

CHAPTER IV

RESULTS AND DISCUSSION

This research was mainly focused on one of industrially important processes, the oxidation of cyclohexane to cyclohexanone and cyclohexanol. Various biomimetic chemical models capable of functionalizing alkanes have in fact shared some common features. In general, these systems are composed of a metal ion or complex as a catalyst, an organic ligand and an oxidant in a reaction medium. These variable factors greatly affect the ratio of products arising from the reaction. In this study, the substrate used was mainly cyclohexane. Other substrates such as cyclopentane, cycloheptane, or other cyclic hydrocarbons were sometimes used for some specific purposes. Both copper salts and copper complexes were utilized as catalysts in this reaction. Solvents were mostly a mixture of pyridine and acetic acid. Other solvents such as acetonitrile, acetone, *etc* were also employed in order to search for an alternatively appropriate solvent system. Two major oxidants employed were hydrogen peroxide and *tert*-butyl hydroperoxide.

The Optimum Conditions for the Oxidation of Cyclohexane

Effects of copper catalyst

In order to seek for appropriate copper catalysts that could catalyze the reaction to convert cyclohexane to cyclohexanone and cyclohexanol, various copper salts and synthesized copper complexes were selected. The results of utilization of various copper catalysts are summarized in Table 4.1.

Table 4.1 The results of the oxidation of cyclohexane catalyzed by various copper catalysts^a

Entry	Cu catalysts	20 min		O/N	
		A (mmol)	B (mmol)	A (mmol)	B (mmol)
1	-	0	0	0	0
2	CuCl	0.922	trace	0.859	trace
3	CuCl ₂ .2H ₂ O	0.525	0.072	0.754	trace
4	CuCl ₂ on Al ₂ O ₃	0.543	trace	0.714	trace
5	CuBr	0.660	trace	0.609	trace
6	CuBr ₂	0.578	trace	0.630	trace
7	CuSO ₄	0.086	trace	0.579	0.080
8	Cu(OAc) ₂ .H ₂ O	0.899	0.058	0.928	0.027
9	Cu(N ₂ O ₆).3H ₂ O	1.006	0.052	0.990	0.031
10	Cu(dipic).2H ₂ O	0	0	0.033	0.019
11	Cu(dipic)(py)	0	0	0.031	0.017
12	Cu(salen)	0	0	0.849	trace
13	Cu(acac) ₂	0.345	0.084	0.628	trace

a. reaction conditions : cyclohexane (20 mmol), copper catalyst (0.2 mmol), pyridine (30 mL), acetic acid (3 mL), H₂O₂ (15 mmol)

A = cyclohexanone, B = cyclohexanol

From Table 4.1, it could clearly be seen that the alkane oxidation catalyzed by copper catalysts proceeded very fast. The reaction was almost finished within 20 minutes or less. This finding was in contrast to the reaction utilizing iron catalysts.⁵³ Whereas the former reaction can take place very rapidly, the latter was found a little bit slower. Blank experiments clearly showed that in the absence of either catalysts or hydrogen peroxide (oxidant), the oxidation did not occur.

Among copper catalysts employed, the utilized copper salts such as CuCl, Cu(N₂O₆).3H₂O, and Cu(OAc)₂.H₂O as catalysts gave higher yields than copper complexes such as Cu(dipic).2H₂O and Cu(dipic)(py). Cu(N₂O₆).3H₂O provided the highest yield but the reaction was not totally homogeneous (entry 9). The reaction employing CuCl and Cu(OAc)₂.H₂O also gave high yield of the desired products. These reactions were homogeneous. Therefore, both copper salts were considered as appropriate catalysts for further investigation.

With regarding of CuCl, CuCl₂.2H₂O, CuCl₂ on Al₂O₃, CuBr and CuBr₂, it suggested that Cu(I) possessed a better reactivity than Cu(II). Cu(I) might participate in the mechanism and make the reaction rate more rapid. The reaction was completed within 20 minutes. However, Cu(I) or Cu(II) were not the only factor that influenced on yield and reaction rate of the reaction. Comparative studies between Cu(II) salts showed that CuCl₂.2H₂O or CuCl₂ on Al₂O₃ and Cu(OAc)₂.H₂O which had different counterions (ligands) gave different yield (entries 3, 4 and 8).

CuCl₂ on Al₂O₃, a commercial available catalyst, was selected to explore its catalytic activity in this reaction and to see whether it could be used as a heterogeneous catalyst in the oxidation reaction. From Table 4.1, it was found that using either this catalyst or CuCl₂.2H₂O did not make the yield of cyclohexanone and cyclohexanol different (entries 3 and 4). Another question arose whether that copper catalyst was dissolved into the reaction medium or was still remained on the adsorbent. A set of experiments was thus performed and the results are tabulated in Table 4.2.

Table 4.2 The effects of CuCl_2 on Al_2O_3 on the oxidation of cyclohexane^a

Procedure	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
A	20	0.792	trace	0.792
	O/N	0.733	trace	0.733
B	20	trace	trace	trace
	O/N	0.217	trace	0.217
C	20	0.749	trace	0.749
	O/N	0.831	trace	0.831

a. reaction conditions : cyclohexane (20 mmol), CuCl_2 on Al_2O_3 (0.2 mmol), pyridine (30 mL), acetic acid (3 mL), H_2O_2 (15 mmol)

A = CuCl_2 on Al_2O_3 was direct used in the reaction.

B = The same procedure as A was carried out. The copper catalyst was filtered and reused in the next reaction.

C = CuCl_2 on Al_2O_3 was dissolved in the solvent system, then filtered. The filtrate was further used in the oxidation reaction.

From Table 4.2, it was found that CuCl_2 was in fact dissolved from the surface of Al_2O_3 to the reaction media. That is the reason why it did not provide different results from using $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ as a catalyst alone.

The effect of the copper catalyst concentration was the next parameter that was evaluated. The results are presented in Table 4.3 and Figure 4.1. It was clearly seen that in the absence of $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$, the oxidation did not occur. The final yield was dependent on the amount of catalyst used. $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ 0.2 mmol gave the highest reaction yield and high selectivity of ketone to alcohol ratio compared with other concentrations tested. The excess of $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ did not give the highest reaction yield. However, it could catalyze the reaction to completion within 20 minutes. On the other hand, when the amount of $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ used was less than 0.2 mmol, the reaction rate decreased. Catalytic turnover was a technical value to point out an

efficiency of catalysts. For instance, the catalytic turnover when $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ 0.2 mmol was used was found to be about 8. This meant that $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ could produce the products about 8 times of the amount of copper catalyst employed.

Table 4.3 The effects of catalyst concentration^a

$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (mmol)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)	Catalytic turnover
0	20	0	0	0	0
	O/N	0	0	0	0
0.01	20	0.051	0.028	0.079	7.90
	O/N	0.198	0.059	0.257	25.70
0.05	20	0.289	0.068	0.357	7.14
	O/N	0.643	0.051	0.694	13.88
0.1	20	0.563	0.062	0.625	6.25
	O/N	0.804	0.055	0.859	8.59
0.2	20	1.497	trace	1.497	7.49
	O/N	1.545	trace	1.545	7.73
0.5	20	1.415	0.055	1.470	2.94
	O/N	1.350	0.056	1.406	2.81
1.0	20	0.927	0.058	0.985	0.99
	O/N	0.930	0.063	0.993	0.99

a. reaction conditions : cyclohexane (20 mmol), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (variable), pyridine (30 mL), acetic acid (1 mL), H_2O_2 (15 mmol)

