

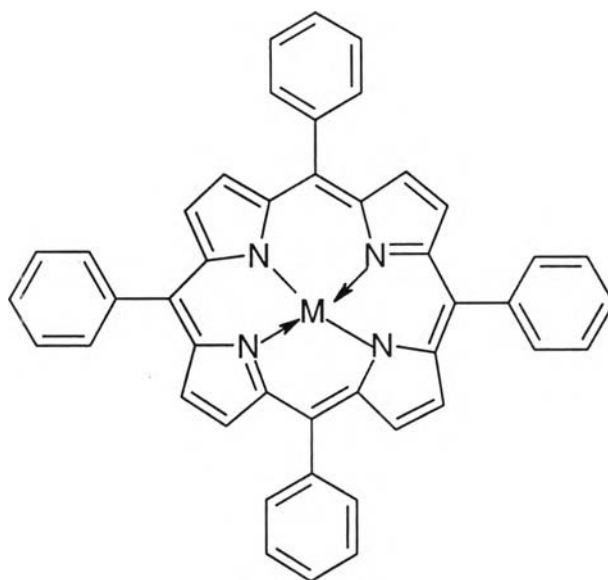
CHAPTER III

RESULTS AND DISCUSSION

This research mainly focuses on the oxidation of cycloalkanes, especially cyclohexane, to ketones and alcohols. Cyclohexane was selected as a substrate for reaction conditions optimization. Other substrates such as *tert*-butylcyclohexane and *n*-pentane were chosen for regioselectivity study. In general, these systems are composed of metal porphyrin complex as a catalyst, zinc grit/air as a source of an oxidant in a reaction medium. A mixture of pyridine and acetic acid was mostly used as a solvent. Other solvents such as acetonitrile, *tert*-butanol, acetone, dichloromethane, isooctane and other oxidizing agents such as *tert*-butyl hydroperoxide, hydrogenperoxide, aldehyde/O₂ were also employed in order to search for another alternatively appropriate oxidation system. Under these particular condition to our best knowledge, there is no report concerning with the oxidation of saturated hydrocarbons.

3.1 Syntheses and characterization of porphyrin ligands and their complexes

Utilizing condensation reaction, ten porphyrin ligands were synthesized by reacting pyrrole with appropriate aromatic aldehydes according to the literature procedure.³¹ Their identities were well-confirmed by IR and NMR techniques prior to use for synthesizing metal porphyrin complexes.



M-TPP

where M = Cu(II), Ni(II), Co(II), Mn(II), Fe(II), Fe(III), Zn(II)

3.2 The optimum conditions for cyclohexane oxidation

3.2.1 Effect of metals

The appropriate transition metal was one of the essential parameters that needed to be first evaluated. Thus, the variation of first row transition metal-TPP complexes was carefully studied. The results are presented in Table 3.1 and Fig 3.1.

Table 3.1 The oxidation of cyclohexane catalyzed by various metal porphyrin catalysts

Entry	Catalysts	2 hours		24 hours		-one/-ol ratio at 24 hours
		-one (mmol)	-ol (mmol)	-one (mmol)	-ol (mmol)	
1	none	0	0	0	0	-
2	FeCl ₂ ·4H ₂ O	0.156	trace	1.089	0.104	10.5
3	Cu(II)-TPP (11)	trace	trace	trace	0.169	-
4	Ni(II)-TPP (12)	0	trace	0	trace	-
5	Co(II)-TPP (13)	0.118	trace	0.266	0.155	1.7
6	Mn(II)-TPP (14)	0.240	0.173	0.333	0.493	0.7
7	Fe(II)-TPP (15)	0.577	trace	1.340	0.249	5.4
8	Fe(III)-TPP (16)	0.360	trace	1.258	0.296	4.3
9	Zn(II)-TPP (17)	trace	trace	trace	0.312	-

Reaction conditions: cyclohexane (30 mmol), catalyst (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

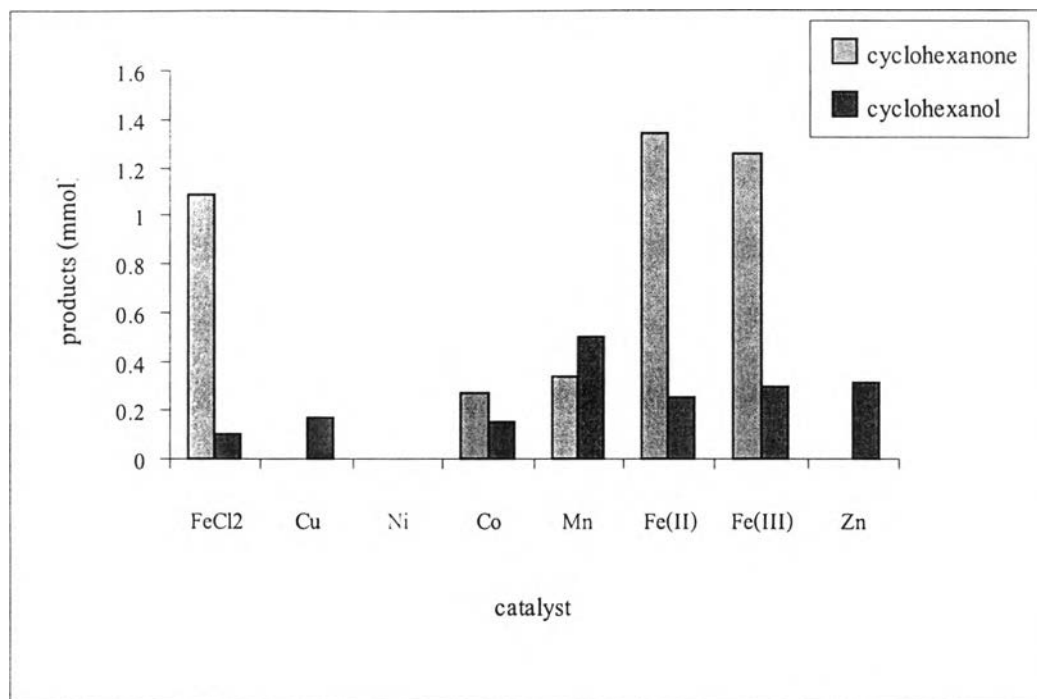


Fig 3.1 The oxidation of cyclohexane catalyzed by various metal porphyrin catalysts

It could clearly be seen from Table 3.1 and Fig 3.1 that the oxidation of cyclohexane could take place using iron catalysts. Comparing with FeCl₂.4H₂O that was employed in Gif^{IV} oxidation system³⁹, the use of Fe (II) and Fe (III)-porphyrin catalysts could enhance the amount of the desired product. The total amount of the oxidized product was found to be 1.33 times over that using FeCl₂.4H₂O as a catalyst, respectively.

In addition, iron (II) porphyrin catalyst gave slightly more cyclohexanone/cyclohexanol ratio than that obtained from iron (III) porphyrin catalyzed system. It is interesting to note that Ni-TPP complex did not produce any oxidized product under this particular conditions. The use of Cu-TPP and Zn-TPP gave only cyclohexanol as a sole product. Co- and Mn-TPP complexes could catalyze the oxidation reaction with smaller extent than iron systems. This observation strongly

supported the concept of metal-dependence in oxidation reaction.⁴⁰ Therefore, iron (II) porphyrin complex was considered as appropriate catalyst for further investigation.

From recent literature, the use of synthetic iron porphyrins as models for the enzyme in the oxidation reaction is now firmly established; however, those models usually gave alcohol as a major product. For example, Mansuy and his colleagues⁴¹ reported that iron (III) porphyrin produced only cyclohexanol as product using cumylhydroperoxide (CumOOH) and iodosobenzene (PhIO) as oxidants and benzene as solvent whereas Rh (III) porphyrin failed to catalyze cyclohexane oxidation, and Cr (III) porphyrin led to low cyclohexanol but similar yields of cyclohexanone.

