost 100%; however, higher conversion was obtained when with the presence of the solvent; i.e. the conversion at 60 minutes increased from 57% to 71%.

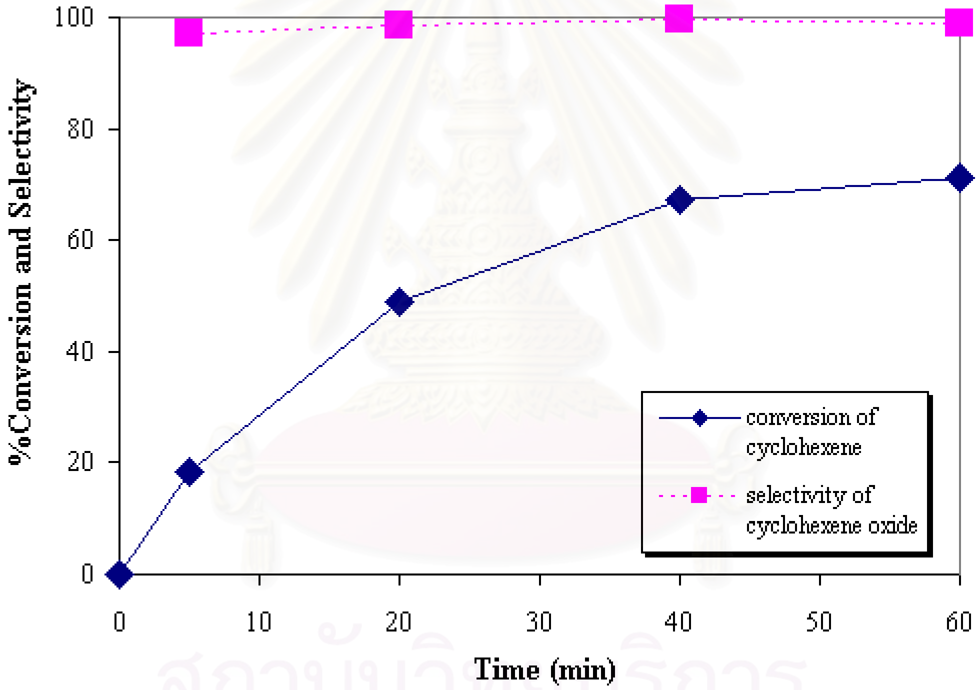


Figure 5.5 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time. (Case 3: Cyclohexene = 9.7 mmol (1 cm^3), oxone = 11.18 mmol (3.69 g), acetone = 27 mmol, stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83 using dichloromethane as a solvent, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 minutes).

This improvement can be explained by considering Figure 5.6. When the solvent is added to then system, acetone can be dissolved in both the aqueous and the organic phases. As a result, the dioxirane can be formed both in the aqueous phase and at the aqueous/ organic interface by the reaction between acetone and KHSO5. Because the dioxirane can be preferentially extracted to the organic phase containing dichloromethane, acetone and cyclohexene, the reaction can take place in the solvent phase and result in higher reaction conversion.

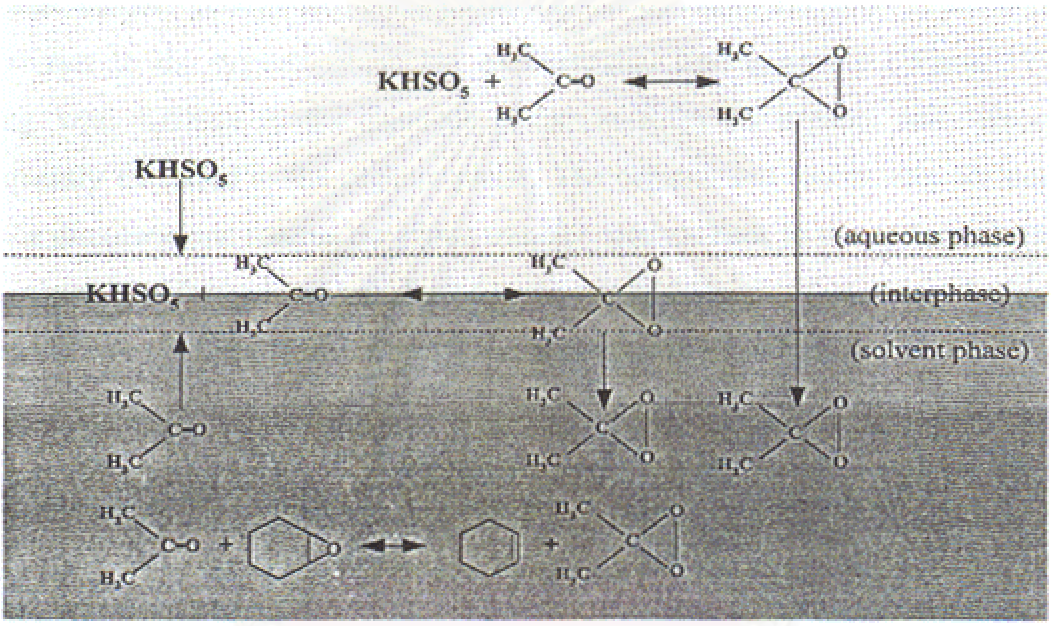


Figure 5.6 The scheme for the synthesis of cyclohexene oxide in Case 3; ▩: organic phase; ⬚: aqueous phase)

Case 4: Epoxidation with $KHSO_5$ + actone using solvent and phase transfer catalyst.

(H_2O + $KHSO_5$ + PTC / Cyclohexene + Acetone + Solvent)

This case is also extractive reaction process. The operating condition was the same as Case 3 but a phase transfer catalyst of Bu_4NHSO_4 was added. The results in Figure 5.7 shows that almost 100% selectivity was obtained; however, when compared to Case 3 the conversion at 60 minutes was improved from 71% to 91%. The phase transfer catalyst helped improve the rate of formation of dioxirane and its transfer rate to the organic phase by, as illustrated by Figure 5.8 (Wang, 1997), reacting with $KHSO_5$ in the aqueous phase to form an organic salt which is subsequently extracted to the organic phase. The organic salt reacts with acetone to form the dioxirane and returns the phase transfer catalyst back to the system. Because the dioxirane was formed and transferred to the organic phase at faster rate, the higher conversion was obtained with the use of the phase transfer catalyst.