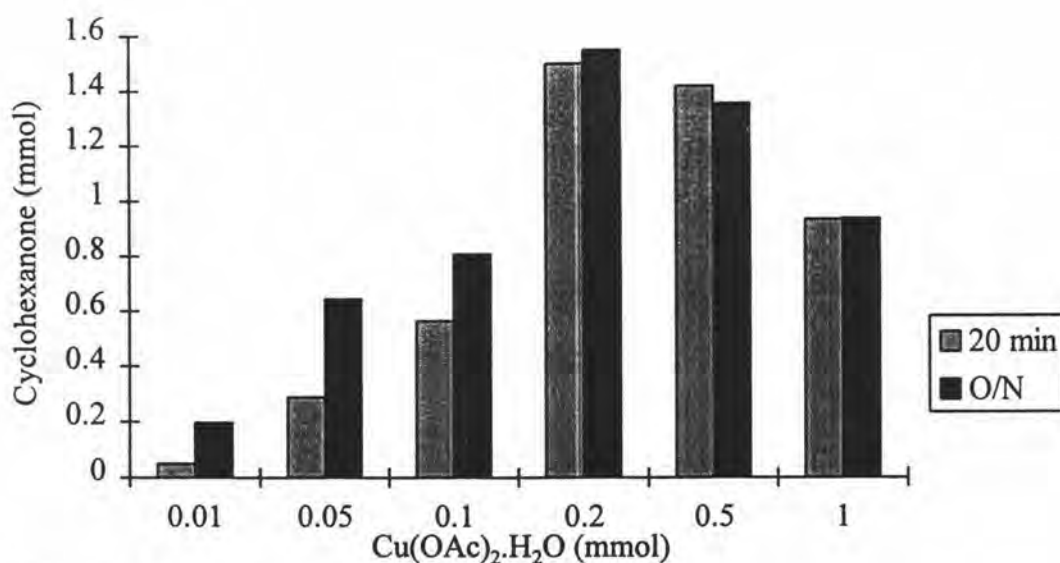


Figure 4.1 The effects of catalyst concentration

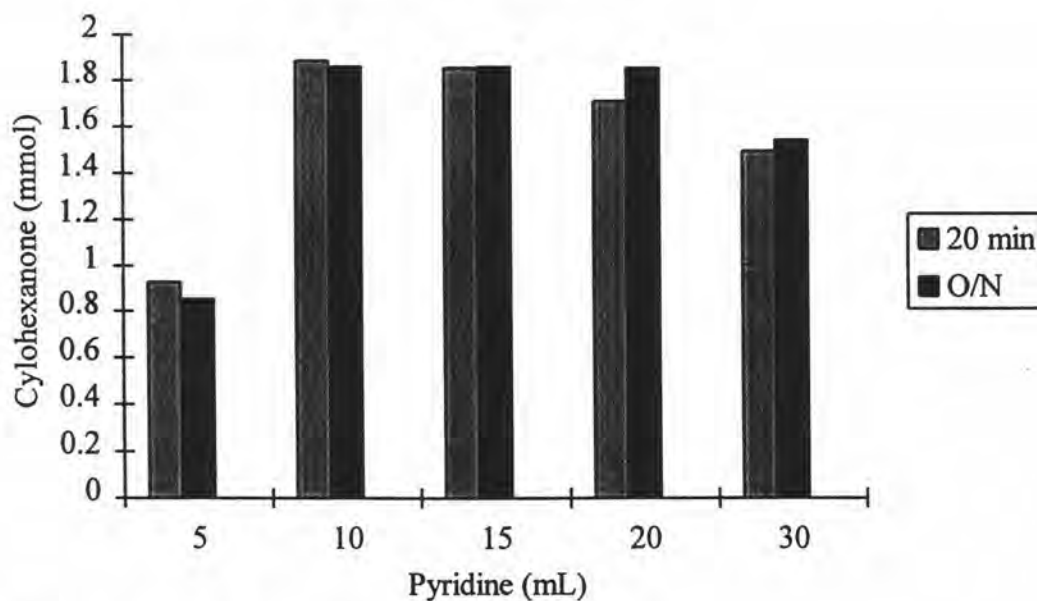
Effects of solvent

The solvent that could provide the homogenize reaction was required in this study. Pyridine was the first chosen as solvent because it could dissolve both substrate and copper catalyst. The effects of the amount of pyridine are tabulated in Table 4.4 and Figure 4.2. In addition to the effect of $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ concentration (see Table 4.3), the final yield was also dependent on the pyridine concentration. The excess amount of pyridine did not give the best result. The amount of pyridine in the range of 10-20 mL was found to be the most appropriate to provide the highest yield of the desired products.

Table 4.4 The effects of the amount of pyridine^a

Pyridine (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
5	20	0.929	0.142	1.071
	O/N	0.885	0.051	0.936
10	20	1.888	0.093	1.981
	O/N	1.862	0.084	1.946
15	20	1.855	0.071	1.926
	O/N	1.862	0.068	1.807
20	20	1.711	0.059	1.770
	O/N	1.855	0.058	1.913
30	20	1.497	trace	1.497
	O/N	1.545	trace	1.545

a. reaction conditions : cyclohexane (20 mmol), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (0.2 mmol), pyridine (variable), acetic acid (1 mL), H_2O_2 (15 mmol)

**Figure 4.2** The effects of the amount of pyridine

Another component, acetic acid, that might have an influence on the outcome of the reaction was studied. The effects of the amount of acetic acid are recorded in Table 4.5 and Figure 4.3. It was found that acetic acid was also essential for this reaction. In the absence of acetic acid, the reaction yield was very low. The most appropriate amount of acetic acid was found to be 1.0 mL (based upon the highest yield observed). The amount of acetic acid more than 1.0 mL made the yield more or less constant.

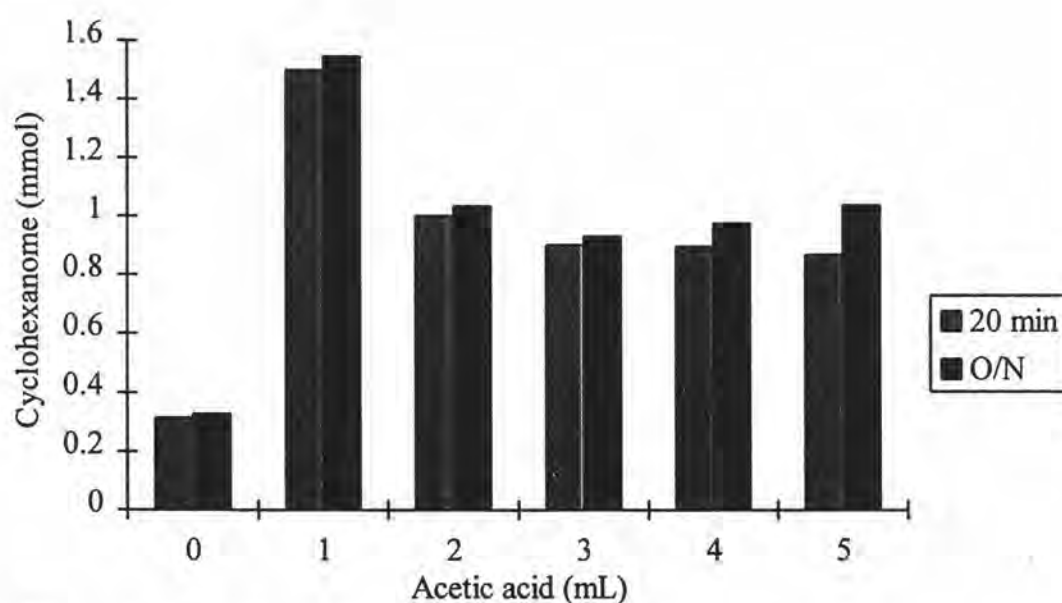


Figure 4.3 The effects of the amount of acetic acid

Table 4.5 The effects of the amount of acetic acid^a

Acetic acid (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	20	0.314	trace	0.314
	O/N	0.327	trace	0.327
1	20	1.497	trace	1.497
	O/N	1.545	trace	1.545
2	20	1.000	0.046	1.046
	O/N	1.032	trace	1.032
3	20	0.899	0.058	0.957
	O/N	0.928	0.027	0.955
4	20	0.893	0.046	0.939
	O/N	0.972	trace	0.972
5	20	0.864	0.080	0.944
	O/N	1.033	trace	1.033

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (variable), H₂O₂ (15 mmol)

A mixture of pyridine-acetic acid seemed to be a good choice for the oxidation reaction. However, the cost of pyridine is generally higher than other common organic solvents such as acetonitrile, acetone, *etc.* The search for other solvents that could replace or partly substitute pyridine without alternating the outcome of the reaction was therefore very essential. The results of the study on the effect of other solvents are shown in Table 4.6. The mixture of acetonitrile and pyridine ratio 1:1 (V/V) provided the higher yield than those obtained from other mixed solvents. The observed yield was comparable with that obtained in the standard reaction (pyridine-acetic acid system). The reason for this result was that acetonitrile was rather polar and may act also as an appropriate ligand for copper like pyridine.

Table 4.6 The effects of the solvent system^a

Additive solvent (15 mL)	Pyridine (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
-	30	20	1.497	trace	1.497
		O/N	1.545	trace	1.545
1,2-dichloroethane	15	20	1.033	trace	1.033
		O/N	1.314	trace	1.314
acetone	15	20	0.692	trace	0.692
		O/N	0.945	trace	0.945
acetonitrile	15	20	1.462	0.081	1.543
		O/N	1.479	0.080	1.559
<i>t</i> -butanol	15	20	0.727	trace	0.727
		O/N	0.889	trace	0.889

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (15 mL), additive solvent (15 mL), acetic acid (1 mL) H₂O₂ (15 mmol)

It was interesting whether all pyridine could be replaced by acetonitrile. Thus various ratios of pyridine to acetonitrile were studied and the results are presented in Table 4.7 and Figure 4.4. The results clearly indicated that acetonitrile could not replace all pyridine. Pyridine was still essential and must be present in the system. The best result was derived when the ratio of pyridine:acetonitrile was 1:1 (V/V). Furthermore, in the system employing acetonitrile as a co-solvent, it was observed that the amount of cyclohexanol was produced much more than that observed from the pyridine-acetic acid system. The amount of cyclohexanol increased when the amount of acetonitrile increased. Using only acetonitrile as solvent, the rate of the reaction was slower than the system comprising of pyridine in the reaction (the reaction was not complete after 20 minutes).