3.2.2 Effects of porphyrin ligands

In order to seek for appropriate metalloporphyrin catalysts that could catalyze the reaction to convert cyclohexane to cyclohexanone and cyclohexanol, various porphyrinic ligands derived from selected aromatic aldehydes were manipulated. The results of the utilization of various porphyrin ligands for iron catalysts are summarized in Table 3.2 and Fig 3.2.

Table 3.2 The effect of iron (II) porphyrin complexes on cyclohexane oxidation

Entry	Catalysts	2 hours		24 hours		Total products at 24 hours (mmol)
		-one (mmol)	-ol (mmol)	-one (mmol)	-ol (mmol)	
1	15	0.577	trace	1.340	0.249	1.589
2	18	0.373	trace	1.777	0.172	1.949
3	19	0.530	trace	2.167	0.228	2.395
4	20	0.593	0.109	1.615	0.337	1.952
5	21	0.841	0	2.447	0.293	2.740
6	22	0.273	trace	0.918	0.199	1.117
7	23	0.389	trace	1.510	0.217	1.727
8	24	0.482	trace	2.139	0.389	2.528
9	25	0.567	0.099	2.086	0.382	2.468
10	26	0.339	0.117	1.150	0.560	1.710

Reaction conditions: cyclohexane (30 mmol), catalyst (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

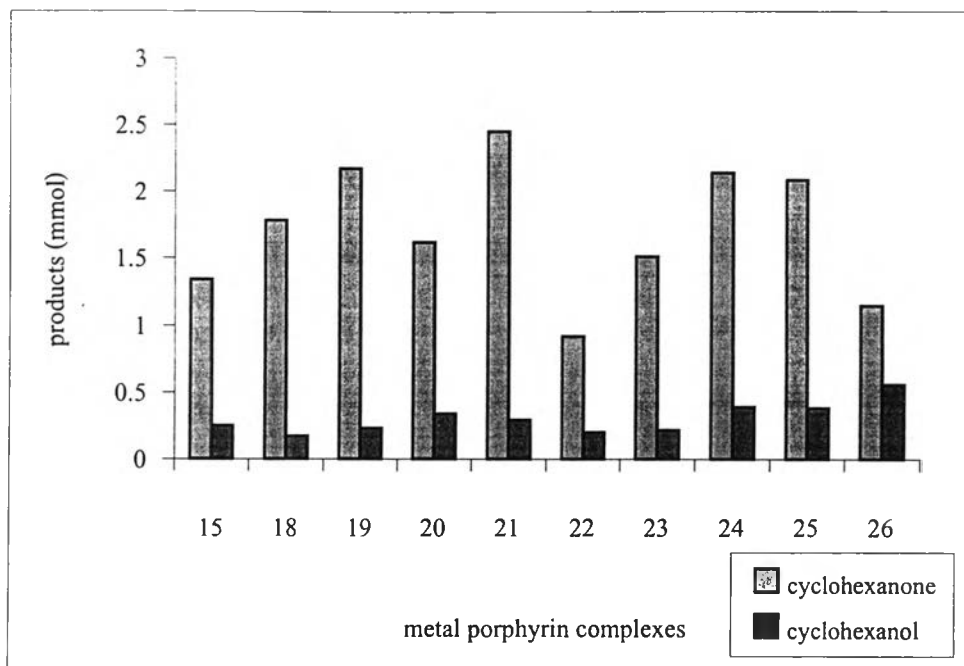
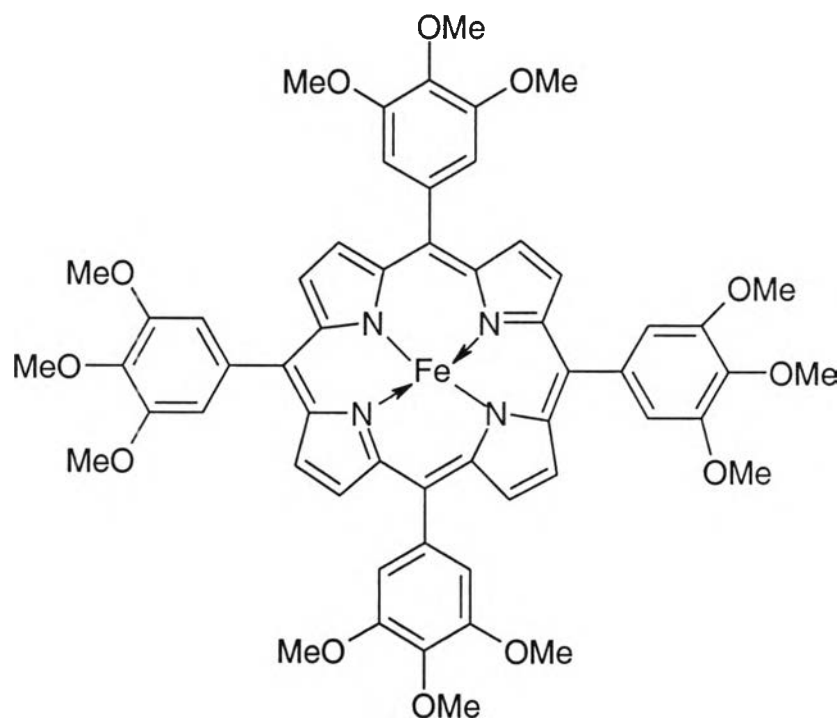


Fig 3.2 The effect of iron (II) porphyrin complexes on cyclohexane oxidation

From Table 3.2 and Fig 3.2, it is interesting to note that iron porphyrin catalysts **19**, **21**, **24** and **25** gave better results than other iron porphyrin catalysts studied. It could also be observed that the oxidation of cyclohexane in this system was dependent on the substituent of a porphyrin ring. Considering the variation of the substituent at *para* position, *p*-tert-butyl (**18**), *p*-Cl (**20**) and *p*-Br (**21**) seemed to be a good substituent because the yields of the desired products utilized these catalysts were better than Fe (II)-TPP complex. *p*-Br substituent gave the highest yield based upon this experiment. Catalyst with electron donating substituent like methyl group (**22**) gave lower yield than Fe (II)-TPP complex. At *meta* position, iron porphyrin catalyst **19** gave higher yields than those attained from using iron porphyrin catalyst **20**. Methoxy group was also found to be a good substituent. For iron porphyrin catalysts **23**, **24** and **25**, the total yields of the desired product were increased

according to the steric hindrance of catalyst. In contrast, iron porphyrin catalyst **26** reduced the yield of cyclohexanone. The substituent at *ortho* position may affect this oxidation system, indicating that the *ortho* substituent hindered itself to the low solubility in this solvent system and could not directly interact with the approaching saturated hydrocarbon molecule.

In this research, justifying from the rate of the reaction (observed at 2 hours) and the amount of total products (detected at 24 hours), iron porphyrin catalyst **25** was selected to employ as a catalyst in most oxidation of cyclohexane and other substrates.



Tetra(3,4,5-trimethoxyphenyl)-porphyrin iron(II) complex (25)

3.2.3 Effect of solvents

During the course of this research, the solvent that could provide a homogeneous reaction was required. From the experiments described above, pyridine

was the first solvent chosen as a reaction medium because it could dissolve both metal porphyrin complex catalyst and organic substrate. Other solvents such as acetone, dichloromethane, isooctane and *tert*-butanol were also selected to examine whether they can substitute pyridine in this oxidation reaction. The effect of various solvents is shown in Table 3.3.

