

CHAPTER III

RESULTS AND DISCUSSION

This research was focused on the epoxidation of alkenes employing Co(II) complexes. After screening for potential Co(II) catalysts, cobalt(II) complexes of calix[4]pyrrole **10**, thiophen-*o*-phen **12**, salophen **13** and saloa **14** emerged to exhibit their superb catalytic activity. In this study, the reaction conditions were optimized using cyclohexene as a chemical model. Other substrates such as 1-dodecene, 1-methylcyclohexene, 4-vinylcyclohexene, α -pinene, β -pinene, α -methylstyrene, *trans*-stilbene, *cis*-stilbene, *trans*-2-hexen-1-ol, *cis*-4-hexen-1-ol, 1,2-dihydronaphthalene, ethyl cinnamate and ethyl 4-methoxycinnamate were selected for examining the capability of this catalyst and for exploring the scope of this developed epoxidation system.

3.1 Characterization of cobalt complexes

Tetrakis(4-methoxyphenyl)-tetramethyl-calix[4]pyrrole **10** and thiophen-*o*-phen **12** ligands were synthesized and confirmed their identities by comparison both physical properties and spectroscopic data including IR and $^1\text{H-NMR}$ with those reported in literature.³⁹

The $^1\text{H-NMR}$ spectrum of calix[4]pyrrole displayed the proton signal of NH group at δ 7.53 ppm. These proton signals were disappeared when this ligand was deprotonated to polyanion. The polyanion was further treated with $\text{CoCl}_2\cdot\text{THF}$ to yield the cobalt complex which did not display the signal in $^1\text{H-NMR}$ because of diamagnetic property of cobalt.

All cobalt complexes of **10**, **12**, **13**, **14**, **15**, **16**, **17**, **18**, **18** and **19** used in this study were depicted as shown in Figure 3.1.



Figure 3.1 All ligands used for complexation with cobalt(II) in this study

3.2 Study on the optimum conditions for the epoxidation of alkenes

In fact, there are various factors that need to be evaluated to optimize the epoxidation reaction explored such as the concentration of catalyst, temperature, type of catalyst and type of oxidant. Based upon the accumulated information derived from previous investigation,⁴⁹ this present work concentrated on two important parameters to be optimized. These included the effect of ligands and effect of the amount of 2-ethylbutyraldehyde. Cyclohexene was chosen as a chemical model.

3.2.1 Effect of ligands

Even though a variety of Co(II) complexes have been investigated as a catalyst in the epoxidation of alkenes. All complexes chosen in this study have never been reported concerning their catalytic activity in the epoxidation reaction in chemical literature except for cobalt complex of **13**.⁴⁹

In order to search for appropriate cobalt complexes that could catalyze the reaction to convert cyclohexene to cyclohexene oxide selectively under this particular condition, various ligands were examined. The results of utilization of various cobalt catalysts are presented in Table 3.1.

Table 3.1 Epoxidation of cyclohexene catalyzed by cobalt(II) complexes

Entry	Catalyst	% yield			oxide one + ol
		Cyclohexene oxide	2-Cyclohexenone	2-Cyclohexenol	
1	10	71.90	0	0	-
2	12	52.40	trace	trace	-
3	13	52.39	4.64	trace	11.29
4	14	52.52	2.57	trace	20.44
5	15	47.89	5.01	2.31	6.54
6	16	30.76	3.34	3.20	4.70
7	17	45.00	3.52	2.85	7.06
8	18	25.46	1.77	3.20	5.12
9	19	28.13	1.94	2.98	5.72

reaction conditions: cyclohexene (5 mmol), catalyst (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 mmol), reaction time (24 hr)