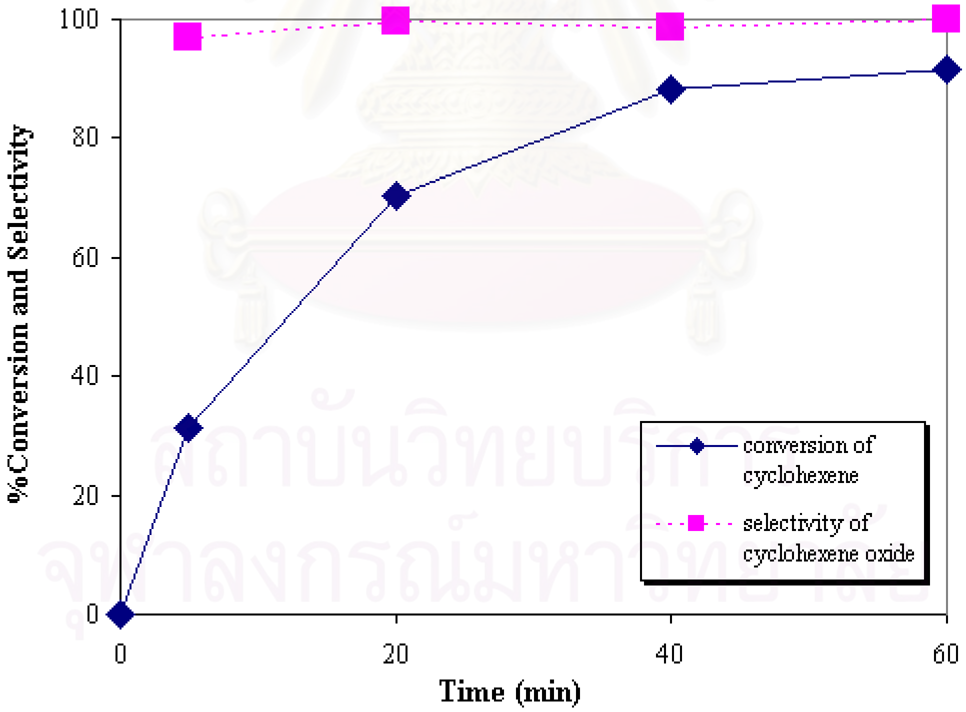


Figure 5.7 The conversion of cyclohexene and the selectivity of cyclohexene oxide as a function of time. (Case 4: Cyclohexene = 9.7 mmol (1 cm^3), oxone = 11.18 mmol (3.69 g), acetone = 27 mmol, Bu_4NHSO_4 = 0.5 mmol (0.17g), stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83 using dichloromethane as a solvent, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 minutes).

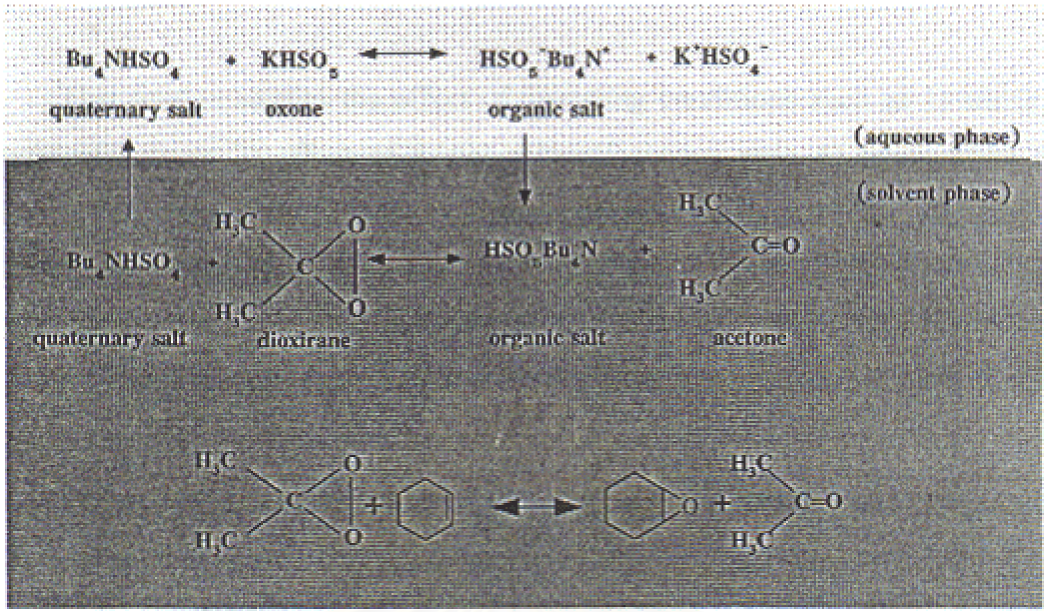


Figure 5.8 The scheme for the synthesis of cyclohexene oxide in Case 3; ▩: organic phase; ⬚: aqueous phase)

By comparing the reaction performance of the above four different preparation methods, it could be concluded that the best performance was obtained when cyclohexene was epoxidized with dioxirane in an extractive reaction system with the presence of the phase transfer catalyst. This method was chosen for studying the effect of operating conditions on the performance of the epoxidation of cyclohexene.

5.2 Effect of operating conditions on the performance of the system.

This section studies the effect of operating conditions such as 1) stirring rate 2) type of solvent 3) effect of initial solvent/aqueous ratio 4) temperature 5) pH 6) amount of catalyst and amount of phase transfer catalyat on the performance of epoxidizing cyclohexene.

5.2.1 Effect of stirring rate

Figure 5.9 shows the effect of the stirring speed on the yield of cyclohexene oxide. The stirring speed was varied between 1200 and 2040 rpm.

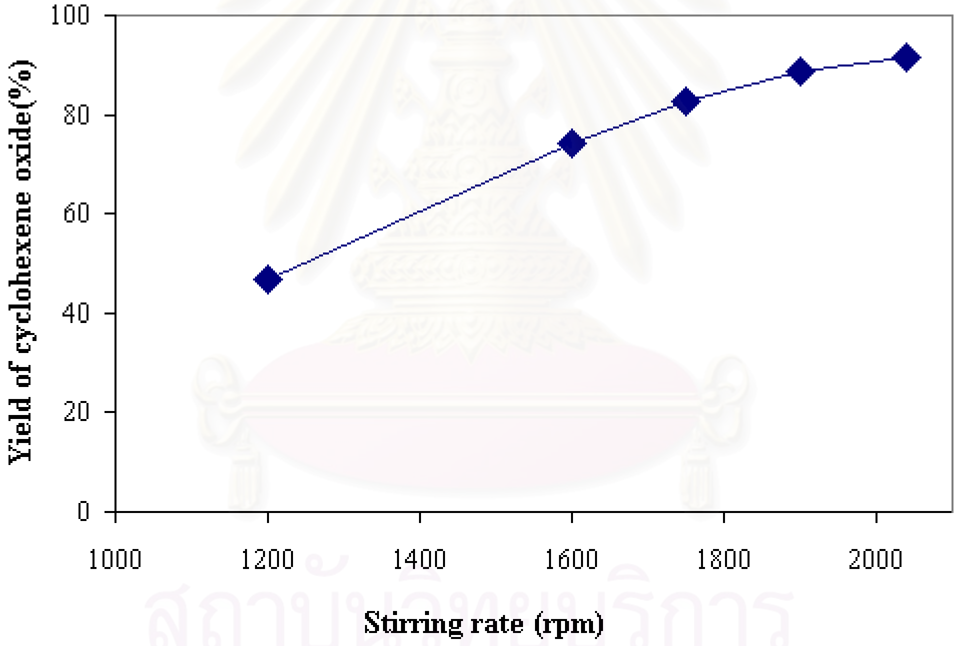


Figure 5.9 Effect of stirring rate on the yields of cyclohexene oxide using dichloromethane as a solvent. (Acetone = 27 mmol, cyclohexene = 2.47 mmol (0.255 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), initial solvent/aqueous ratio = 0.83, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 minutes).