Table 3.3 The effect of solvents in the oxidation reaction

Entry	Solvent	2 hours		24 hours	
		-one (mmol)	-ol (mmol)	-one (mmol)	-ol (mmol)
1	Pyridine	0.567	0.099	2.086	0.382
2	Acetonitrile	0	trace	trace	trace
3	Acetone	0	0	0	0
4	Dichloromethane	0	0	0	0
5	Isooctane	0	0	0	0
6	<i>tert</i> -Butanol	0	0	0	0

Reaction conditions: cyclohexane (30 mmol), **25** (0.25 mmol), solvent (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

From Table 3.3, acetonitrile, acetone, dichloromethane, isooctane and *tert*-butanol were examined whether they could replace pyridine in this oxidation reaction. It was found that when acetonitrile was used as the reaction media, the oxidation reaction provided only a small amount of product. In the case of employing acetone, dichloromethane, isooctane and *tert*-butanol, the oxidation reaction was not taken place. This may be explained that unwanted side reactions may rapidly occur instead.

Since the high toxicity and high cost of pyridine, the attempts to reduce the amount of pyridine were performed. In addition, the variation of the ratio of ketone to alcohol may be affected by the solvent systems. Thus, the variation of the amount of pyridine and co-solvent (acetonitrile) was examined and the results are shown in Table 3.4.

Table 3.4 The effect of the amount of pyridine and acetonitrile in cyclohexane oxidation

Entry	Pyridine : CH ₃ CN (mL : mL)	2 hours		24 hours		-one/-ol ratio at 24 hours
		-one (mmol)	-ol (mmol)	-one (mmol)	-ol (mmol)	
1	28 : 0	0.567	0.099	2.086	0.382	5.5
2	21 : 7	0.431	0.099	1.631	0.413	4.0
3	14 : 14	0.354	0.122	0.865	0.336	2.6
4	7 : 21	Trace	0	0.160	0.119	1.3
5	0 : 28	0	trace	trace	trace	-

Reaction conditions: cyclohexane (30 mmol), **25** (0.25 mmol), solvent (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

From Table 3.4, it was observed that when the amount of acetonitrile increased, the amount of total product was reduced and the ratio of cyclohexanone/cyclohexanol was decreased. According to these experiments, pyridine 28 mL was found to be the most appropriate solvent to provide the highest yield of the desired product.

3.2.4 Effect of the oxidants

Zinc grit coupled with air was a primary oxidant used for the oxidation of saturated hydrocarbon in this study. However, many oxidants besides zinc grit/air may be appropriate for this oxidation reaction. The results of the variation of oxidants in cyclohexane oxidation using iron (II) catalyst **25** are presented in Table 3.5 and Fig 3.3.

Table 3.5 Effect of oxidants in cyclohexane oxidation reaction^a

Entry	Oxidant	2 hours		24 hours	
		-one (mmol)	-ol (mmol)	-one (mmol)	-ol (mmol)
1	None	0	0	0	0
2	Zinc/Air	0.5670	0.099	2.086	0.382
3	2-Ethylbutyraldehyde/O ₂	trace	0	0.112	Trace
4	TBHP	0	0	0	0
5	TBHP ^b	1.540	0.653	1.679	0.644
6	H ₂ O ₂	0.427	0.225	1.285	0.331

a. Reaction conditions: cyclohexane (30 mmol), **25** (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), oxidizing agent (15 mmol) at RT

b. at 70 °C.

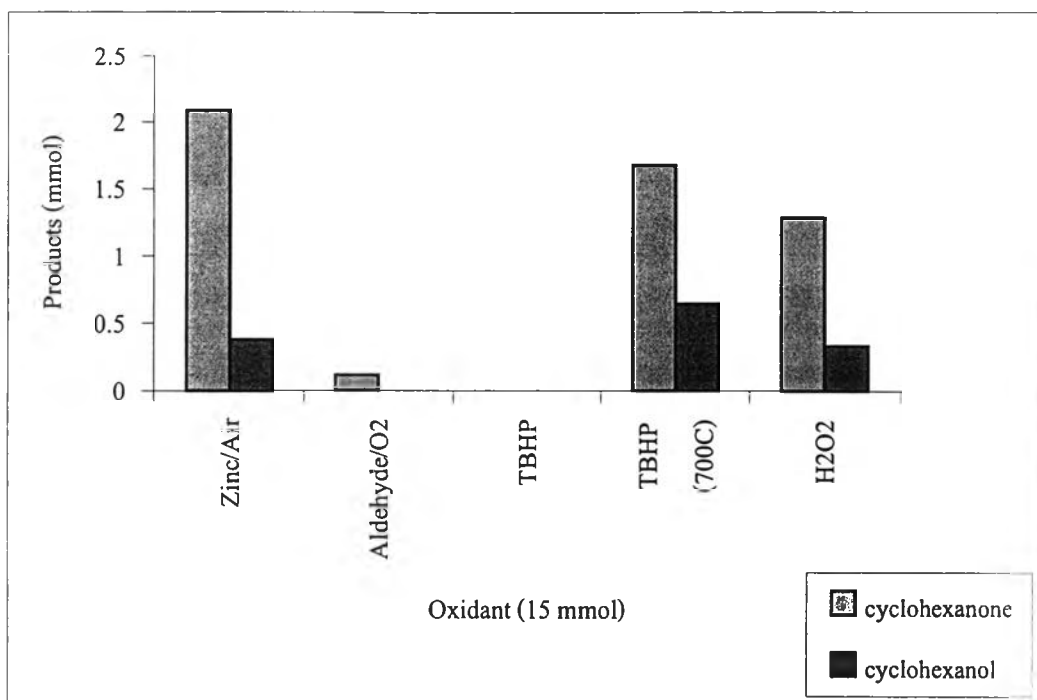


Fig 3.3 Effect of oxidants in cyclohexane oxidation reaction

Concerning the amount of the desired products and the rate of the reaction, it was found that zinc grit/air was significantly better oxidant than 2-ethylbutyraldehyde/O₂, *tert*-butyl hydroperoxide (TBHP) 70% in water and hydrogen peroxide 30% in water for the oxidation of cyclohexane at room temperature and atmospheric pressure. The reaction employing 2-ethylbutyraldehyde/O₂ produced only small amount of cyclohexanone and trace amount of cyclohexanol. TBHP was found not to be a good oxidant at room temperature. However, the oxidation reaction using TBHP as oxidant was proceeded smoothly at 70 °C. It could clearly see that the rate of the reaction with TBHP at 70 °C was almost completed within 2 hours. This result implied that TBHP was more efficient in term of the rate of the reaction. Further study on cyclohexane oxidation using TBHP as an oxidant is presented in

section 3.6. However, as shown in a blank experiment, the oxidation of cyclohexane will not take place without oxidant.

3.3 Kinetic study on the reaction rate of cyclohexane oxidation

Various recent catalytic models mimicking enzymatic systems had been developed in order to be of a capability to proceed at room temperature and atmospheric pressure. Nevertheless, the rates of these reactions were generally slow and needed to spend more time to complete the reaction. Consequently, the catalytic systems that consume less time to complete the reaction should be illicitly required. The kinetic analysis results of cyclohexane oxidation are presented in Fig 3.4.