Table 4.7 The effects of the ratio of pyridine-acetonitrile in the oxidation of cyclohexane^a

CH ₃ CN (mL)	Pyridine (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
30	-	20	0.255	0.150	0.405
		O/N	0.418	0.375	0.793
20	10	20	1.377	0.124	1.501
		O/N	1.395	0.122	1.517
17	13	20	1.196	0.072	1.268
		O/N	1.351	0.085	1.436
15	15	20	1.462	0.081	1.543
		O/N	1.479	0.080	1.559
-	30	20	1.497	trace	1.497
		O/N	1.545	trace	1.545

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol),

pyridine+acetonitrile (30mL), acetic acid (1 mL), H₂O₂ (15 mmol)

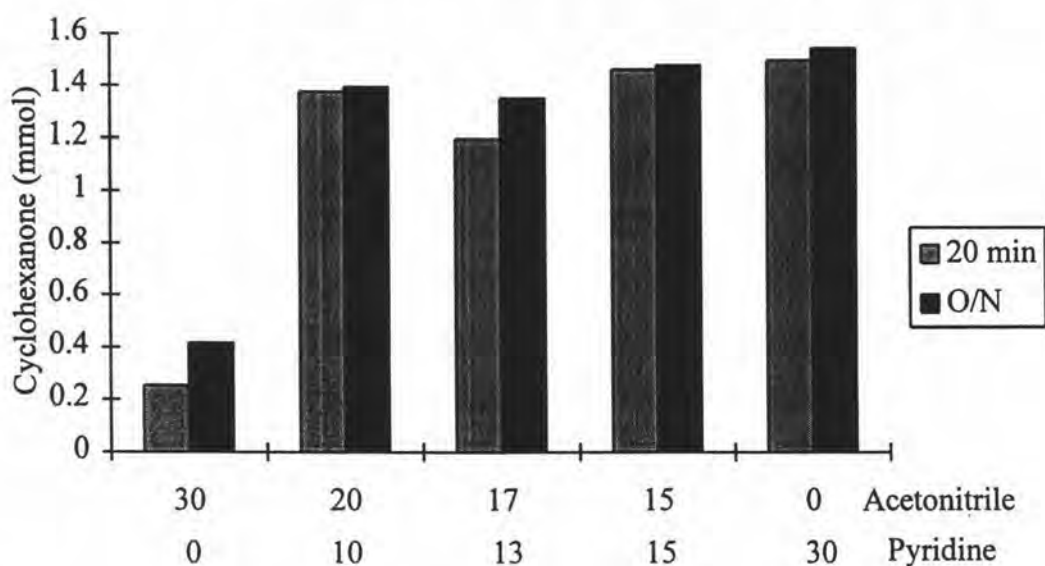


Figure 4.4 The effects of the amount of pyridine-acetonitrile

As stated earlier, the results from Table 4.5 indicated that acetic acid was essential in this solvent system. From Table 4.7, certain amount of pyridine could be replaced with acetonitrile. Thereby, it was interesting whether acetic acid was still necessary in the mixed pyridine and acetonitrile system. The results are summarized in Table 4.8 and Figure 4.5. It was indicated that acetic acid must be present in the reaction. The most appropriate amount of acetic acid was found to be in the range of 1.0-2.0 mL (based upon the highest yield observed). The amount of acetic acid more than 1.0-2.0 mL made the yield more or less constant.

Table 4.8 The effects of the amount of acetic acid in pyridine-acetonitrile system^a

AcOH (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	20	0.290	trace	0.290
	O/N	0.372	trace	0.372
1	20	1.462	0.081	1.543
	O/N	1.479	0.080	1.559
2	20	1.502	0.074	1.576
	O/N	1.480	0.068	1.548
3	20	1.335	0.063	1.398
	O/N	1.141	trace	1.141
5	20	1.074	0.069	1.143
	O/N	0.908	trace	0.908

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (15 mL), acetonitrile (15 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

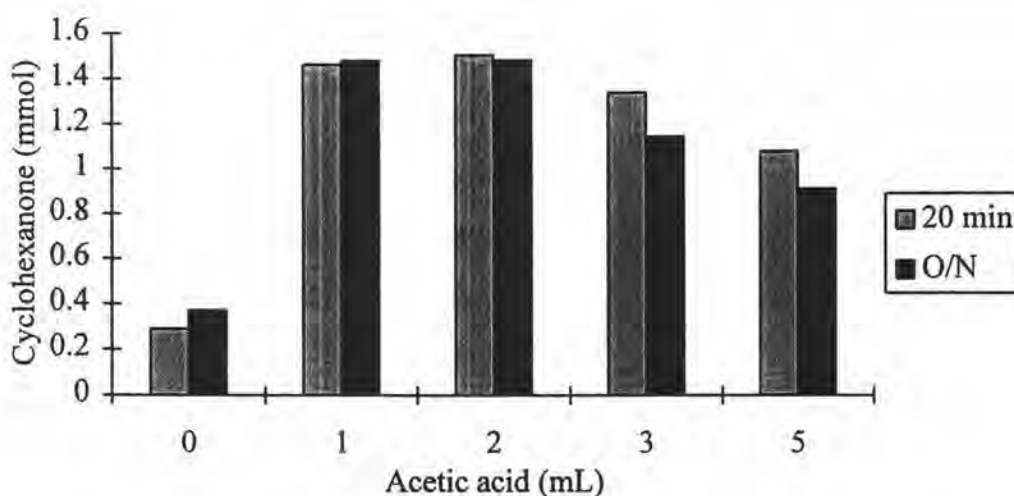


Figure 4.5 The effects of the amount of acetic acid in pyridine-acetonitrile system

Effects of substrate concentration

The effects of the substrate concentration was the next parameter that was evaluated. The results are summarized in Table 4.9 and Figure 4.6. It was clearly seen that the amount of cyclohexanone and cyclohexanol increased when the amount of substrate increased. However, the conversion of cyclohexane was found to be decreased. It was about 18 % conversion when using cyclohexane 5 mmol and about 10 % when using cyclohexane 20 mmol. However, when the cyclohexane concentration was more than 20 mmol, the reaction yield was almost constant. The use of cyclohexane 50 mmol made the reaction not homogeneous. From this result, it suggested that the yield was dependent on cyclohexane concentration. The appropriate cyclohexane concentration was about 20-30 mmol for the standard condition. The higher efficiency of hydrogen peroxide may be explained as competitive reactions occurred in the system. These competitive reactions included the oxidation of cyclohexane and the decomposition of hydrogen peroxide to water and dioxygen. Both processes are well known to take place *via* metal-catalyzed reactions.⁹ Therefore, the more cyclohexane (substrate) was present in the reaction system, the more oxidation reaction proceeded and the more decomposition process of hydrogen peroxide suppressed.

Table 4.9 The effects of substrate concentration^a

Cyclohexane (mmol)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)	% efficiency of H ₂ O ₂ ^b
5	20	0.827	0.035	0.862	11.19
	O/N	0.779	0.029	0.808	10.77
10	20	1.311	0.061	1.372	18.29
	O/N	1.281	0.055	1.336	17.81
15	20	1.687	0.079	1.766	23.55
	O/N	1.515	0.069	1.584	21.12
20	20	1.888	0.093	1.981	26.41
	O/N	1.862	0.084	1.946	25.95
30	20	1.884	0.119	2.003	26.71
	O/N	1.792	0.115	1.907	25.43
50	20	1.804	0.140	1.944	25.92
	O/N	1.637	0.088	1.725	23.00

a. reaction conditions : cyclohexane (variable), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

b. see appendix A

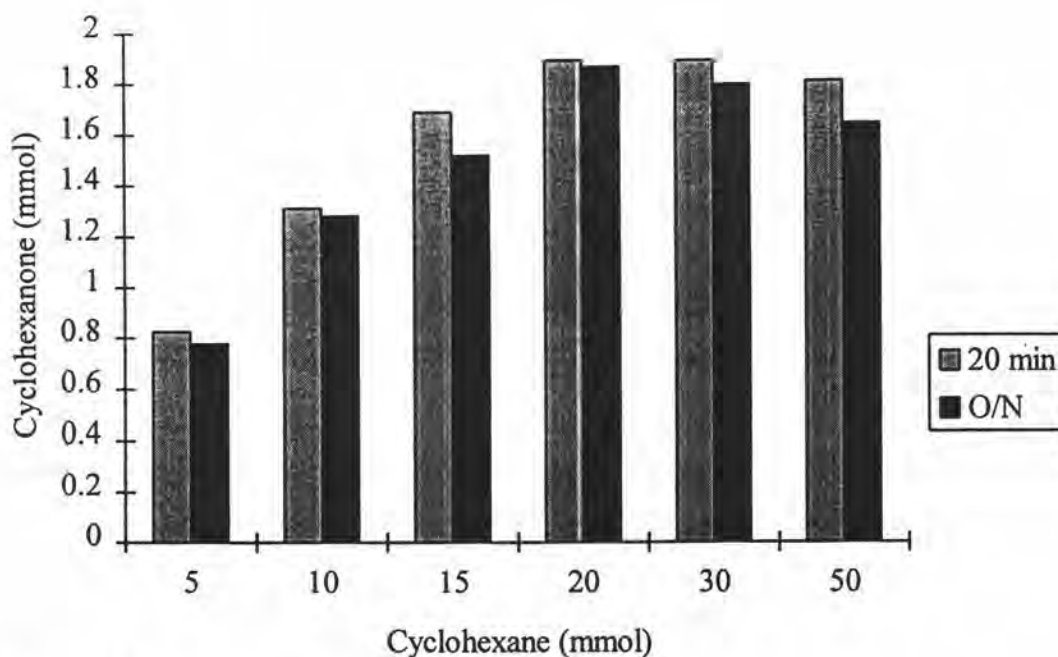


Figure 4.6 The effects of cyclohexane concentration

Effects of oxidant

Hydrogen peroxide was a primary oxidant used for the oxidation of cyclohexane in this study. However, many oxidants besides hydrogen peroxide might be good for this reaction. The results of the effects of various oxidants in the oxidation of cyclohexane are presented in Table 4.10. Concerning with the amount of the desired products and the reaction time, it was found that hydrogen peroxide (H_2O_2) was a significantly better oxidant than *tert*-butyl hydroperoxide for the oxidation of cyclohexane. The reaction employing *tert*-butyl hydroperoxide produced only trace amount of both cyclohexanone and cyclohexanol. This result implied that the activation step in both systems should be different.