It was observed that the stirring rate had significant effect on the yield of cyclohexene oxide. The higher the stirring rate, the higher cyclohexene oxide yield. Because the extractive reaction system is biphasic, stirring rate is very important to ensure sufficient contact between the two phases. However, due to the limitation of the equipment, the maximum speed of 2040 was used in the studies.

5.2.2 Effect of type of solvent

Three types of solvent; i.e. benzene, toluene and dichloromethane were chosen to study the effect of solvent type on the reaction performance. The solvent volume of 25 cm^3 was used for all the experiment. The conversions of cyclohexene are shown in Figure 5.10.

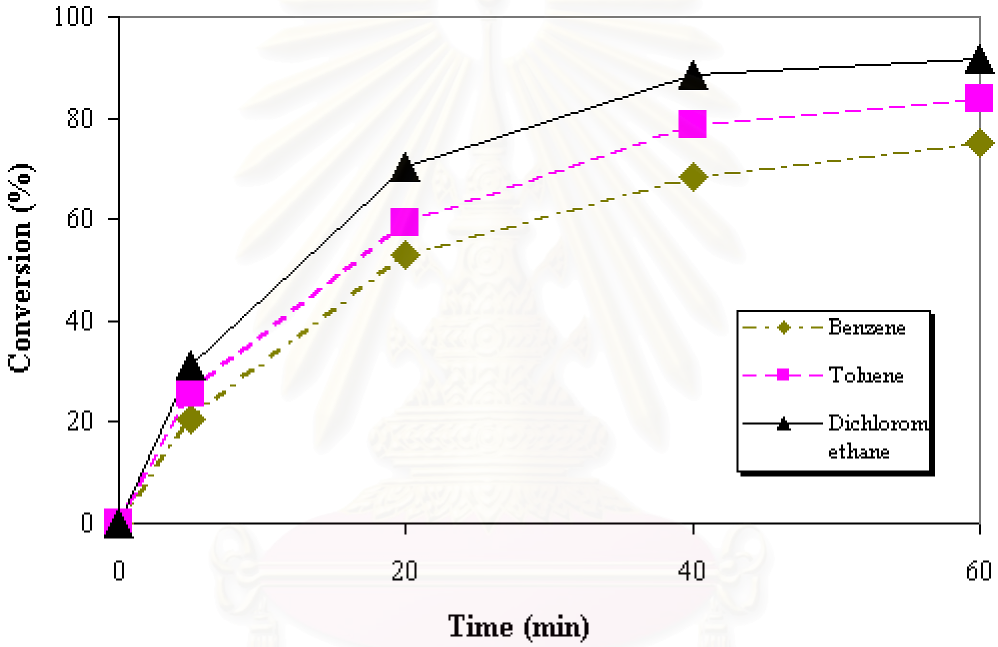


Figure 5.10 The conversion of cyclohexene oxide as a function of time in biphasic system using different solvent as extractant. (Acetone = 27 mmol, cyclohexene = 9.7 mmol (1 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 minutes).

From Figure 5.10, the best conversion was obtained when dichloromethane was used as a solvent. Because of the presence of the phase transfer catalyst in the system, the polarity of the organic solvent is an important factor affecting the conversion and the reaction rate (Wang, 1997). If the organic solvent has more polarity, the quaternary organic salt will be more extracted. A higher yield is achieved in dichloromethane/water system because of its high polarity compared to the others.

5.2.3 Effect of initial solvent/aqueous ratio

The effect of initial solvent/aqueous ratio on the cyclohexene oxide yield was studied in the dichloromethane/water system. The range varied from 0.50 to 1.17 at 3 stirring rates of 1200, 1600 and 2040 rpm. Figure 5.11 shows the yield of cyclohexene oxide at 60 minutes.

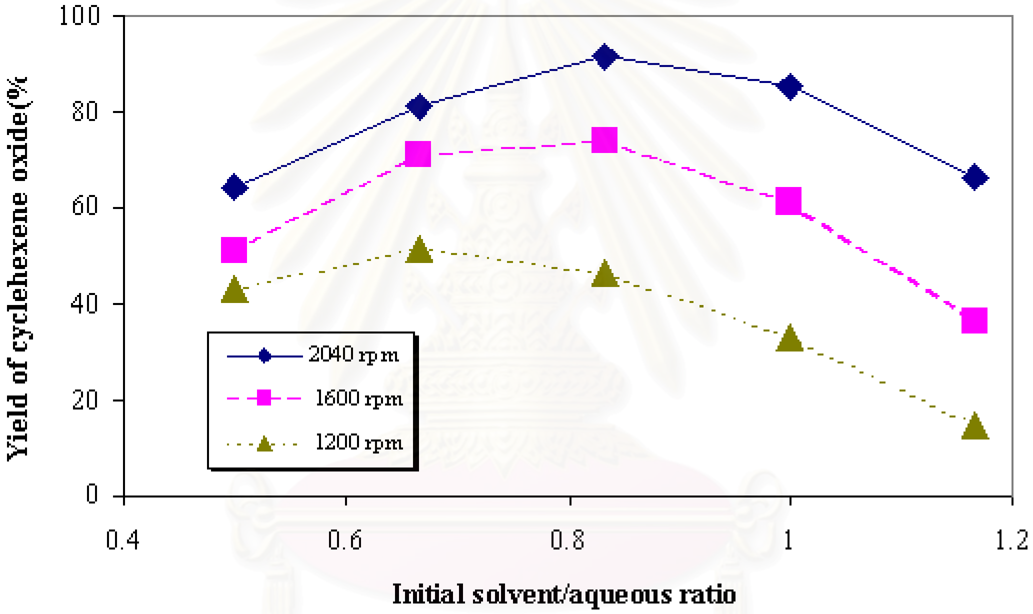


Figure 5.11 Effect of initial solvent/aqueous ratio on the yields of cyclohexene oxide at various stirring rates. Using dichloromethane as a solvent. (Acetone = 27 mmol, cyclohexene = 2.47 mmol (0.255 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 60 min.).

It was found that there existed an optimum initial solvent/aqueous ratio which offered the highest yield for each stirring rate. In the range that the yield of cyclohexene oxide increased with increasing initial solvent/aqueous ratio, because the more solvent is used, the more amount of product is extracted. For the range that the yield of cyclohexene oxide decreased with increasing initial solvent/aqueous ratio, it could be explained by the mass transfer effect. Increasing the amount of solvent while keeping the stirring rate constant leads to insufficient contact between two phases, causing the decrease of the yield of cyclohexene oxide. When the stirring rate increased, the optimum performance was achieved at higher initial solvent/aqueous ratio due to the better contact between two phases. Apart from the mass transfer effect, slow rate of reaction due to diluted reactant may be another reason that caused the decrease of yield. When too many solvent was added, the reactant was very diluted and, consequently, the rate of reaction was slow.

In this study, at the highest stirring rate, the optimum performance was achieved at the initial solvent/aqueous ratio of 0.83, thereby this ratio was used in following studies.