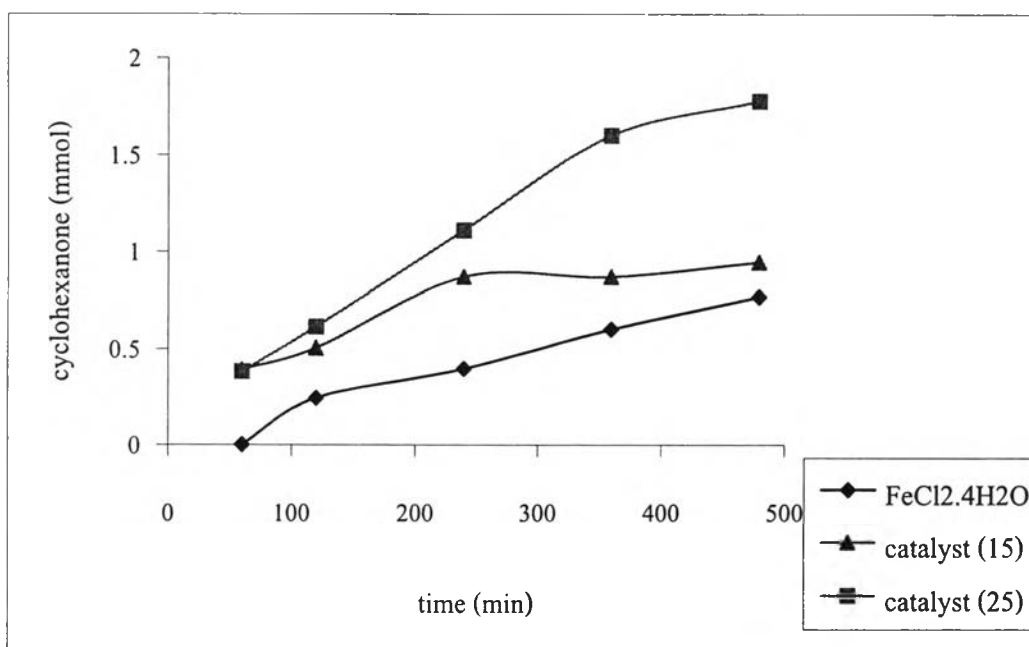


Fig 3.4 Kinetic study on cyclohexane oxidation catalyzed by selected iron catalysts

From Fig 3.4, it was found that the rate of the reaction employing iron (II) porphyrin catalyst **25** was significantly better than that utilized iron (II) porphyrin catalyst **15** and $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$. The desired product was taken place when the reaction time was about 60 minutes by using either iron porphyrin catalyst **25** or **15**. From this result, it could be observed that under this particular system the reaction with catalyst **25** proceeded the oxidation reaction pretty fast. Moreover, cyclohexane oxidation using the series of iron (II) porphyrin complex catalysts reinforced the concept of the importance of ligand around metal ion. The appropriate ligand as proposed should be hindered substituents in the porphyrin rings and may affect the rate and selectivity of the oxidation reaction.

3.4 Chemoselectivity study

Another important factor that needs to be carefully examined is the selectivity. The addition of an additive to the reaction system would provide some clues for the selectivity of the studied system. Four additives, namely ascorbic acid, imidazole, triphenylphosphine and carbon tetrachloride were chosen in this study.

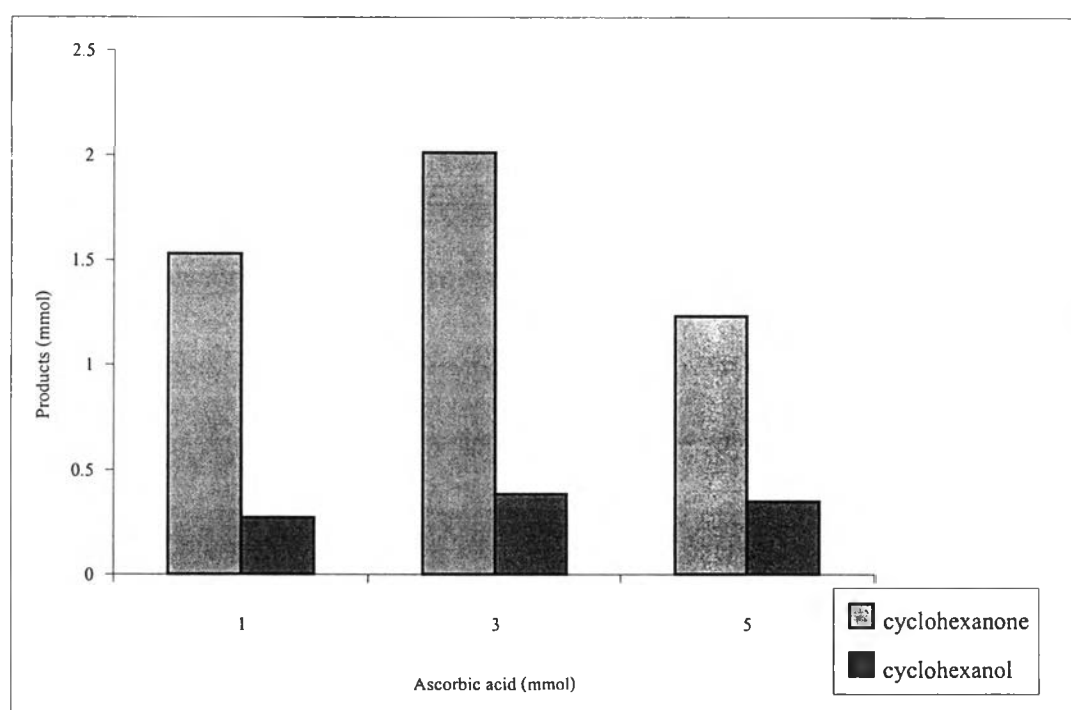
3.4.1 Effect of ascorbic acid

Ascorbic acid was a well-known biochemical reductant. The variation of the amount of ascorbic acid was examined and the results are presented in Table 3.6 and Fig 3.5.

Table 3.6 Effect of ascorbic acid in cyclohexane oxidation

Entry	Ascorbic acid (mmol)	24 hours		Total yields at 24 hours	-one/-ol ratio at 24 hours
		-one (mmol)	-ol (mmol)		
1	none	1.340	0.249	1.589	5.4
2	1	1.528	0.270	1.798	5.7
3	3	2.015	0.384	2.399	5.2
4	5	1.231	0.349	1.580	3.5

Reaction conditions: cyclohexane (30 mmol), **15** (0.25 mmol), ascorbic acid (varied), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

**Fig 3.5** Effect of ascorbic acid in cyclohexane oxidation

The results obtained from Table 3.6 clearly revealed that ascorbic acid had an effect on the cyclohexane oxidation. The maximum yield was gained upon the addition of this additive 3 mmol. This may be explained that ascorbic acid itself may react with oxygen to produce superoxide, as zinc grit does. That makes the reaction proceeded with more efficiency. The addition of ascorbic acid 5 mmol provided the decreasing of total yields. It may be explained that ascorbic acid reacted with oxygen to produce more superoxide. Then, unwanted side reaction may compete with the desired oxidation reaction to produce another products. Other explanation was ascorbic acid may form buffer with pyridine like pyridine-acetic acid system and decreased the efficiency of reducing agent. Considering the cyclohexanone/cyclohexanol ratio, it was observed that this ratio had a tendency to decrease when adding more ascorbic acid to the system. The reason was probably derived from the reduction of cyclohexyl hydroperoxide intermediate.

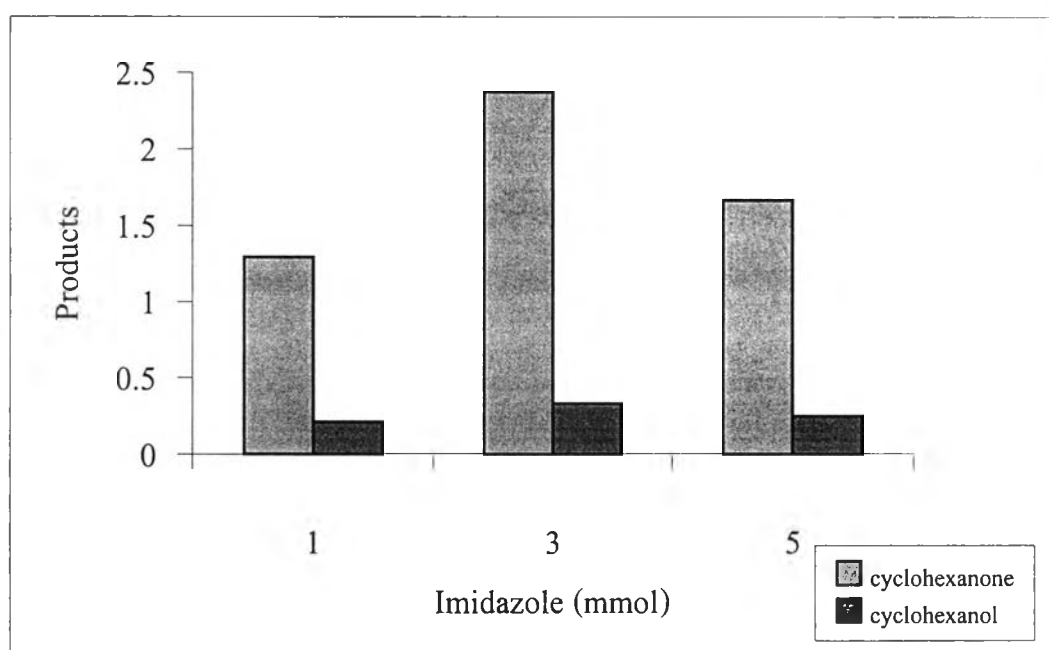
3.4.2 Effect of imidazole

Imidazole was another additive selected to observe its effect on the oxidation reaction. A nitrogenous like imidazole used to be reported to act as a very efficient cocatalyst for the oxidation of cyclohexane. The results are presented in Table 3.7 and Fig 3.6.