Table 4.10 The effects of various oxidants in the oxidation of cyclohexane^a

Oxidants (15 mmol)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
H ₂ O ₂	20	0.899	0.058	0.957
30% in H ₂ O	O/N	0.927	0.027	0.955
TBHP ^b	20	trace	trace	trace
70% in H ₂ O	O/N	trace	trace	trace
TBHP 3.3M	20	trace	trace	trace
in isooctane	O/N	trace	trace	trace

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (3 mL), oxidant (variable)

b. TBHP = *tert*-butyl hydroperoxide

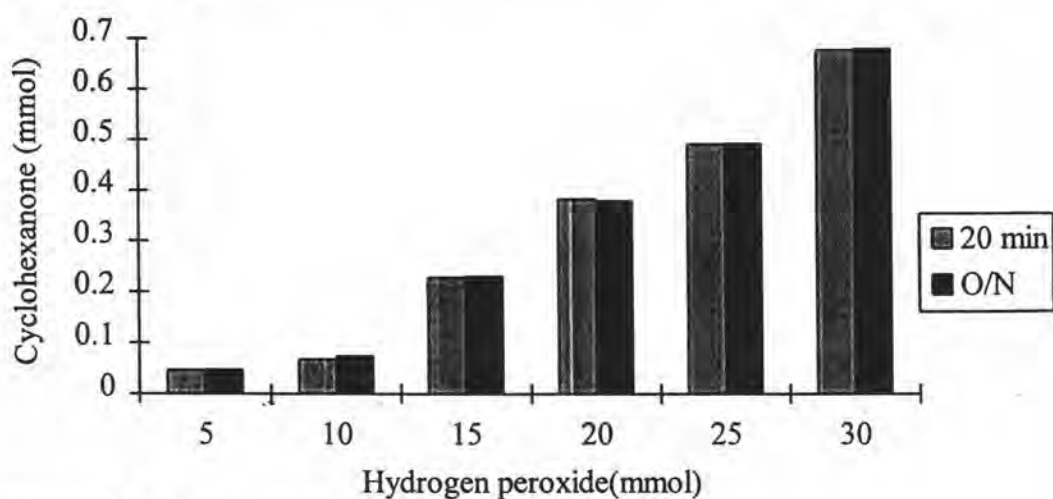
The effects of hydrogen peroxide concentration are presented in Table 4.11 and Figure 4.7. It was found that in the absence of hydrogen peroxide, the oxidation was not occurred. The yield of the oxidation products was directly varied to the amount of hydrogen peroxide employed. Thus, the yield could be easily improved by increasing the amount of hydrogen peroxide. The efficiency of hydrogen peroxide increased when hydrogen peroxide increased. However, the efficiency of hydrogen peroxide was found to reach the highest figure when the oxidant concentration changed from 10 mmol to 15 mmol.

Table 4.11 The effects of oxidant concentration^a

H ₂ O ₂ (mmol)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)	% efficiency of H ₂ O ₂ ^b
0	O/N	0	0	0	0
5	20	0.046	trace	0.046	1.85
	O/N	0.048	trace	0.048	1.92
10	20	0.068	trace	0.068	1.36
	O/N	0.075	trace	0.075	1.50
15	20	0.229	trace	0.229	3.06
	O/N	0.231	trace	0.231	3.08
20	20	0.383	trace	0.383	3.83
	O/N	0.379	trace	0.379	3.79
25	20	0.491	0.045	0.536	4.29
	O/N	0.492	0.046	0.538	4.30
30	20	0.677	0.066	0.743	4.95
	O/N	0.679	0.067	0.746	4.97

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (0 mL), H₂O₂ (variable)

b. see appendix A

**Figure 4.7** The effects of oxidant concentration

In typical experiments 30% hydrogen peroxide in water was used. Water itself could perhaps play an important role in this chemistry since μ -oxo dimeric species, particularly for iron were postulated as active catalysts for the ketonization process.⁵⁴ Thus, water might have an influence on the reaction yield or the rate of ketonization. The effects of water on the oxidation of cyclohexane are presented in Table 4.12.

Table 4.12 The effects of water added in the oxidation of cyclohexane^a

H ₂ O (mL)	Time (min)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	20	1.257	trace	1.257
	O/N	1.175	trace	1.175
0.5	20	1.176	trace	1.176
	O/N	1.222	trace	1.222
1.0	20	1.256	trace	1.256
	O/N	1.221	trace	1.222
3.0	20	1.047	0.054	1.101
	O/N	1.162	trace	1.162

a. reaction conditions : cyclohexane (20 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (1 mL), H₂O₂ (15 mmol), water (variable)

From Table 4.12, it was found that the amount of water added (up to 3 mL) did not change the reaction yield of this reaction. It was unlikely to the iron catalyst systems that the reaction did depend on the amount of water added.⁵⁵ This result may lead to the conclusion that the formation of a μ -oxo dimeric active species did not appear in the copper catalyst system. Thus, water from hydrogen peroxide should not have any effect to this oxidation reaction.

Kinetic study on the reaction rate of the oxidation of cyclohexane

Various catalytic systems that mimic enzymatic systems could catalyze reactions to proceed at room temperature and atmospheric pressure. However, the rates of these reactions were generally slow. Thus it needed to spend more time to complete the reaction. The catalytic systems that consume less time to complete the reaction should therefore be investigated. The rate of the cyclohexane oxidation catalyzed by copper catalyst was studied and the results are shown in Figure 4.8. It was found that the rate of the reaction obtained from this system was significantly better than those of other copper complexes. The half-life of the reaction was approximately 10 minutes and the reaction time was about 30 minutes. This reaction time was faster than many catalysis systems reported, for example, $\text{Fe}(\text{PA})_2 / \text{H}_2\text{O}_2 / (\text{Py})_4\text{HOAc}$ (reaction time 4h.)²⁷, $\text{Co}(\text{bPy})_2^{2+} / \text{H}_2\text{O}_2 / (\text{MeCN})_4\text{Py}$ (reaction time 6 h.)³⁰, $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O} / \text{H}_2\text{O}_2 / \text{Py}$ (reaction time 2 h.)³⁷, etc.

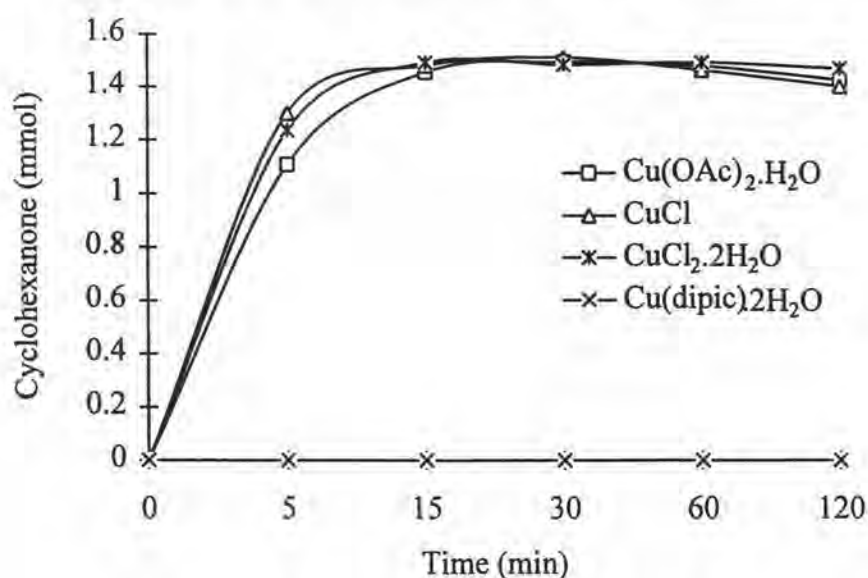










Figure 4.8 The reaction rate of cyclohexane oxidation catalyzed by copper catalysts

From this result, it could be observed that among biological mimic systems reported, this particular system could proceed the oxidation reaction pretty fast (half-life about 10 minutes).