5.2.4 Effect of temperature

The epoxidation experiments were carried out at different temperatures ranging between 10-30 ^{O}C. Figure 5.12 shows the effect of temperature on the cyclohexene oxide yield. It can be seen that the optimum temperature was 25 ^{O}C with the maximum yield of 93.55 %. The reason for the presence of the optimum temperature can be explained by considering two competing effects taking place in the system. The reaction rate increases with increasing temperature. However, it was noted earlier that $KHSO_5$ was decomposed at faster rate at higher temperature (Curci *et al*., 1980). Moreover, the extent of ring expansion of epoxy groups increased with increasing temperature (Roy *et al.,* 1991). As a result, the yield of cyclohexene oxide existed the maximum.

5.2.5 Effect of pH

To study the effect of pH on the cyclohexene oxide yield, the pH value was varied from 5 to 8. The findings are presented in Figure 5.13.

A maximum yield occurred at the pH of 7.5. The reaction rate increases when the pH value increases but at pH higher than 7.5 the rate of decomposition of $KHSO_5$ increased rapidly resulting in lower values for the cyclohexene oxide yield (Connell *et al*., 1998).

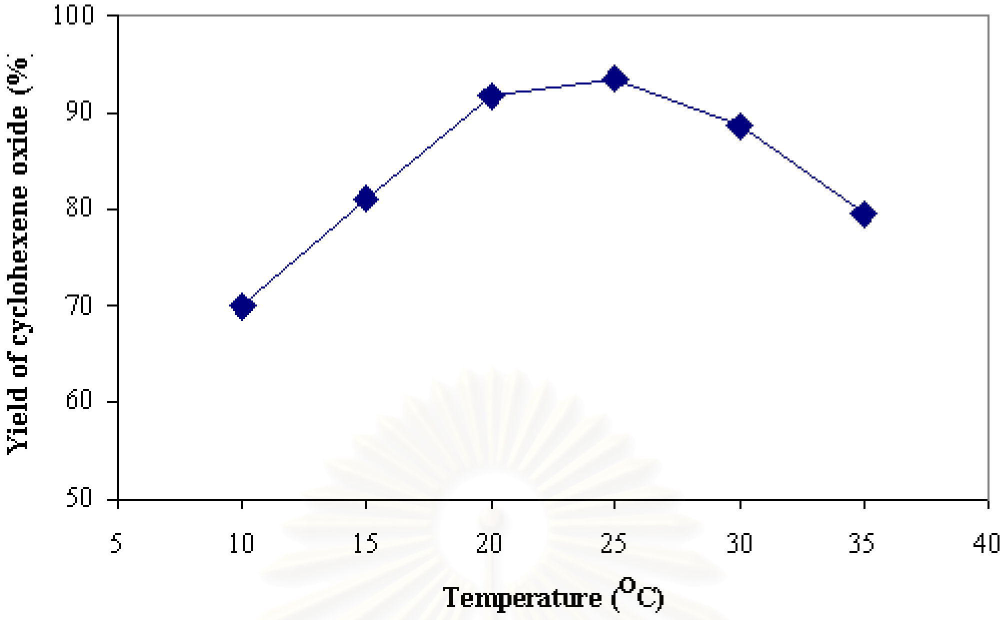


Figure 5.12 Effect of temperature on the cyclohexene oxide yield. (Acetone = 27 mmol, cyclohexene = 2.47 mmol (0.255 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83, pH 7.5 and reaction time = 60 minutes).

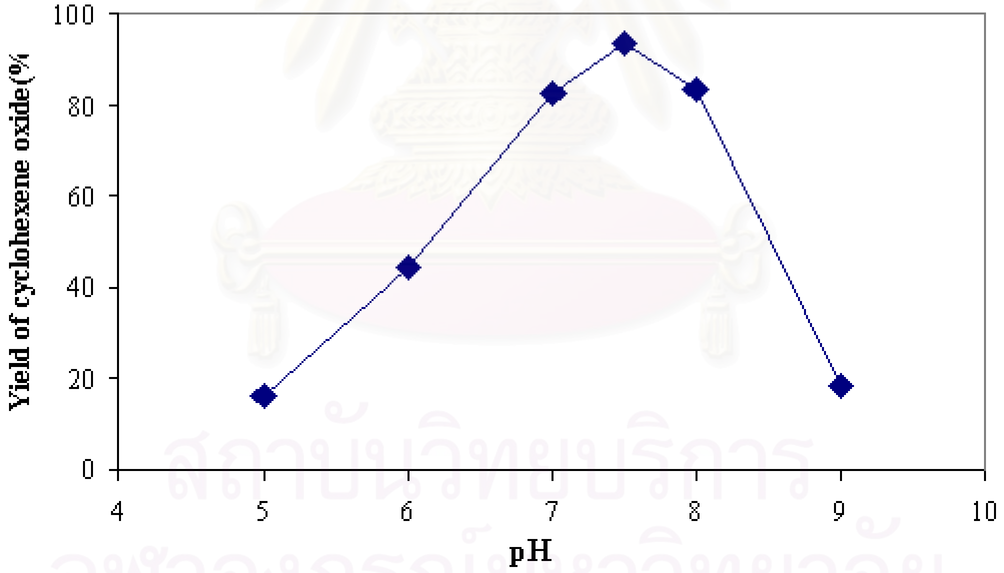


Figure 5.13 Effect of pH on the cyclohexene oxide yield. (Acetone = 27 mmol, cyclohexene = 2.47 mmol (0.255 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83, reaction temperature = 25 ^{O}C and reaction time = 60 minutes).

5.2.6 Effect of amount of catalyst (acetone)

The influence of the amount of catalyst on the cyclohexene oxide yield is shown in Table 5.1.

Table 5.1 Effect of the acetone amount on the yields of cyclohexene oxide.

Amount of acetone (mmol)	Yield of cyclohexene oxide (%)
0	14.10
6.8	42.65
13.6	63.09
27	93.55
68	97.51

(Using cyclohexene = 2.47 mmol (0.255 cm^3), Bu_4NHSO_4 = 0.5 mmol (0.17g), dichloromethane as a solvent, stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83, pH = 7.5, reaction temperature = 25 ^{O}C and reaction time = 1 minutes).

It is clearly shown that the extent of reaction depends on the amount of acetone. The higher the amount of catalyst, the higher cyclohexene oxide yield. It should be noted that cyclohexene oxide was formed even in the absence of ketone. This was due to the direct reaction between $KHSO_5$ and cyclohexene but the yield of cyclohexene oxide at this condition was very low.

5.2.6 Effect of amount of phase transfer catalyst

To study the effect of phase transfer catalyst on the performance of epoxidizing cyclohexene, the amount of phase transfer catalyst was varied from 0-0.7 mmol. The results are shown in Table 5.2

Table 5.2 Effect of the amount of phase transfer catalyst on the yields of cyclohexene oxide.

Amount of Bu_4NHSO_4 (mmol)	Yield of cyclohexene oxide (%)
0	71.25
0.3	82.46
0.5	91.68
0.7	95.87

(Using cyclohexene = 2.47 mmol (0.255 cm^3), Acetone = 27 mmol, dichloromethane as a solvent, stirring rate = 2040 rpm, initial solvent/aqueous ratio = 0.83, pH = 7.5, reaction temperature = 20 ^{O}C and reaction time = 1 minutes).