Table 3.7 Effect of imidazole on cyclohexane oxidation

Entry	Imidazole (mmol)	24 hours		Total yields at 24 hours	-one/-ol ratio at 24 hours
		-one (mmol)	-ol (mmol)		
1	none	1.340	0.249	1.589	5.4
2	1	1.293	0.212	1.505	6.1
3	3	2.370	0.331	2.701	7.2
4	5	1.665	0.252	1.917	6.6

Reaction conditions: cyclohexane (30 mmol), **15** (0.25 mmol), imidazole (varied), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

**Fig 3.6** Effect of imidazole in cyclohexane oxidation

With the addition of imidazole, the oxidation reaction could perform efficiently and provided a large increase in the amount of ketone formed. Similar to

the addition of ascorbic acid, the addition of imidazole 3 mmol provided the highest yield of the desired products. However, the addition of imidazole did not affect on the cyclohexanone/cyclohexanol ratio. Moreover, this attained results were in good agreement with those experimented by Nam and coworkers that oxidation of alkanes in the presence of imidazole gave significant amount of the corresponding ketone and alcohol.⁴²

3.4.3 Effect of triphenylphosphine

Triphenylphosphine was another additive selected for chemoselectivity study.

The results are exhibited in Table 3.8 and Fig 3.7.

Table 3.8 Effect of triphenylphosphine on cyclohexane oxidation

Entry	PPh ₃ (mmol)	24 hours		Total yields at 24 hours	-one/-ol ratio at 24 hours
		-one (mmol)	-ol (mmol)		
1	None	1.340	0.249	1.589	5.4
2	1	1.321	0.568	1.889	2.3
3	3	1.860	1.331	3.191	1.4
4	5	0.690	1.529	2.219	0.5
5	7	0.773	1.904	2.677	0.4
6	10	0.624	1.997	2.621	0.3

Reaction conditions: cyclohexane (30 mmol), **15** (0.25 mmol), triphenylphosphine (varied), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

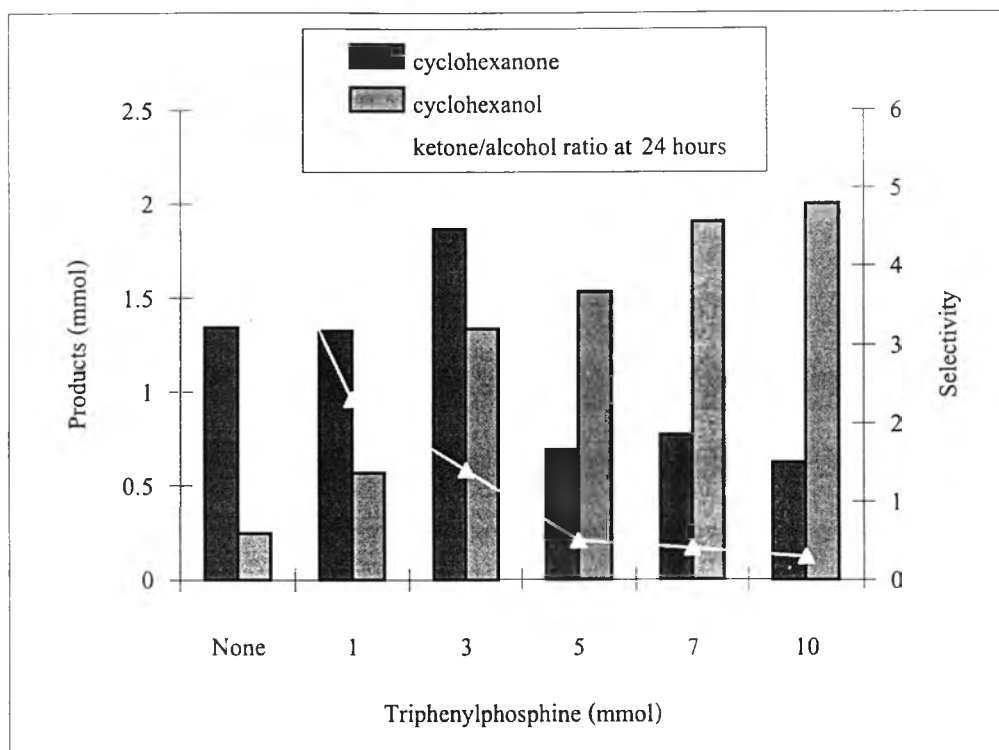


Fig 3.7 The effects of triphenylphosphine

The results obtained from the addition of triphenylphosphine provided very impressive results. Upon the addition of this additive, the activation process was taken place more efficiently. The total yields of the oxidized products were increased. Interestingly, the production of alcohol under this particular conditions was found to be prevailed over that of ketone. This manifestly implied the reduction of the alkyl hydroperoxide intermediate as it was noticed in the former case, ascorbic acid.

It could be seen that the outcome from chemoselectivity study provided important clues for mechanistic study. The addition of triphenylphosphine, or another reducing agent such as ascorbic acid, strongly supported the idea for the presence of an intermediate, possibly alkyl hydroperoxide. Therefore, at least two distinct

intermediates should appear along the pathway of transformation of alkanes to ketones. The details of mechanistic discussion will be addressed in section 3.8.

3.4.4 The effect of carbon tetrachloride

Carbon tetrachloride was another additive that would prove the idea for the existence of an intermediate. In order to gain insight the possible mechanism of the cyclohexane oxidation catalyzed by iron (II) porphyrin catalyst **25**, carbon tetrachloride was selected to use as a trapping agent. The results are shown in Table 3.9.

Table 3.9 Effect of carbon tetrachloride in cyclohexane oxidation

Entry	Carbon tetrachloride (mmol)	24 hours			Total yields at 24 hours
		Cyclohexene (mmol)	-one (mmol)	-ol (mmol)	
1	None	0	1.340	0.249	1.589
2	3	trace	1.303	0.214	1.517
3	10	0.625	0.158	trace	0.158
4	20	1.371	0	0	0

Reaction conditions: cyclohexane (30 mmol), **15** (0.25 mmol), carbon tetrachloride (varied), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

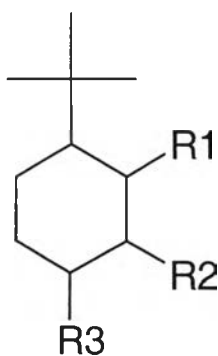
When carbon tetrachloride 3 mmol was added to the reaction media, cyclohexanone and cyclohexanol were still detected as major products. In the presence of carbon tetrachloride 10 mmol, the amount of cyclohexanone and cyclohexanol were reduced and did not give any cyclohexanone or cyclohexanol

when carbon tetrachloride 20 mmol was added. High yield of cyclohexene was instead detected. This result indicated that the trapping agent, carbon tetrachloride, may trap the intermediate of the reaction and transform to cyclohexylchloride. Then, the unstable cyclohexylchloride under this particular condition will be take place *via* an elimination reaction to produce cyclohexene. The addition of carbon tetrachloride to inhibit the reaction process supported the proposed mechanism which was taken place *via* at least two intermediates.