Comparative Studies on the Relative Reactivity of Cyclic Saturated Hydrocarbons

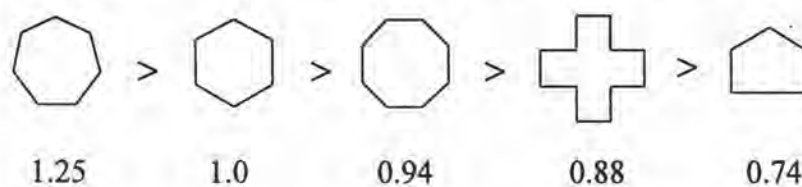
Mechanistic study of this reaction system is another challenging aspect. There were two possible mechanisms proposed for the oxidation of cyclohexane catalyzed by metal catalysts. First, the reaction occurred *via* a free radical pathway. The other was believed not to involve the radical reaction. To evaluate these proposals, the comparison of a series of saturated hydrocarbons with bromination by BrCCl_3 was presented.⁵⁶ For the radical bromination, the relative reactivity was cyclooctane (3.3) > cyclododecane (1.9) > cyclopentane (1.3) > cyclohexane (1.0). For the non-radical, the relative reactivity was cyclohexane (1.0) > cyclooctane (0.76) > cyclopentane (0.69) > cyclododecane (0.63). Moreover, it is noteworthy that the reaction was occurred by the radical reaction when the relative reactivity of cyclopentane/cyclohexane was more than 1.0; on the other hand, when the relative reactivity of cyclopentane/cyclohexane was less than 1.0, the reaction was occurred by the non-radical reaction.⁵⁷ To answer whether the mechanism of the oxidation of saturated hydrocarbons catalyzed by copper in this study was radical or not, the comparison of relative reactivity order per hydrogen towards a series of cyclic saturated hydrocarbons was studied. The results are summarized in Table 4.13.

Table 4.13 Comparison of reactivity order per hydrogen for a series of cyclic saturated hydrocarbons^a

R ¹ H	R ² H	R ¹ H or R ² H (mmol)	R ¹ =O (mmol)	R ² =O (mmol)	Rel. React. R ² (H)/R ¹ (H)
		10	0.555	0.342	0.74
		10	0.547	0.795	1.25
		10	0.554	0.692	0.94
		10	0.581	1.025	0.88

a: reaction conditions: substrates (10 mmol each), copper catalyst (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

Reactivity of various cyclic saturated hydrocarbons can be calculated compared with the relative of cyclohexane. The results is shown below.



From Table 4.13, it was found that the relative reactivity for a series of cyclic saturated hydrocarbons was cycloheptane (1.25) > cyclohexane (1.0) > cyclooctane (0.94) > cyclododecane (0.88) > cyclopentane (0.74). In addition, it was found that the relative reactivity of cyclopentane/cyclohexane in this study was less than 1.0, thus the reaction was occurred by non-radical intermediate. Moreover, this reactivity agreed with the comparison relative reactivity of oxidation of cycloalkane catalyzed by iron catalyst⁵⁸ (Gif-type system), *i.e.* cycloheptane (1.15) > cyclohexane (1.0) > cyclopentane (0.85) > cyclooctane (0.75) > cyclododecane (0.43). The relative

reactivity of oxidation of cyclohexane was nearly 1.2 as reactive as cyclopentane in Gif-type system and this system was clearly proved not undergo the radical process. From these data, it suggested that the mechanism of the oxidation of saturated hydrocarbons catalyzed by copper catalysts in this study should also not occur *via* the radical pathway.

Copper-catalyzed Oxidation of Cyclohexene

In order to compare and contrast the copper-catalyzed oxidation reaction in this study with various systems reported, the oxidation of cyclohexene was investigated. The results of cyclohexene oxidation catalyzed by copper acetate are shown in Table 4.14.

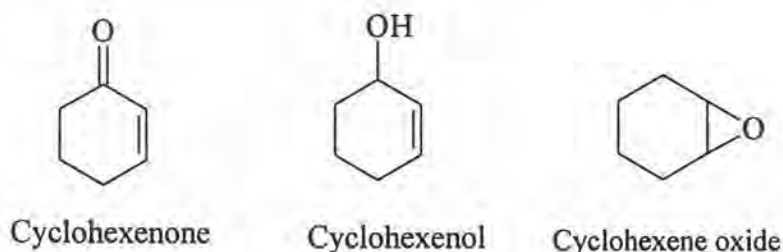


Table 4.14 The copper-catalyzed oxidation of cyclohexene^a

Time (min)	Cyclohexenone (mmol)	Cyclohexenol (mmol)	Cyclohexene oxide (mmol)	Total (mmol)
20	0.808	trace	trace	0.808
300	0.852	trace	0	0.852
1 day	0.791	trace	0	0.791

a. reaction conditions : cyclohexene (20 mmol), Cu(OAc)₂·H₂O (0.2 mmol), pyridine (10 mL), acetic acid (1.0 mL), H₂O₂ (15 mmol)





From Table 4.14, it was found that cyclohexenone was a major product. The epoxidation of cyclohexene to cyclohexene oxide did not take place. This result was different from other reported systems. For instance chlorodimethylferriporphyrin

IX with iodosylbenzene system²⁴ and Cu(OH)₂ with aldehydes system³⁸ where the major product was cyclohexene oxide. However, the allylic oxidation of cyclohexene to produce cyclohexenone and cyclohexenol was found to be resemble to some biomimetic systems reported. Co(bpy)₂²⁺ system³⁰ and Cu(bpy)₂⁺ system⁵⁹ are among those examples.

Competitive Studies on the Oxidation of Cyclohexane, Cyclohexene, and Ethylbenzene

In order to examine the characteristic of the copper-catalyzed oxidation system, the competitive studies on the oxidation between cyclohexane and cyclohexene, cyclohexane and ethylbenzene were investigated. The outcome of the reactions is tabulated in Table 4.15. The results were found to be striking since the relatively weak C-H bond energy as that in ethylbenzene (benzylic C-H bond: 85 kcal/mol)²⁸ should be easily oxidized compared with inert C-H bond in cyclohexane. The same trend was also observed when compared cyclohexane with allylic C-H bond in cyclohexene. The results therefore implied that the high valence oxidation state Cu (formulated as Cu^{IV}=O) should selectively activate the C-H bond of alkanes. This observation was found to be similar to that using Fe^{II} or Fe^{III} as catalysts.²⁸

Table 4.15 Competitive study of the oxidation between cyclohexane and cyclohexene and cyclohexane and ethylbenzene^a

R ¹ H	R ² H	R ¹ H or R ² H (mmol)	R ¹ O ^A (mmol)	R ² O ^{B,C} (mmol)	Ratio R ¹ O / R ² O
		10	0.542	0.495	1.095
		10	0.740	0.306	2.418


a: reaction conditions: substrates (10 mmol each), copper catalyst (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

A = cyclohexanone, B = cyclohexenone, C = acetophenone

Chemoselectivity

Another important feature of the system that needs to be carefully evaluated is the chemoselectivity. By comparing with the normal oxidation system, the addition of equal amount of additive to the system would provide some clues for the chemoselectivity of the study system. Cyclooctane was chosen for this study because it was sufficiently non-volatile so that a good mass balance could be obtained with respect to the hydrocarbon and its oxidation products, cyclooctanone and cyclooctanol. The results are presented in Table 4.16.

Table 4.16 The chemoselectivity study^a

Entry	Additive (10 mmol)	Time (min)	Percentage			% Mass Balance
			Cyclo- octane	Cyclo- octanone	Cyclo- octanol	
1	-	20	86.94	9.14	trace	96.08
		O/N	87.41	10.20	trace	97.61
2		20	91.76	4.99	trace	96.75
		O/N	92.73	5.07	trace	97.80
3	EtOH	20	90.28	6.99	trace	97.27
		O/N	91.01	6.53	trace	97.54
4	(CH ₃) ₂ CHOH	20	90.03	6.55	trace	96.58
		O/N	93.00	6.89	trace	99.89
5	(CH ₂ OH) ₂	20	97.34	6.81	trace	104.15
		O/N	95.97	6.83	trace	102.80
6	PhPh	20	96.61	7.78	trace	104.39
		O/N	96.69	7.65	trace	104.34
7	PhOMe	20	89.85	7.01	trace	96.86
		O/N	89.37	6.57	trace	95.94
8	PhCO ₂ Me	20	94.23	8.03	trace	102.26
		O/N	95.96	8.37	trace	104.33
9	Ph ₂ S	20	96.69	6.26	trace	102.95
		O/N	98.91	6.53	trace	104.72
10	PPh ₃	20	95.09	0.83	trace	95.92
		O/N	94.97	0.86	trace	95.83

a. reaction conditions: cyclooctane (10 mmol), additive (10 mmol), H₂O₂ (15 mmol)

Cu(OAc)₂·H₂O (0.2 mmol), pyridine (20 mL), acetic acid (1 mL)

b. recovered cyclooctane

From Table 4.16, it could be seen that in the presence of alcohols, the well known easily oxidizable compounds such as cyclohexanol, ethanol, isopropanol or ethylene glycol (entries 2-5), the alkane oxidation process was a little suppressed by the effect of these additives. The activation process of saturated hydrocarbon was still occurred to produce the corresponding ketone and alcohol. This observation implied that the high valent intermediate generated should selectively oxidize C-H bonds of saturated hydrocarbons. More striking results were obtained from the competition reaction between cyclooctane and ethanol. The results are tabulated in Table 4.17

Table 4.17 The effects of ethanol concentration in the oxidation of cyclohexane^a

EtOH (mmol)	Time (min)	Percentage		% Mass Balance
		Cyclooctane ^b	Cyclooctanone	
0	20	86.94	9.14	96.08
	O/N	87.41	10.20	97.61
10	20	90.28	6.69	97.27
	O/N	91.01	6.53	97.54
20	20	94.57	5.01	99.58
	O/N	97.00	5.11	102.11
30	20	97.60	4.50	102.10
	O/N	96.95	4.77	101.72
50	20	93.69	3.46	97.15
	O/N	98.57	3.64	102.21

a. reaction conditions : cyclooctane (10 mmol), ethanol (variable), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H₂O₂ (15 mmol)


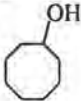

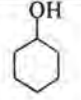
b: recovered cyclooctane

It could clearly see from this table that even in the presence of an excess amount of ethanol, the oxidation process of alkane still took place. Therefore, the

proposed high valent Cu intermediate responsible for oxidation of alkanes should somewhat have a preference to oxidize saturated hydrocarbons to ketone.