It was found that the higher yield of cyclohexene oxide was achieved when the higher amount of phase transfer catalyst was used. Because the extent of generating rate of dioxirane depended on the amount of phase transfer catalyst, the increment of amount of phase transfer catalyst caused the improvement of generating rate of dioxirane and this resulted the high yield of cyclohexene oxide.

CHAPTER VI

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Extractive reaction for the epoxidation of cyclohexene to cyclohexene oxide using dioxirane was studied in this research. The following conclusions can be drawn from the investigation.

1. In the study on the comparison of different preparation methods, the best preparation method was achieved when cyclohexene was epoxidized with dioxirane in an extractive reaction system with the presence of phase transfer catalyst. Dioxirane is a high reactive and efficient oxidizing agent therefore it helped improve the yield and selectivity of cyclohexene oxide. By a principle of extractive reaction, solvent was added in the system to extract a desired product into the organic solvent phase thereby bypassing the equilibrium limitation and preventing its further reaction. Phase transfer catalyst was used to help improve the rate of generation of dioxirane. By these reasons, the extent of reaction and the yield of desired product increased and it could be concluded that the performance of an extractive reaction process was superior to the conventional single-phase process.

2. In the study on effect of operating conditions,
    - 2.1 The yield of cyclohexene oxide increased with increasing stirring rate.
    - 2.2 Dichloromethane was the best solvent for this system in this study.
    - 2.3 At the maximum stirring rate of 2040 rpm, the highest yield at the reaction time of 1 hour was achieved at the initial solvent/aqueous ratio of 0.83, temperature of 25 ^{O}C and pH of 7.5.

2.4 The higher cyclohexene oxide yield was obtained with the increased amount of catalyst and phase transfer catalyst.

Recommendations

This work studied an extractive reaction process for the epoxidation of cyclohexene with dioxirane. The process was only studied in lab-scale level. Although, in the experiments, an extractive reaction process provided a very high yield of desired product but it still could not be used in industry level. The further studies should investigate the continuous extractive reaction process and explored an extractive reaction process using other reactions.

REFERENCES

Anderson, A. K., and T. Veysoglu. A simple procedure for the epoxidation of acid-sensitive olefinic compound with m-chloroperbenzoic acid in an alkaline biphasic solvent system. J. Org. Chem. 38 (1973): 2267.

Alders L. Liquid-Liquid Extraction Theory and Laboratory Experiments. New York, (1955). Baumstark, A. L. and P. C. Vasquez. Epoxidation by dimethyldioxirane: Electronic and steric effects. J. Org. Chem. 53 (1988): 3437.

Brandstrom, A. Chemical protection by phase separation and phase transfer catalysis. J. Mol. Catal. 20 (1983): 93.

Campaci, F. and S. Campestrini. Catalytic olefin epoxidations with $KHSO_5$: The first report on manganese hemiporphyrazines as vatalysts in oxygenation. J. Mol. Catal. 140 (1999): 121.

Carey, F. A. and R. J. Sunberg, Advanced Organic Chemistry Part B. New York, (1990).

Cicala, G., R. Curci, M. Fiorentino and O. Laricchiuta. Stereo- and regioselectivities in the epoxidation of some allylic alcohol by the dioxirane intermediate generated in the reaction of potassium caroate with acetone. J. Org. Chem. 47 (1982): 2670.

Coca, j., G. Adrio, C. Y. Jeng, and S. H. Langer, Preparative and Production Scale Chromatography. New York, (1993).

Connell, A., T. Smyth and K. Benjamin. The epoxidation of cyclohexene by dioxiranes over ketone catalysts. Catal. Today. 32 (1996): 273.

Connell, A., T. Smyth and K. Benjamin. In-situ epoxidation using dioxiranes: Evaluation of reactivity and selectivity. J. Chem. Technol. Biotechnol. 72 (1998): 60.

Corey, P. F. and F. E. Ward. Bufferd potassium peroxymonosulfate-acetone epoxidation of α,β-unsaturated acids. J. Org. Chem. 51 (1986): 1925.

Curci, R., M. Fiorentino, L. Troisi, J. O. Edwards and R. H. Pater. Epoxidation of alkenes by dioxirane intermediates generated in the reaction of potassium caroate with ketones. J. Org. Chem. 45 (1980): 4758 .

DeGarmo, J. L., V. N. Parulekar, and V. Pinjala. Consider reactive distillation. Chem.

Eng. Prog. 3 (1992): 43.

Dohertv\y, M. F.and G. Buzasd. Reactive distillation by design. Trans. Inst. Chem. Eng. 70 (1992): 448.

Fife, W. K. and Y. Xin. Inverse phase-transfer catalysis: probing its mechanism with competitive transacylation. J. Am. Chem. Soc. 109 (1987): 1278.

Freeman, H. H. Industrial applications of phase transfer catalysis (PTC): past, present and future. Pure Appl. Chem. 58 (1986): 857.

Gaikar, V. G. and M. M. Sharma. New Strategies for separations through reactions. Proc. Ind. Acad. Sci., Eng. Sci. 10 (1987): 163.

Georgea. Olah. Oxidation-Oxygenation. Hydrocarbon chemistry (1995).

Hegarty, A. F. Comprehensuve Organic Chemistry. 2 (1983): 1108.

Hirata, M., T. Ishimine and A. Hirata. Development of novel method for enzymatic peptide synthesis utilizing extractive reaction. J. Chem. Eng. Jpn. 30 (1997): 467.

Hori, T. and K. B. Sharpless. Synthetic applications of arylselenenic and arylseleninic acids. Conversion of olefins to allylic alcohols and epoxides. J. Org. Chem. 43 (1978): 1689.

King, M. L., A. L. Forman, C. Orella and S. H. Pines. Extractive hydrolysis for pharmaceuticals. Chem. Eng. Prog. 5 (1985): 36.

Krishnakumar, V. K. and M. M. Sharma. Synthesis of triarylphosphates via phase transfer catalysis. Synthesis 7 (1983): 558.

Krishnakumar, V. K. and M. M. Sharma. A novel method of recovering phenolic substances from aqueous waste streams. Ind. Eng. Chem. Proc. Des. Dev. 23 (1984): 410.

Krishnakumar, V. K. and M. M. Sharma. Kinetics of formation of triphenyl phosphage: phase transfer catalysis. Ind. Eng. Chem. Proc. Des. Dev. 24 (1985): 1293.

Kuo, M. C. and T. C. Chou. Kinetics and mechanism of the catalyzed epoxidation of oleic acid with oxygen in the present of benzaldehyde. Ind. Eng. Chem. Res.

2(1987): 277.

Lele, S. S., R. R. Bhave and M. M. Sharma. Fast and very slow liquid-liquid reactions: Phase transfer catalysis. Chem. Eng. Sci. 22 (1983):765.

Lindblom, L. and M. Elander. Phase transfer catalysis in the production of pharmaceuticals. Pharm. Technol. 4 (1983): 59.

Mahajani, S. M. Reactions of glyxylic acid with aliphatic alcohols using cationic exchange rasins as catalysts. React. Funct. Polym. 43 (2000): 253.