3.5 Regioselectivity study

For further study on regioselectivity of this developed oxidation system, the oxidation of *tert*-butylcyclohexane (**27**) and *n*-pentane (**34**) was investigated using iron (II) porphyrin complex **25** as catalyst. The results are shown in Tables 3.10 and 3.11.

3.5.1 Oxidation of *tert*-butylcyclohexane using iron (II) porphyrin complex as catalyst



- (27) $R^1 = H, R^2 = H, R^3 = H$
 (28) $R^1 = C=O, R^2 = H, R^3 = H$
 (29) $R^1 = H, R^2 = C=O, R^3 = H$
 (30) $R^1 = H, R^2 = H, R^3 = C=O$
 (31) $R^1 = OH, R^2 = H, R^3 = H$
 (32) $R^1 = H, R^2 = OH, R^3 = H$
 (33) $R^1 = H, R^2 = H, R^3 = OH$

Table 3.10 The oxidation of *tert*-butylcyclohexane catalyzed by iron (II) porphyrin complex **25**

Products	Oxidants		
	Zinc grit/air ^a		TBHP ^b
	2 hours (mmol)	24 hours (mmol)	24 hours (mmol)
28	trace	0.028	0.178
29	0.291	0.901	1.089
30	0.128	0.386	0.427
31	0	trace	trace
32	trace	trace	trace
33	0	trace	trace

a. Reaction conditions: *tert*-butylcyclohexane (30 mmol), **15** (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

b. same as (a) except at 70 °C

From Table 3.10, it was found that the positions 3- and 4- in *tert*-butylcyclohexane were preferentially oxidized and little oxidation occurred at the 2-position. The ratio of 2-one : 3-one : 4-one (**28** : **29** : **30**) was 1 : 32 : 14 when zinc grit/air was used as an oxidant and 1 : 6 : 2 when *tert*-butyl hydroperoxide as an oxidant was utilized. This ratio was obviously pointed out that zinc grit/air system gave higher selectivity than that using *tert*-butyl hydroperoxide. When the reaction was performed for 2 hours, 3- and 4-*tert*-butylcyclohexanones gave similar yields, and 3-*tert*-butylcyclohexanone gave high yield when the reaction was proceeded for 24 hours. This observation displayed that *tert*-butyl substituent on cyclohexane had a profound effect on the oxidation reaction and induced the oxidation took place at 3-

position. This selectivity was found to be the same as the former report. Nappa and his colleague was able to oxidize *tert*-butylcyclohexane using iron (III) porphyrin as catalyst and iodozobenzene as an oxidant to give similarly selectivity but alcohol is the major product.⁴³

3.5.2 Oxidation of *n*-pentane using iron (II) porphyrin complex **25** as catalyst

Another selected important substrate hydrocarbon to be examined is *n*-pentane.

The results of the oxidation of *n*-pentane is presented as shown in Table 3.11.

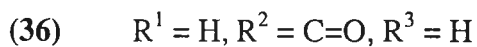
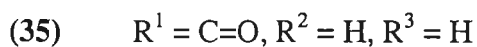
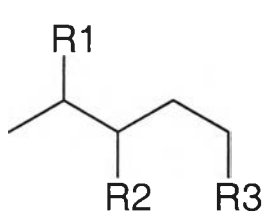


Table 3.11 The oxidation of *n*-pentane catalyzed by iron (II) porphyrin complex

Products	Oxidants	
	Zinc grit/air ^a	TBHP ^b
	24 hours (mmol)	24 hours (mmol)
2-pentanone (34)	trace	2.140
3-pentanone (35)	0.990	trace
1-pentanol (36)	0.235	0
2-pentanol (37)	0	trace
3-pentanol (38)	0.051	0

a. Reaction conditions: *n*-pentane (30 mmol), **25** (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

b. Same as (a) except at 70 °C

From Table 3.11, there is the difference between two reactions studied using different oxidants. When zinc grit/air was used as an oxidant, it was clearly seen that 3-pentanone was a major product. In contrast, when *tert*-butyl hydroperoxide was employed as an oxidant, 2-pentanone was surprisingly found to be a major product. From the same literature cited above, Nappa also oxidized *n*-pentane using iron (III) porphyrin as catalyst and iodosobenzene as an oxidant. 2-Pentanone was a major product. The selectivity may be depended on the oxidant used in the oxidation reaction. The oxidation reaction using iodosobenzene or *tert*-butyl hydroperoxide as an oxidant was believed to take place *via* radical pathway, while the oxidation reaction using zinc grit/air was proved to be non-radical fashion. Considering from the difference of products obtained, another effect such as solvent may perhaps affect the selectivity of each reaction condition.

3.6 Oxidation of cyclohexane in the absence of organic solvent

In this study, the oxidation reaction was proceeded in the absence of organic solvent. Cyclohexane itself was used as a solvent. The effect of the small amount of pyridine present in the reaction was also examined. Due to the efficiency of *tert*-butyl hydroperoxide (TBHP) as described in Table 3.5 and Fig 3.3, TBHP 15 mmol was employed as an oxidizing agent at 70°C instead of zinc grit/air. The results are tabulated in Table 3.12 and Fig 3.8.

Table 3.12 The effect of the amount of pyridine in cyclohexane oxidation

Entry	Pyridine (mL)	24 hours		Total products (mmol)	-one/-ol at 24 hours
		-one (mmol)	-ol (mmol)		
1	0	4.748	4.061	8.809	1.169
2	1	4.469	3.162	7.631	1.414
3	3	3.002	3.035	6.037	0.967
4	5	1.808	1.870	3.678	0.989

Reaction conditions: cyclohexane (30 mmol), **25** (0.20 mmol), pyridine (varied), TBHP (15 mmol) at 70°C.

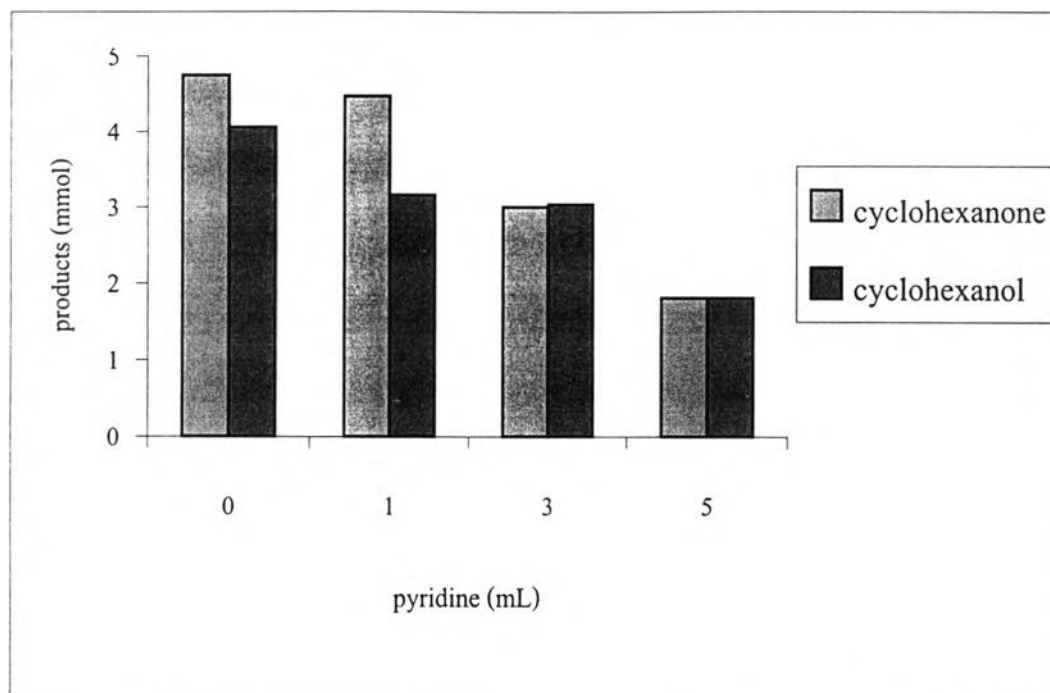
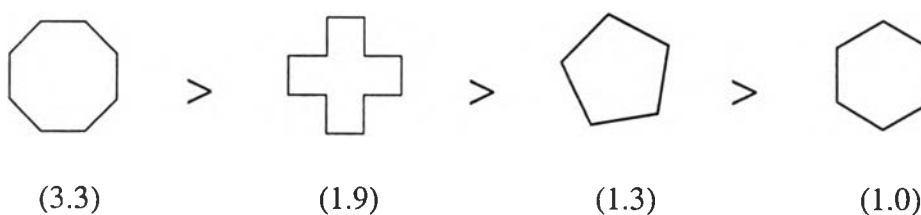