In addition, the competitive studies on the oxidation between cyclohexane and cyclooctanol and *vice versa* between cyclooctane and cyclohexanol were investigated. The results are summarized in Table 4.18.

Table 4.18 The competitive studies on the oxidation of cyclohexane and cyclooctanol and between cyclohexanol and cyclooctane^a

R ¹ H (10mmol)	R ² OH (10 mmol)	Time (min)	R ¹ =O (mmol)	R ² =O (mmol)	R ² OH ^b (mmol)
		20 O/N	0.807 0.736	0.848 0.814	8.473 8.333
		20 O/N	0.546 0.562	0.239 0.232	8.252 8.274

a: reaction conditions: substrates (10 mmol each), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

b: recovered cyclooctanol or cyclohexanol

From Table 4.18, it was found that cyclohexane and cyclooctane were still preferentially oxidized. These observation confirmed the aforementioned results that the high valent Cu intermediate responsible for oxidation of alkanes should have a preference to oxidize saturated hydrocarbons to ketone.

Reconsidering the outcome from Table 4.16, as a test of a possible electron transfer mechanism, biphenyl, anisole and methyl benzoate (entries 6-8) were used for this purpose. Those compounds had slightly effect on the oxidation process. The oxidation of cyclooctane was still found to be prevailed. Therefore, the oxidation process occurred *via* electron transfer mechanism should not be possible.

Further interesting results were obtained by the addition of a sulfur compound. In addition to the above results, diphenyl sulfide also showed little effect on the oxidation process.

Triphenylphosphine was the last chosen substance for chemoselectivity study. It is well known that triphenylphosphine was a good reducing agent. This substance significantly affects the oxidation process. It reduced the oxidation of cyclooctane to be only 0.08 mmol of cyclooctanone. It was highly possible that hydrogen peroxide preferentially oxidized triphenylphosphine to triphenylphosphine oxide. Thereby, the oxidation of cyclooctane was not occurred.

The Use of *tert*-Butyl Hydroperoxide as an Oxidant

Comparative Study on the Use of Hydrogen Peroxide and *tert*-Butyl Hydroperoxide as an Oxidant

There are many fruitful oxidants employed in biologically mimicking systems. The report on the use of Zn, O_2 in Gif^{dV} system⁶⁰ or the utilization of dioxygen and aldehyde disclosed by Mukaiyama and colleagues⁶¹ are among those examples. *tert*-Butyl hydroperoxide (TBHP) has been well-known as an oxidant for alkane epoxidation.⁶² Nonetheless, during the last decade TBHP has also turned out to be a powerful oxidizing agent in several metal-catalyzed oxidations of alkanes.⁶³ Based upon the results derived from the use of hydrogen peroxide as an oxidant, the extension of the use of TBHP was carried out in more details to compare their similarity and difference. The results of the oxidation of cyclooctane oxidized by various oxidants are summarized in Table 4.19.

Table 4.19 The results of the oxidation of cyclooctane oxidized by various oxidants^a

Oxidants (10 mmol)	Temperature (^o C)	Time (hr)	Cyclooctanone (mmol)	Cyclooctanol (mmol)	Total (mmol)
H ₂ O ₂ 30% in H ₂ O	room temperature ^b	1	0.266	0.044	0.310
		6	0.283	0.040	0.316
		24	0.281	0.046	0.327
urea.H ₂ O ₂	room temperature	1	0.615	0.008	0.623
		6	0.794	0.033	0.827
		24	0.758	0.028	0.786
TBHP 70% in H ₂ O	room temperature	1	0.005	0.041	0.046
		6	0.025	0.011	0.036
		24	0.075	0.055	0.130
TBHP 3.3M in isooctane	room temperature	1	0	0	0
		6	0.023	0.012	0.035
		24	0.089	0.032	0.121
TBHP 70% in H ₂ O	60	1	0.709	0.543	1.252
		6	2.620	0.818	3.203
		24	6.972	1.055	8.027
TBHP 3.3M in isooctane	60	1	0.642	0.383	1.025
		6	3.066	0.771	3.837
		24	6.922	0.780	7.702

a. reaction conditions : cyclooctane (50 mmol), Cu(OAc)₂.H₂O (0.2 mmol), pyridine (30 mL), acetic acid (3 mL), oxidant (variable)

b. room temperature = 30^oC

From Table 4.19, it was found that both 30% H₂O₂ in water and urea.H₂O₂ were good oxidants in this reaction. The reaction could occur at room temperature and gave higher yield than that using *tert*-butyl hydroperoxide 70% in water or *tert*-butyl hydroperoxide 3.3M in isooctane as an oxidant. On the other hand, when the reaction

proceeded at 60⁰C, *tert*-butyl hydroperoxide 70% in water and *tert*-butyl hydroperoxide 3.3M in isooctane gave superior results.

The comparative studies between using hydrogen peroxide and *tert*-butyl hydroperoxide revealed many different characteristics. Whereas the oxidation reaction using hydrogen peroxide as an oxidant took place very rapidly at room temperature, the other required higher temperature. However, the yield of the latter case was far better. It was possible that the mechanism operated in the case of TBHP may involve a free radical reaction. The initial step might be the homolytic cleavage stage, which required a higher temperature to produce *t*-butyloxy radical (+O•) or *t*-butyl peroxy radical (+OO•). The next step should therefore be similar to other autoxidation processes.

Copper-catalyzed Functionalization of Saturated Hydrocarbons

From the above results, the oxidation of cyclohexane catalyzed by copper catalyst using TBHP could occur at temperature around 60⁰C. The major product was cyclohexanone and cyclohexanol was a minor one. Base upon the mechanistic pathway postulated in Gif-type systems⁶⁴ that there were at least two intermediates involved in the oxidation reaction, the copper-catalyzed oxidation reaction in this study using hydrogen peroxide was believed to have similar mechanistic pathway. In order to gain insight the possible mechanism of the reaction and at the same time to search for the the new route to functionalize saturated hydrocarbons catalyzed by copper catalysts, bromotrichloromethane was selected to use as a trapping agent.

Bromocyclohexane

In order to see the similarity and difference between the systems catalyzed by iron and copper, the effect of a trapping agent, bromotrichloromethane was studied. The results are tabulated in Table 4.20.

Table 4.20 The effects of bromotrichloromethane in the oxidation of cyclohexane using H_2O_2 as an oxidant^a

BrCCl_3 (mmol)	Time (min)	Bromocyclohexane (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
15	20	0.040	trace	trace	0.040
	O/N	0.062	trace	trace	0.062
20	20	0.032	trace	trace	0.032
	O/N	0.052	trace	trace	0.052

a. reaction conditions: cyclohexane (20 mmol), BrCCl_3 (variable), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H_2O_2 (15 mmol)

Unlike the system using iron as a catalyst⁵⁶, the oxidation reaction catalyzed by copper catalyst in the presence of bromotrichloromethane did not give an alkyl bromide as a major product. Only trace amount of cyclohexyl bromide was observed. Other two products, cyclohexanone and cyclohexanol were also detected as very minor products. This revealed that the addition of bromotrichloromethane to this system made the C-H activation process not occur. The reason was probably derived from the self-reaction between bromotrichloromethane and hydrogen peroxide catalyzed by copper salt. In order to make certain that the addition of bromotrichloromethane inhibited the activation process, the addition of this reagent at different time interval was examined. The results are shown in Table 4.21.