Mello, R., M. Fiorentino, O. Sciacovelli and R. Curci. On the isolation and characterization of methyl (trifluoromethyl)dioxirane. J. Org. Chem. 53 (1988): 3890.

Mersmann, A. and M. Kind. Chemical engineering aspects of precipitation from solution. Chem. Eng. Tech. 11 (1988):264.

Meunier, B., M. E. De carvalho and A. Robert. J. Mol. Catal. 41 (1987):185.

Mimoun, H. J. Mol. Catal. 7 (1980): 1.

Murakami, Y. and A. Hirata. Continuous enzymatic synthesis of aspartame precursor at low pH using an extractive reaction. J. Ferment. Bioeng. 84 (1997): 264.

Murakami, Y., T. Yoshida and A. Hirata. Enzymatic synthesis of N-formyl-L-aspartyl-L-phenylalanine methyl ester (aspatame percursor) utilizing an extractive reaction in aqueous/organic biphasic medium. Biotechnol. Lett. 20 (1998): 767.

Murakami, Y., S. Hayashi, A. Takehara and A. Hirata. Pulsed column reactor as a novel tool for continuous enzymatic synthesis of peptide in an aqueous/organic biphasic medium. Biotechnol. Tech. 13 (1999): 165.

Murakami, Y., T. Oda, K. Chiba and A. Hirata. Continuous enzymatic synthesis of peptide precusor masking introduction into cells utilizing extractive reaction. Kagaku. Kogaku. Ronbunshu. 25 (1999): 206.

Murray, W. Robert and Ramasubbu Jeyaraman. Dioxiranes: Synthesis and reactions of methyldioxiranes. J. Org. Chem. 50 (1985):2847.

Ogata, Y. and Y. Sawaki. In organic syntheses by oxidation with metal compounds. New York (1986).

Poorter De, B., B. Meunier. Nouv. J. Chim. 9 (1985): 393.

Roy, S., B. R. Gupta, and B. R. Maiti. Effect of acid concentration and other reaction parameters on epoxidation of natural rubber latex. Ind. Eng. Chem. Res. 30 (1991)2573 .

Samant, K. D. and K. M. Ng. Synthesis of extractive reaction processes. AICHE J. 44 (1998): 1363.

Samant, K. D. and K. M. Ng. Effect of kinetics and mass transfer on design of extractive reaction process. AICHE J. 44 (1998): 2212.

Samant, K. D. and K. M. Ng. Design of multistage extractive reaction processes. AICHE J. 44 (1998): 2689.

Semenov, A. N., Yu. L. Khmelnitski, I. V. Berezin and K. Martinek. Water-organic solvent two-phase systems and media for biocatalytic reactions. Biocatalysis. 1 (1987): 3.

Sharma, M. M. Multiphase reactions in the manufacture of fine chemicals. Chem. Eng. Sci. 43 (1988): 1749.

Starks, C. M. Phase transfer catalysis. New chemistry, catalysts and applications. Am. Chem. Soc. U.S.A.(1987).

Strukul, G., R. Sinigalia, A. Zanardo, F. Pinna and R. A. Michelin. Inorg. Chem. 28 (1989): 554.

Talley, J. J. and C. B. Berman. Phase transfer catalyzed preparation of triarylphosphorothinates. J. Chem. Eng. Data. 32 (1987): 279.

Tonkovich, A. L. Y. and R. W. Carr. Modeling of the simulated countercurrent moving-bed chromatographic reactor used for the oxidativge coupling of methane. Chem. Eng. Sci. 49 (1994): 4657.

Troisi, L., L. Cassidei, L. Lopez, R. Mello and R. Curci. Oxidations by methyl trifluoromethyl dioxirane-epoxidation of enol ethers. Tetrahedron lett. 30 (1989): 257.

Tsotsis, T. T., A. M. Champagnie, R. G. Minet and P. K. T. Liu. Catalytic membrane reactors. Computer Aided Design of Catalysts: R. E. Becker and C. Pereira, eds., Dekker. New York (1993).

Venturello, C. and E. Alneri. A new effect catalytic system for epoxidation of olefins by hydrogen peroxide under phase-transfer conditions. J. Org. Chem. 48 (1983): 3831.

Wang, S., Z. Wang, Z. Xu, Y. Wang, S. Wu and X. Huang. Study on the Hofmann reagents in a two phase system. Chem. Abstr. 101 (1984): 90361.

Wang K. L. Kinetic modeling of catalytic phase transfer systems. Handbook of Phase Transfer Catalysis (1997).

Yadav, G. D. and M. M. Sharma. Kinetics of reaction of benzyl chloride with sodium acetate/Benzoate : Phase transfer catalysts in solid-liquid system. Ind. Eng. Chem. Proc. Des. Dev. 20 (1981): 385.

Zhu, W. and W.T. Ford. Oxidation of alkenes with aqueous potassium peroxymonosulfate and no organic solvent. J. Org. Chem. 56 (1991): 7022.

APPENDICES

APPENDIX A

GAS CHROMATOGRAPH

A1 Operating condition

Flame ionization detector gas chromatographs, model 14B were used to analyze the concentration of cyclohexene and cyclohexene oxide.

The operating conditions for gas chromatograph are described below:

GC model	Shimadzu GC-14B
Detector	FID
Column	Capillary
Nitrogen flow rate	50 ml/min
Column temperature	
- initial	40 ^{O}C
- program rate	5 ^{O}C / min
- final	80 ^{O}C
Injector temperature	200 ^{O}C
Detector temperature	250 ^{O}C

A2 Calibration curve

The calibration curves of cyclohexene and cyclohexene oxide in dichloromethane, toluene and benzene are illustrated in the following figures.

$$\text{RATIO PEAK AREA} = \frac{\text{Area peak of sample}}{\text{Area peak of internal standard}}$$

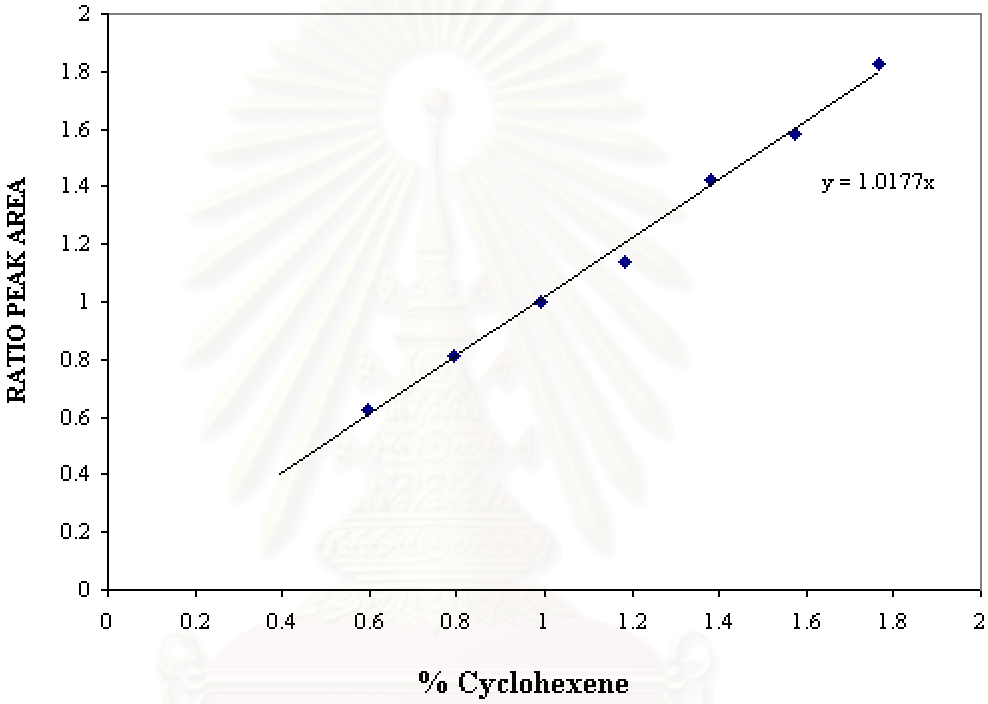


Figure A-1 The calibration curve of cyclohexene in dichloromethane.