Fig 3.8 Variation of the amount of pyridine in cyclohexane oxidation

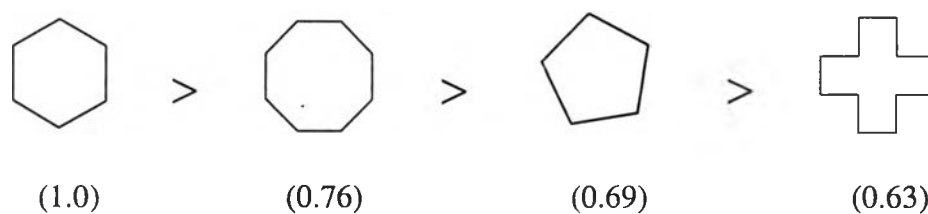
From Table 3.12 and Fig 3.8, it was found that the reaction using iron (II) porphyrin **25** as catalyst and TBHP as oxidant at 70⁰C could take place smoothly and efficiently in the absence of any organic solvent. In contrast, the reactions performed with increasing quantities of pyridine did not give the increment of the amount of cyclohexanol formed. It was seen that the total amount of products decreased with the increasing amount of pyridine. The addition of pyridine in fact gave important clues for the mechanistic study. Generally, the reaction proceeded *via* radical pathway could be trapped by appropriate trapping agents such as bromotrichloromethane, pyridine, etc. Under this particular conditions using TBHP as an oxidant, the reaction was clearly proved to occur *via* radical fashion. The more pyridine added, the less oxidized products obtained.

3.7 Comparative study on relative reactivity of cycloalkanes in oxidation reaction

Mechanistic study of this oxidation system is another challenging aspect. It is widely known that there are two possible mechanisms proposed for the oxidation of cyclohexane catalyzed by metal catalysts. First, the reaction took place *via* a free radical pathway. The other was believed not to involve the radical reaction. From literature, the comparison of a series of saturated hydrocarbons with bromination by BrCCl_3 was presented. For the radical bromination, the relative reactivity could be arranged as following to this order⁴⁴ :











On the other hand, for non-radical mechanism, the relative reactivity could be shown as following to this order :



Moreover, it is noteworthy that the reaction was taken place *via* the radical reaction when the relative reactivity of cyclopentane/cyclohexane was more than 1.0. In contrast, when the relative reactivity of cyclopentane/cyclohexane was less than 1.0, the reaction was proceeded by the non-radical reaction.⁴⁵ To justify whether the

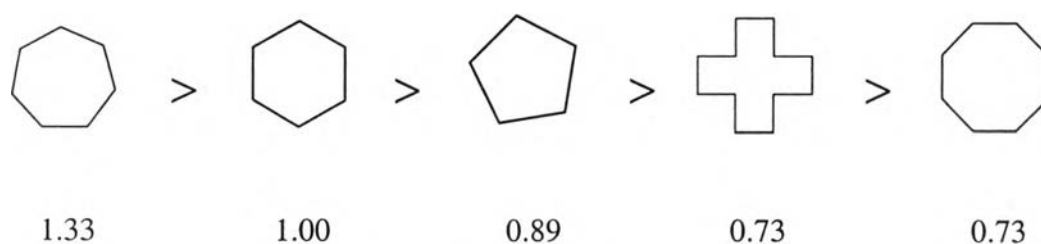
mechanism of the oxidation of saturated hydrocarbons catalyzed by metal porphyrin complex in this research was taken place *via* radical reaction or not, the comparison of relative reactivity order per hydrogen towards a series of cyclic saturated hydrocarbons was systematically studied. The results are summarized in Table 3.13.

Table 3.13 Comparison of reactivity order per hydrogen for a series of cyclic saturated hydrocarbons

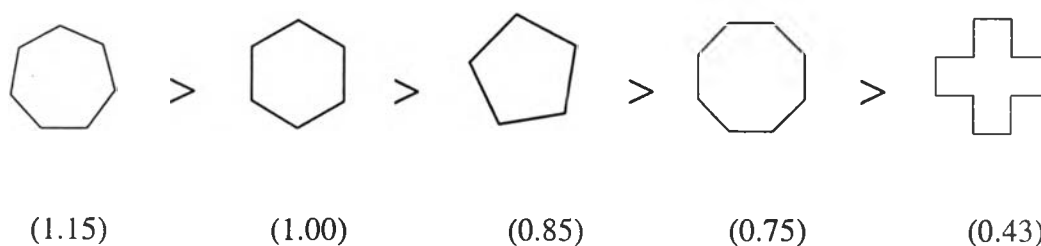
R ¹ H	R ² H	R ¹ H or R ² H (mmol)	Products (mmol)		Relative Reactivity R ² (H)/R ¹ (H)
			R ¹ =O	R ² =O	
		15	0.943	0.701	0.893
		15	0.579	0.897	1.328
		15	0.770	0.751	0.731
		15	0.506	0.743	0.733

Reaction conditions: substrates (15 mmol each), **25** (0.25 mmol), pyridine (28 mL), acetic acid (2.3 mL), zinc grit (1.31 g) at RT

From Table 3.13, it was found that the relative reactivity for a series of cyclic saturated hydrocarbons catalyzed by iron (II) porphyrin complex (**25**) was :



In addition, this reactivity was almost be the same as the comparison relative reactivity in the oxidation reaction of cycloalkanes catalyzed by iron catalyst in Gif-type system⁴⁶ :