Table 4.21 The effects of adding bromotrichloromethane at different time interval^a

Time added BrCCl ₃ (min)	Time (min)	Bromo- cyclohexane (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	20	0.040	trace	trace	0.040
	300	0.062	trace	trace	0.062
5	20	trace	1.152	0.075	1.227
	300	0.055	1.011	0.037	1.066
10	20	trace	1.250	0.056	1.306
	300	0.084	1.092	0.054	1.230
20	20	trace	1.272	0.058	1.330
	300	0.093	1.182	0.054	1.329

a. reaction conditions: cyclohexane (20 mmol), BrCCl₃ (15 mmol), Cu(OAc)₂·H₂O (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), H₂O₂ (15 mmol)

From Table 4.21, it was clearly shown that the oxidation power in the system was destroyed in the presence of bromotrichloromethane. When this reagent was added after the addition of hydrogen peroxide, for instance 5 minutes, the oxidation process leading to the formation of cyclohexanone and cyclohexanol was still exist. Therefore, this reagent was not an appropriate reagent for transforming alkanes to their bromo derivatives in this particular conditions. On the other hand, the addition of bromotrichloromethane into the system employing TBHP as an oxidant provided an alternative route to convert cyclohexane to bromocyclohexane. The results are presented in Table 4.22

Table 4.22 The effects of bromotrichloromethane in *tert*-butyl hydroperoxide system at 60°C^a

Time (min)	Bromocyclohexane (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
20	0.756	trace	0	0.756
300	1.224	0.138	trace	1.362
1 day	2.148	0.181	trace	2.329

a. reaction conditions: cyclohexane (20 mmol), BrCCl₃ (15 mmol), Cu(OAc)₂·H₂O (0.2 mmol), pyridine (20 mL), acetic acid (1 mL), TBHP (15 mmol), T = 60°C

The amount of bromocyclohexane was found to be prevailed over other oxidized products. This result suggested that one of the reaction intermediates along the reaction pathway was trapped by bromotrichloromethane. The proposed mechanistic scheme was discussed later on the next section.

Chlorocyclohexane

Learning from previous result that cyclohexyl bromide could be obtained from the system using TBHP as an oxidant in the presence of bromotrichloromethane. The attempt to produce cyclohexyl chloride was tried by using carbon tetrachloride. However, upon addition of carbon tetrachloride to the oxidation reaction, the major product obtained was still cyclohexanone.

When the copper catalyst was changed from Cu(OAc)₂·H₂O to CuCl, it was observed that certain amount of chlorocyclohexane along with cyclohexanone and cyclohexanol were produced from the reaction. Therefore, the reaction that responded to the production of cyclohexyl chloride may involve ligand exchange process.⁹ To prove this observation, CuCl 5 mmol was used in the reaction. The results are tabulated in Table 4.23.

Table 4.23 The functionalization of cyclohexane to chlorocyclohexane

Time (day)	Chlorocyclohexane (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
1	1.615	0.182	trace	1.797
2	1.523	trace	trace	1.523
3	1.600	trace	trace	1.600

a. reaction conditions: cyclohexane (50 mmol), pyridine (30 mL), acetic acid (1 mL), CuCl (5 mmol), TBHP (15 mmol), T = 60°C

The results in Table 4.23 clearly revealed that chlorocyclohexane was produced as a main product in this system. The reaction was completed in 1 day. Cyclohexanone and cyclohexanol were derived as minor products. The result implied that CuCl may act in two roles; as a catalyst and as a chlorine donor. Thus, using less CuCl and adding another chloride source such as lithium chloride (LiCl) may make this reaction be more understandable. The results are tabulated in Table 4.24 and Figure 4.9.

Table 4.24 The effects of adding LiCl^a

LiCl (mmol)	Chlorocyclohexane (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	0.479	1.015	0.255	1.749
1	1.301	0.923	0.203	2.427
5	3.565	1.080	0.187	4.832

a. reaction conditions: cyclohexane (50 mmol), LiCl (variable), CuCl (0.5 mmol), pyridine (30 mL), acetic acid (1 mL), TBHP (10 mmol), T=60°C, reaction time 1 day

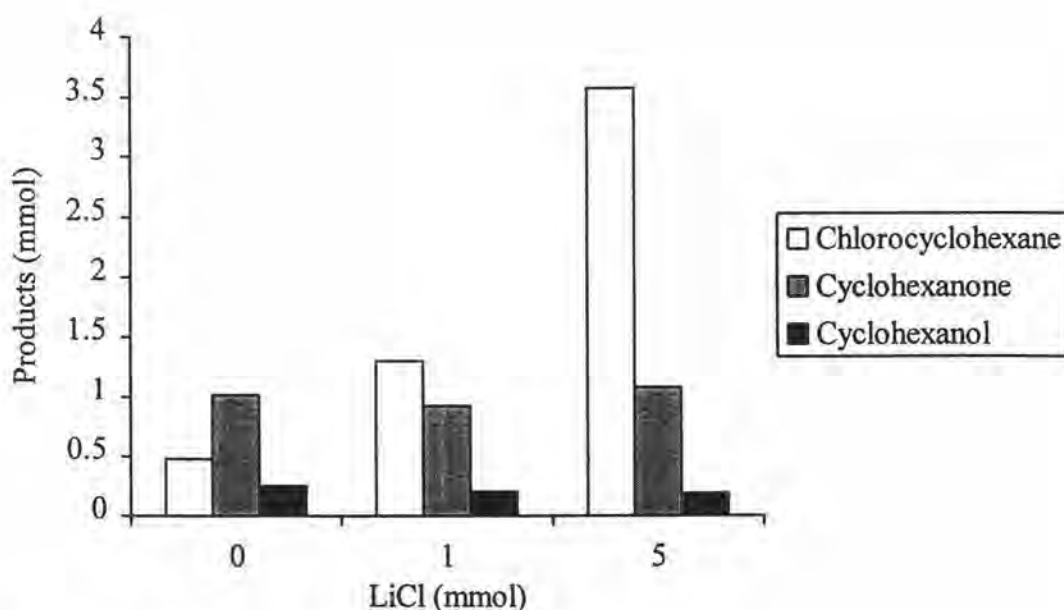


Figure 4.9 The effects of adding LiCl

From Table 4.24 and Figure 4.9, it was found that chlorocyclohexane could also be produced upon adding LiCl to the reaction. The reaction may take place as expected. To illustrate this, in the case of no LiCl added chlorocyclohexane was produced only 0.479 mmol, which was clearly seen that all chlorine was derived from CuCl. This reaction had quite high efficiency, almost 100%. The yield of cyclohexyl chloride increased when adding LiCl up to 5 mmol. However, both cyclohexanone and cyclohexanol were still significantly produced in all cases of adding LiCl.

The formation of cyclohexanone and cyclohexanol was believed to stem from the reaction between a reaction intermediate (say cyclohexyl radical) and molecular oxygen. In order to prove this, the same reaction was carried out under nitrogen atmosphere for 1 day, it was found that chlorocyclohexane 4.762 mmol was produced with only trace amount of cyclohexanone and cyclohexanol detected. Therefore, it is clear to draw a conclusion in this step that the production of oxidizing products (ketones and alcohols) came from dioxygen, while the chloroalkane should derive from the interception of a reaction intermediate along the pathway with appropriate trapping reagents.

Cyclohexyl azide

In order to construct C-N bond directly from C-H bonds of alkane, the addition of sodium azide (NaN_3) instead of LiCl was carried out. The results are summarized in Table 4.25 and Figure 4.10.

Table 4.25 The functionalization of cyclohexane to cyclohexyl azide^a

NaN_3 (mmol)	Time (day)	Cyclohexyl azide (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Total (mmol)
0	1	0	1.328	0.278	1.606
	2	0	1.480	0.290	1.770
1	1	0.346	1.193	0.369	1.908
	2	0.293	1.564	0.330	2.187
5	1	0.419	0.348	0.148	0.915
	2	0.976	0.511	0.137	1.624
10	1	0.341	0.278	0.119	0.738
	2	0.908	0.447	0.115	1.470
20	1	0.603	0.273	0.079	0.955
	2	1.354	0.493	0.099	1.946

a. reaction conditions: cyclohexane (50 mmol), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (0.5 mmol), pyridine (20 mL), acetic acid (1 mL), TBHP (15 mmol), $T = 60^\circ\text{C}$