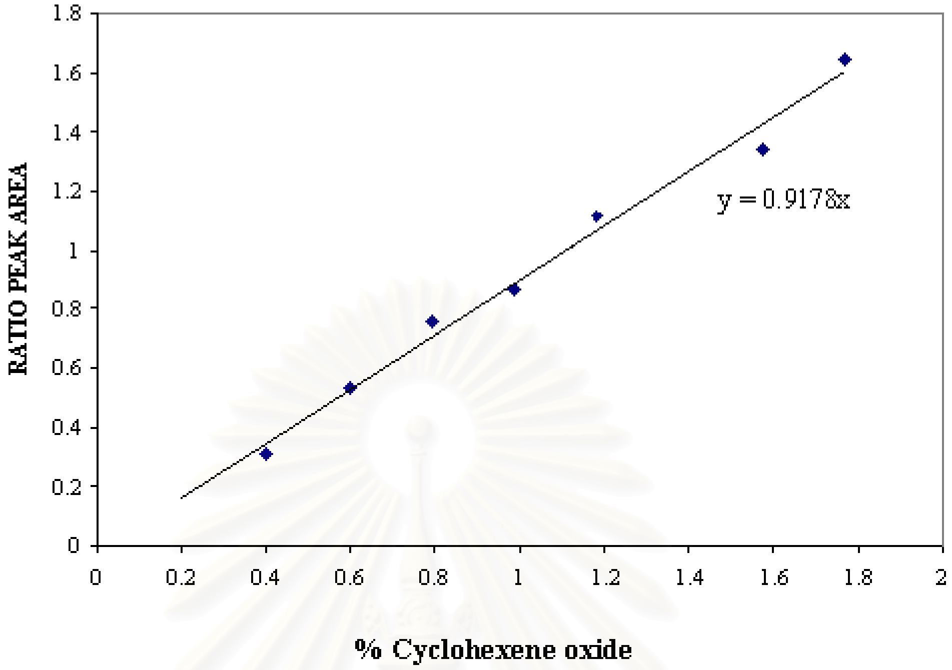


Figure A-2 The calibration curve of cyclohexene oxide in dichloromethane.

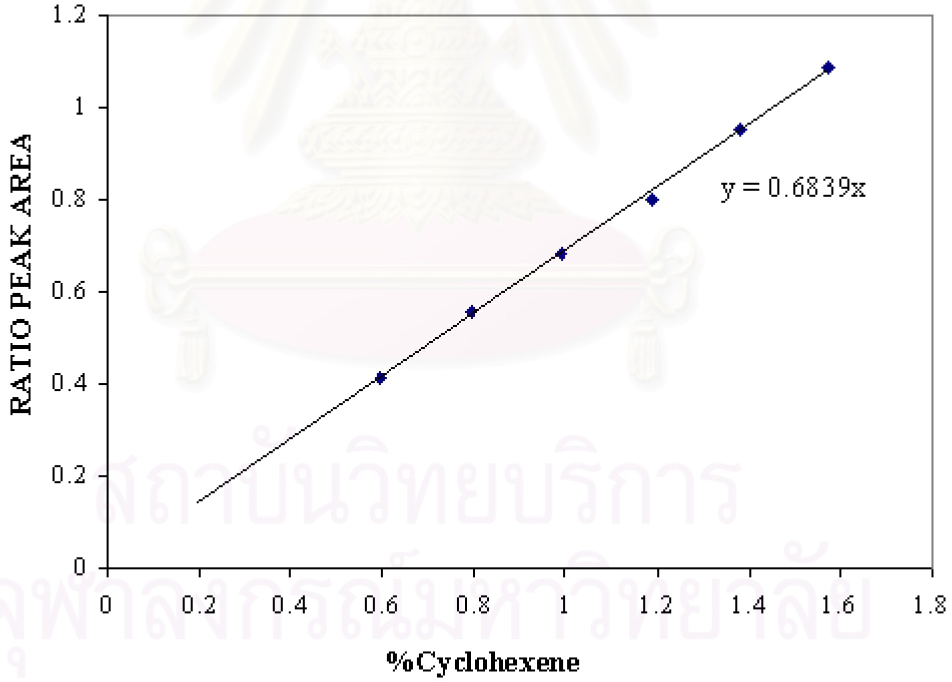


Figure A-3 The calibration curve of cyclohexene in toluene.

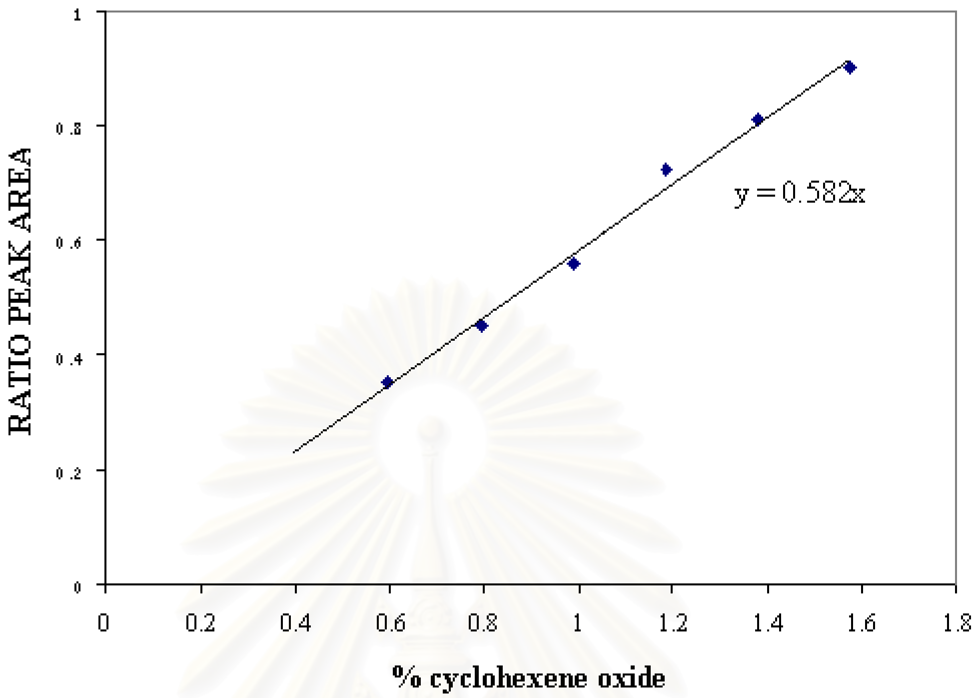


Figure A-4 The calibration curve of cyclohexene oxide in toluene.