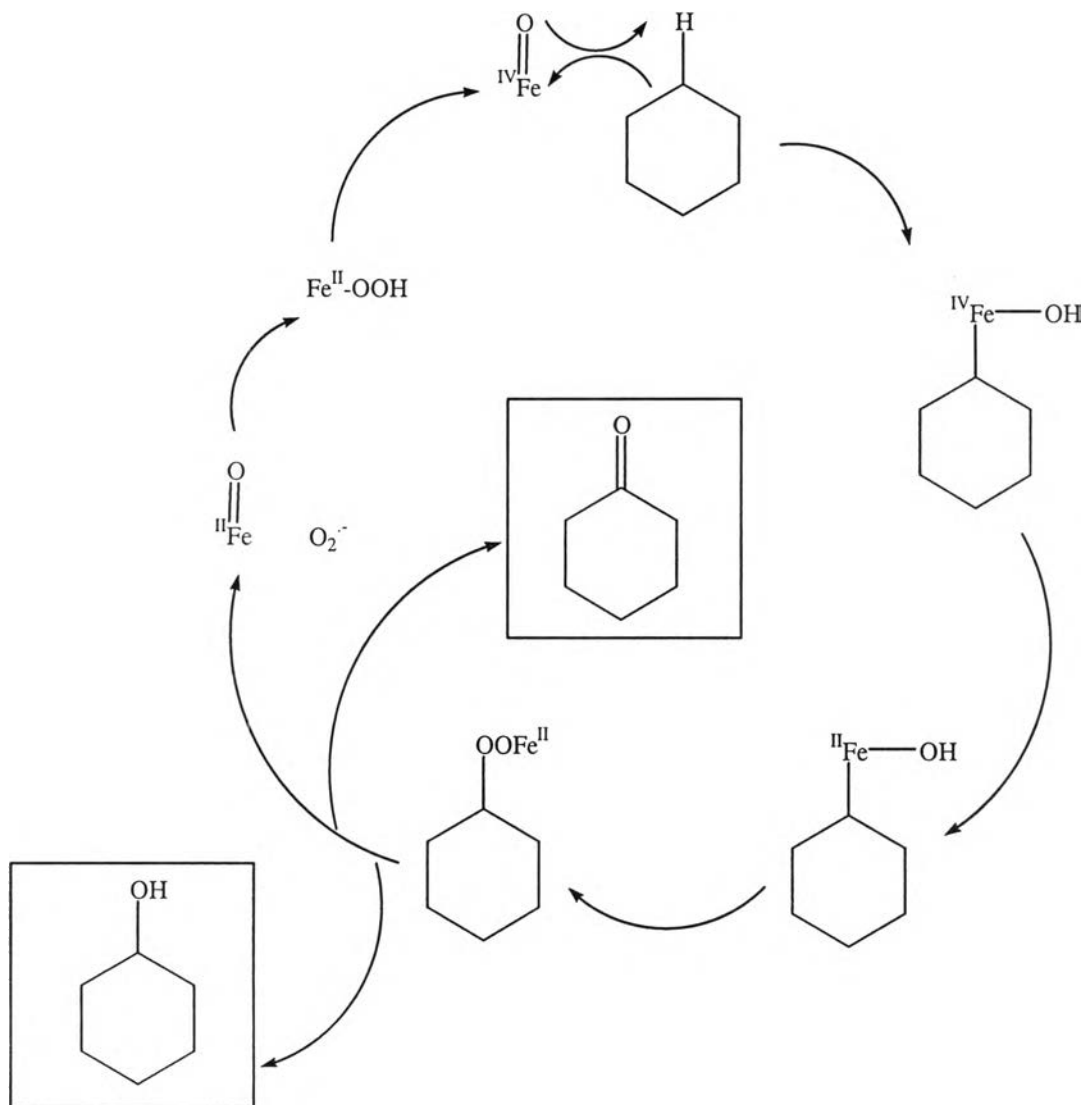
Moreover, the relative reactivity of cyclopentane/cyclohexane in this study was less than 1.0. This data supported the idea that the mechanism of the oxidation of cycloalkanes catalyzed by metal porphyrin complex catalysts in this study not take place *via* the radical pathway.

3.8 The proposed mechanistic pathway for Fe (II) porphyrin-catalyzed oxidation of cycloalkane

3.8.1 Proposed mechanism of cyclohexane oxidation using zinc grit/air as an oxidant

Besides the chemoselectivity study, the comparative study on the relative reactivity of saturated hydrocarbon from the above results (section 3.7) also indicated that the mechanism of this oxidation reaction was not proceeded *via* free radical pathway. It was proposed that zinc grit will reduce oxygen in the air to be superoxide.

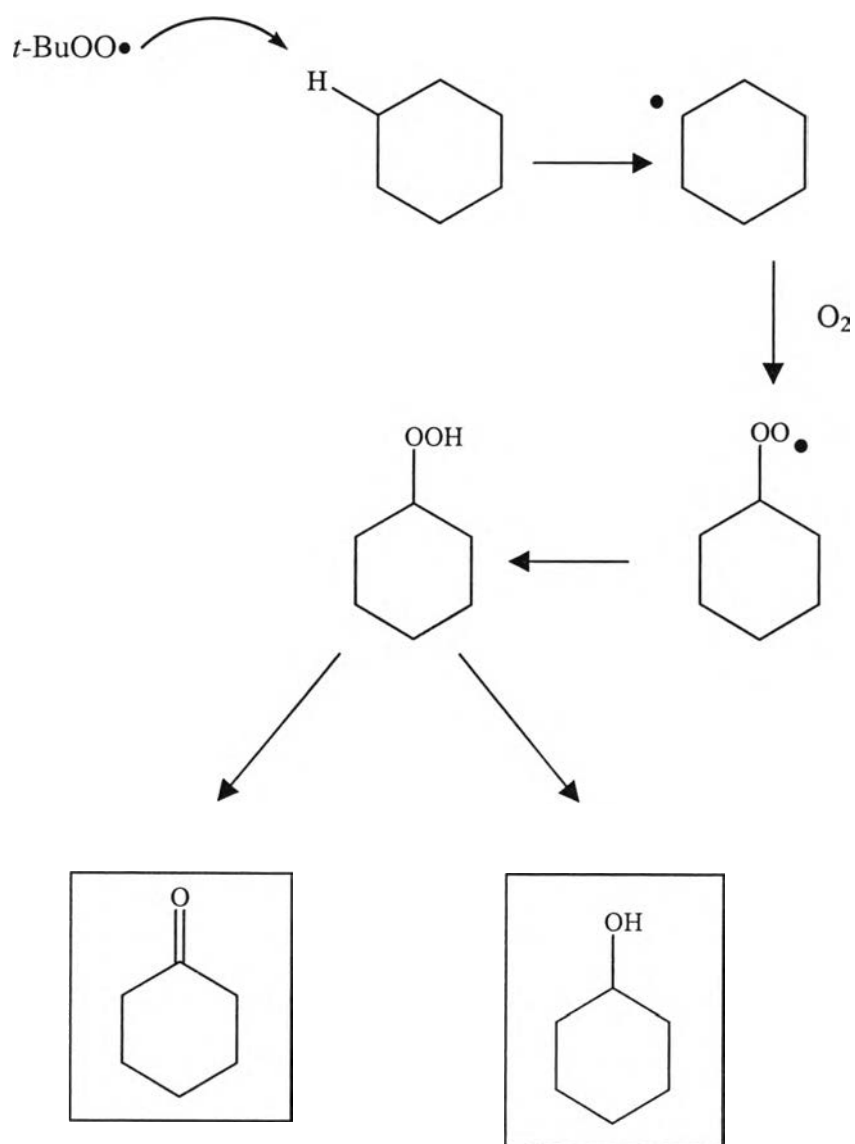
Then, superoxide was transferred to iron (II) and the oxidation was carried out by high-valent iron (IV) oxo species. After that, the insertion reaction of high-valent iron (IV) oxo species will be taken place. After the reduction, oxygen insertion will occur to be cyclohexyl hydroperoxide and then cyclohexanone and cyclohexanol will be formed. The proposed mechanism of the iron (II) porphyrin-catalyzed oxidation of cyclohexane using zinc grit/air as an oxidant is shown in Scheme 3.1.⁴⁷



Scheme 3.1 The proposed mechanism of the iron (II)-catalyzed oxidation of cyclohexane using zinc grit/air as an oxidant

3.8.2 Mechanism of cyclohexane oxidation using *tert*-butyl hydroperoxide as an oxidant

From the results of the variation of the oxidants aforesaid (section 3.2.4), the possible mechanistic pathway of the reaction employing TBHP as an oxidant may involve a free radical reaction. The reaction could not proceed at room temperature but required a higher temperature. At that temperature, TBHP may homolytically cleavage and produce *t*-butyl peroxy radical (*t*-BuOO•). This radical might abstract hydrogen from cyclohexane and hence produced cyclohexyl radicals. Oxygen may then react with the produced carbon radical to form cyclohexyl hydroperoxide which then collapsed to the final products. The proposed mechanism of the iron (II)-catalyzed functionalization of cyclohexane using TBHP as an oxidant is shown in Scheme 3.2.



Scheme 3.2 The proposed mechanism of the iron (II) porphyrin-catalyzed oxidation of cyclohexane using *tert*-butyl hydroperoxide as an oxidant