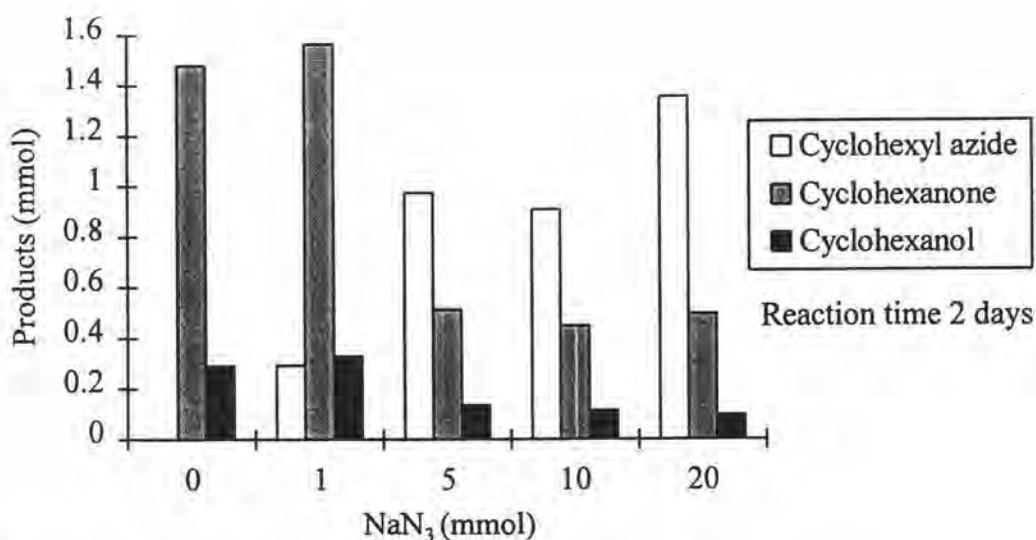


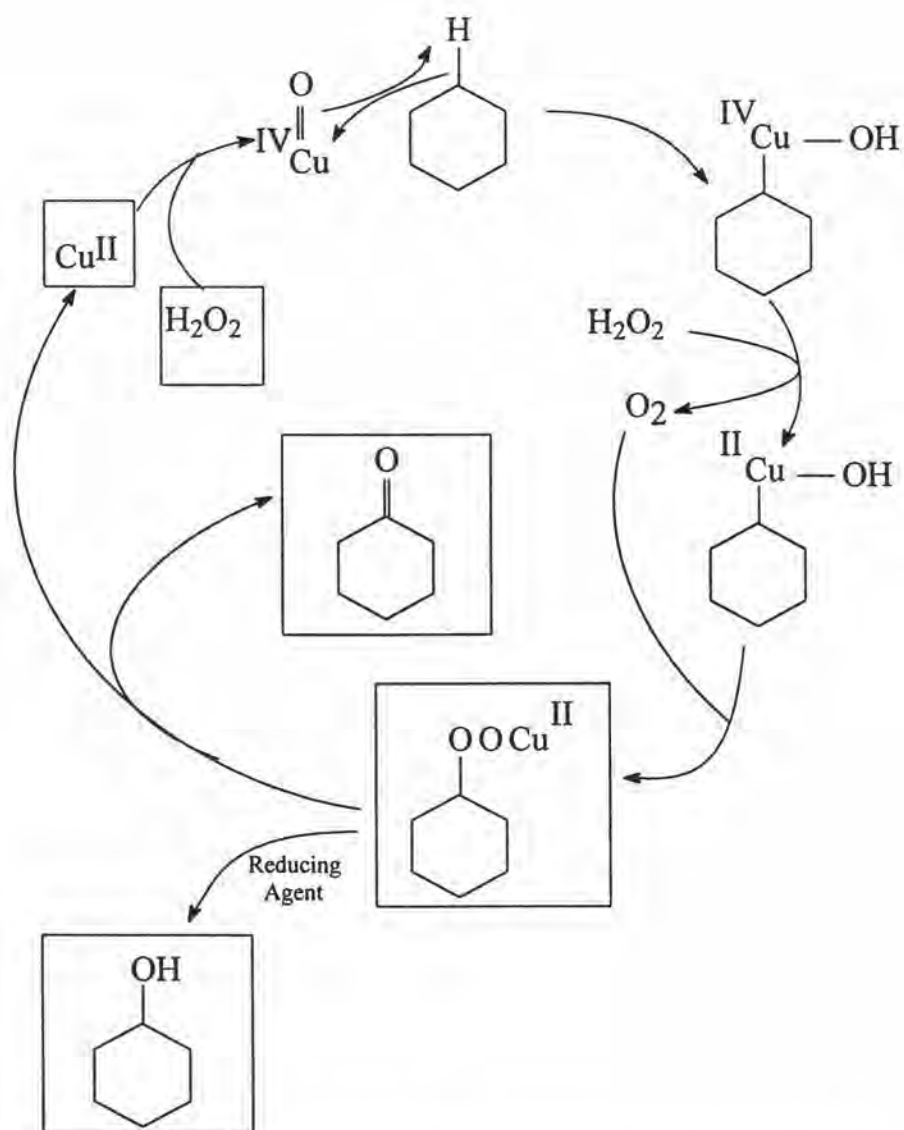
Figure 4.10 The functionalization of cyclohexane to cyclohexyl azide

From Table 4.25 and Figure 4.10, it was revealed that sodium azide showed the similar effect to that of adding lithium chloride to the oxidation process. Cyclohexyl azide produced was varied with the amount of sodium azide added and the reaction time. However, cyclohexanone and cyclohexanol were still the products of the reaction. Within the same manner, when this reaction was carried out under nitrogen atmosphere using sodium azide 5 mmol the cyclohexyl azide 3.892 mmol was produced. Cyclohexanone and cyclohexanol were detected as minor products.

Mechanism of the Copper-catalyzed Oxidation of Cyclohexane

- Using Hydrogen peroxide as an oxidant

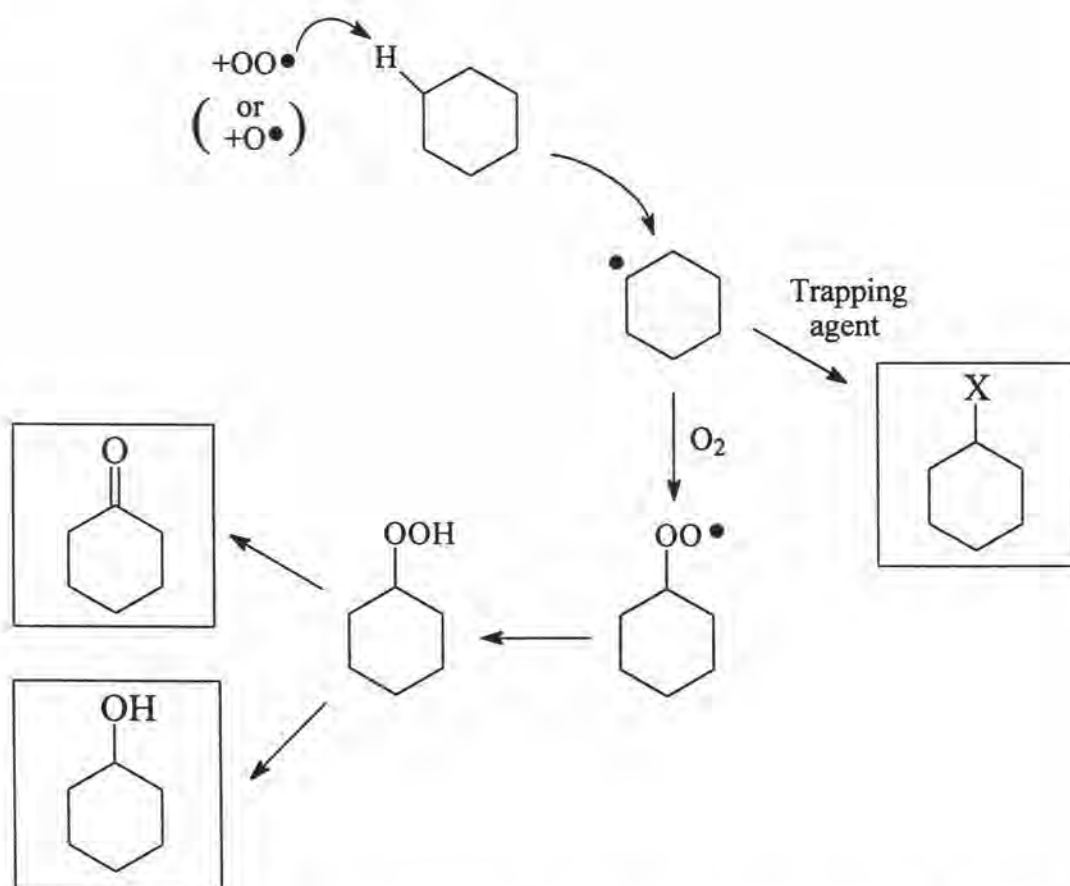
From the above results of the comparative studies on the relative reactivity of cyclic saturated hydrocarbons, it was found that the mechanism of the oxidation of cyclohexane in this study should not occur *via* free radical pathway. In addition, the results from chemoselectivity confirmed this proposal. These results are analogous with Gif-type systems,⁶⁴ thus the high valence oxidation state Cu (formulated as $\text{Cu}^{\text{IV}}=\text{O}$) should selectively activate the C-H bond of cyclohexane and the proposed mechanism of the copper-catalyzed oxidation of cyclohexane using H_2O_2 as an oxidant is shown in Scheme 4.1.



Scheme 4.1 The proposed mechanism of the copper-catalyzed oxidation of cyclohexane using H_2O_2 as an oxidant

- Using *tert*-butyl hydroperoxide as an oxidant

From the results of the copper-catalyzed oxidation of cyclohexane using TBHP as an oxidant, the possible mechanism may involve a free radical reaction. The oxidation reaction required a higher temperature to produce *t*-butyloxy radical ($+O\bullet$) or *t*-butyl peroxy radical ($+OO\bullet$). Those radicals might abstract H from alkanes and hence produced alkyl radicals. The proposed mechanism of the copper-catalyzed functionalization of cyclohexane using *tert*-butyl hydroperoxide as an oxidant is shown in Scheme 4.2.



Scheme 4.2 The proposed mechanism of the copper-catalyzed functionalization of cyclohexane using *tert*-butyl hydroperoxide as an oxidant