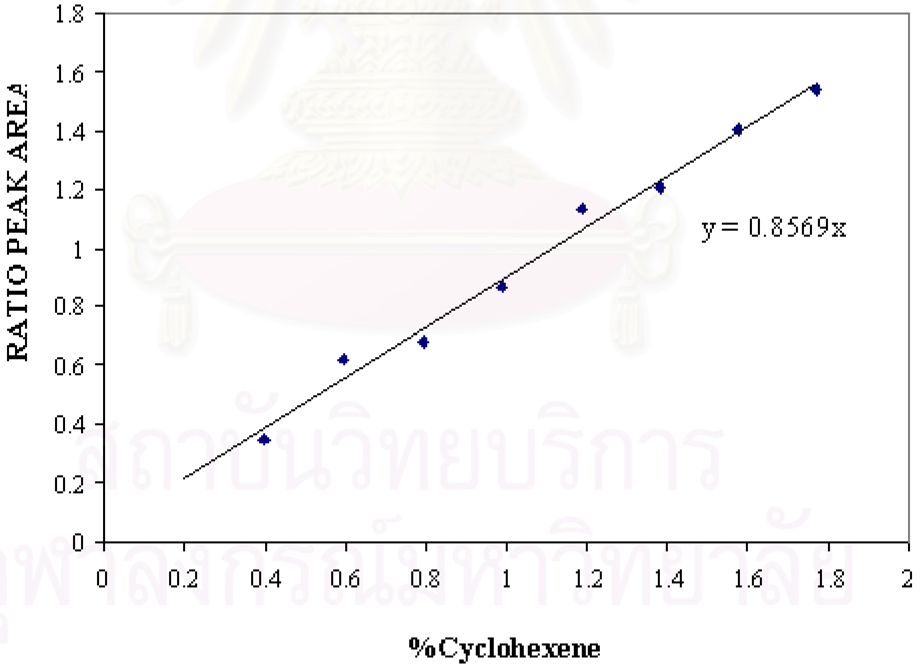


Figure A-5 The calibration curve of cyclohexene in benzene.

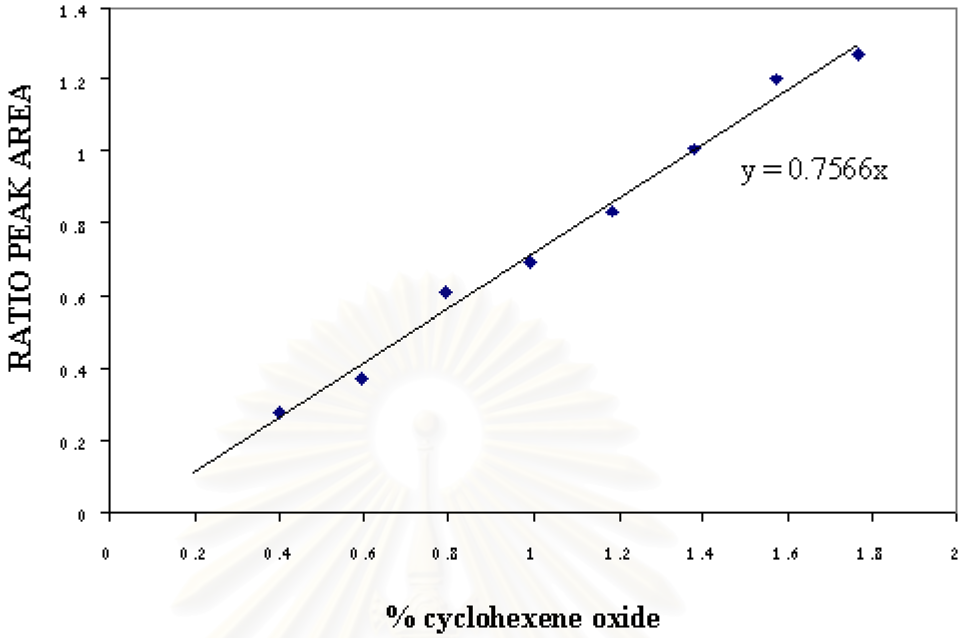


Figure A-6 The calibration curve of cyclohexene oxide in benzene.

APPENDIX B

DATA OF EXPERIMENTS

Table B - 1 Data of Figure 5.1

Time (min)	%Conversion of cyclohexene	%Selectivity of cyclohexene oxide
0	0	-
5	4.86	34.41
20	8.11	46.14
40	10.25	49.06
60	12.71	53.30

Table B - 2 Data of Figure 5.3

Time (min)	%Conversion of cyclohexene	%Selectivity of cyclohexene oxide
0	0	-
5	23.97	98.40
20	45.09	95.43
40	54.71	98.12
60	57.42	99.64

Table B - 3 Data of Figure 5.5

Time (min)	%Conversion of cyclohexene	%Selectivity of cyclohexene oxide
0	0	-
5	18.44	97.25
20	49.09	98.65
40	67.21	99.54
60	71.25	98.87

Table B - 4 Data of Figure 5.6

Time (min)	%Conversion of cyclohexene	%Selectivity of cyclohexene oxide
0	0	-
5	31.24	96.81
20	70.31	99.71
40	88.35	98.62
60	91.68	99.89

Table B - 5 Data of Figure 5.7

Stirring rate (rpm)	%Yield of cyclohexene oxide
1200	46.61
1600	74.25
1750	82.69
1900	88.55
2040	91.68

Table B - 6 Data of Figure 5.8

Time (min)	%Conversion of cyclohexene		
	Benzene	Toluene	Dichloromethane
0	0	0	0
5	20.48	25.68	31.24
20	53.11	59.22	70.31
40	68.54	78.84	88.35
60	74.96	83.61	91.68

Table B - 7 Data of Figure 5.9

Solvent/aqueous ratio	%Conversion of cyclohexene		
	2040 rpm	1600 rpm	1200 rpm
0.50	64.49	51.01	42.81
0.67	81.35	71.15	51.43
0.83	91.68	74.25	46.61
1.00	85.36	61.22	33.12
1.17	66.28	36.34	14.74

Table B - 8 Data of Figure 5.10

Temperature (^{O}C)	%Yield of cyclohexene oxide
10	69.96
15	80.95
20	91.68
25	93.55
30	88.51
35	79.48

Table B - 9 Data of Figure 5.11

pH	%Yield of cyclohexene oxide
5	16.47
6	44.32
7	82.35
7.5	93.55
8	83.48
9	18.45

VITA

Miss. Piyanuch Kachasakul was born on August 27, 1978 in Bangkok. She received the Bachelor degree of Chemical Technology from Faculty of Science, Chulalongkorn University in 1999. She continued her Master's Study at Chulalongkorn University in June, 1999.