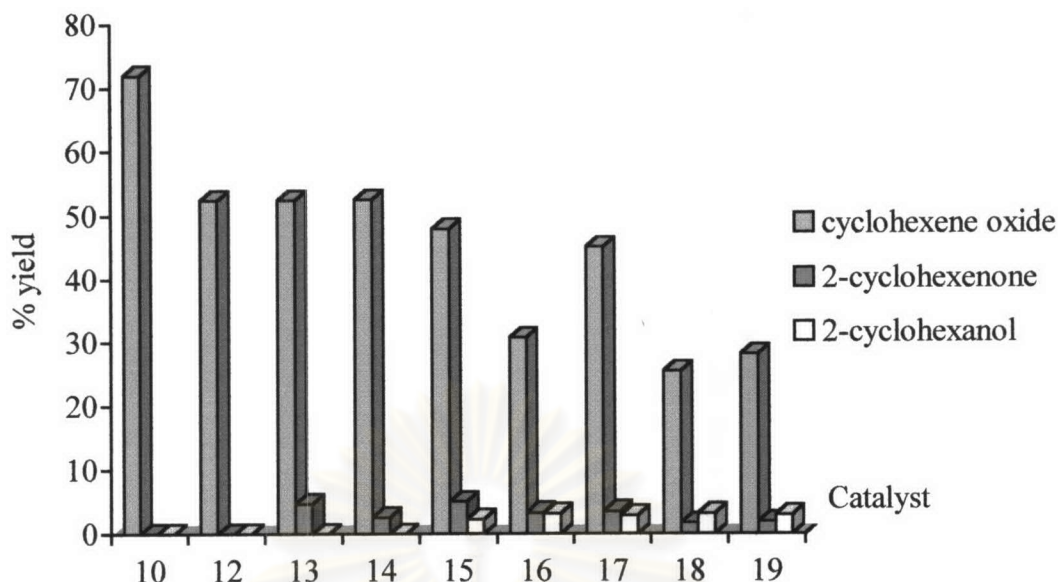


Figure 3.2 The epoxidation of cyclohexene catalyzed by selected cobalt complexes

From Table 3.1 and Figure 3.2, nine cobalt complexes bearing different ligands were screened for potentially catalytic epoxidation ability. It was found that the epoxidation of cyclohexene greatly depended on type of ligands. The cobalt(II) complexes of ligand such as calix[4]pyrrole **10**, thiophen-*o*-phen **12**, salophen **13** and saloa **14** exhibited promising catalytic ability for alkene epoxidation. Among them, cobalt(II) complex of calix[4]pyrrole **10** provided the highest yield of cyclohexene oxide and gave the best selectivity for the production of cyclohexene oxide (entry 1). Thus, in this research cobalt(II) complex of calix[4]pyrrole **10** was mainly utilized as a catalyst for alkene epoxidation. The comparative study on the epoxidation of alkenes employing cobalt(II) complexes of calix[4]pyrrole **10**, thiophen-*o*-phen **12**, salophen **13** and saloa **14** complexes will be discussed in the following topic.

According to the above results, cobalt complexes studied could be divided into four groups. The first was classified for cobalt(II) complexes of thiophen-*o*-phen **12**, salophen **13**, saloa **14**, saloa **15**, and salen* **17**. This group gave moderate yield of epoxide product. The second was cobalt(II) complex of calix[4]pyrrole **10**, provided the best percentage yield of epoxide and the highest selectivity (oxide/one + ol). This good result might stem from the planar structure of cobalt complex of the first and second groups that assisted the active site of the catalyst facilely interacting with the oxidant. The third group was cobalt(II) complex of salt **19** which obliged the poor yield of epoxide and less selectivity. The possible reason why cobalt(II) complex of

saltn **19** produced a small quantity of epoxide could be derived from the cluster structure of these ligands that were of flexible three methylene groups. The last group comprising cobalt(II) complexes of salen OMe **16** and salophen OMe **18** consisted of methoxy groups in ligand structure. The existence of methoxy groups may obstruct the epoxidation proceeding by steric hindrance effect.

3.2.2 Effect of the amount of 2-ethylbutyraldehyde

The epoxidation reaction was normally carried out by using an excess of O₂ and aldehyde. The aldehyde coupled with O₂ was utilized as an oxidant in this reaction. In this research availed 2-ethylbutyraldehyde was used as an oxidant, and the amount of 2-ethylbutyraldehyde was summarized as shown in Table 3.2 and Figure 3.3.

Table 3.2 The effect of the amount of 2-ethylbutyraldehyde on the epoxidation reaction

Entry	Substrate	2-ethylbutyraldehyde (mmol)	% yield
1	cyclohexene	10	71.90
2		20	66.46
3	1-dodecene	10	64.34
4		20	72.32
5	1-methylcyclohexene	10	52.76
6		20	86.33

reaction conditions: substrate (5 mmol), cobalt(II) complex of calix[4]pyrrole **10** (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

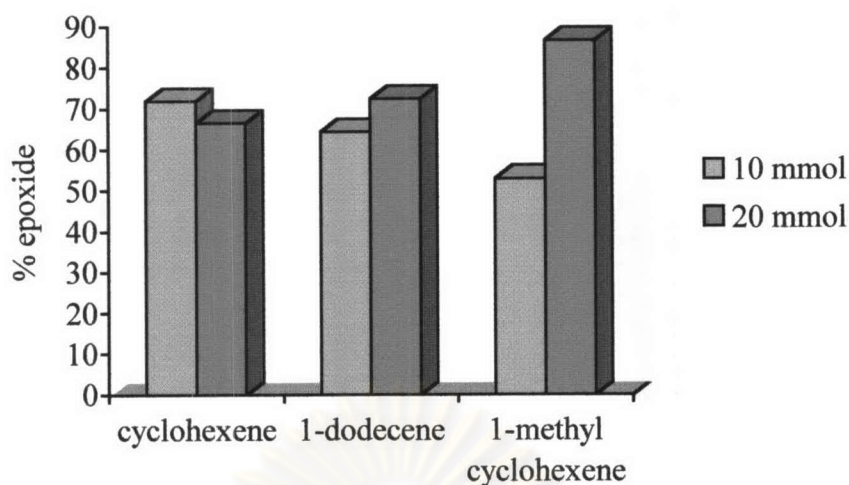




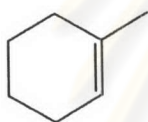
Figure 3.3 The effect of the amount of 2-ethylbutyraldehyde on the epoxidation of alkenes

As a result from Table 3.2 and Figure 3.3, the use of different amount of 2-ethylbutyraldehyde affected the outcome of the reaction. The most appropriate conditions were observed when 2-ethylbutyraldehyde 10 mmol and 20 mmol was employed, cyclohexene was epoxidized to cyclohexene oxide in 72% and 66%, respectively (entries 1,2). With 20 mmol of 2-ethylbutyraldehyde (entry 2), the percentage yield of epoxide was less than that of entry 1 which utilized 2-ethylbutyraldehyde 10 mmol. The large amount of 2-ethylbutyraldehyde might react with the epoxide product, the product quantity was therefore reduced. The use of 2-ethylbutyraldehyde 20 mmol for the epoxidation of 1-dodecene and 1-methylcyclohexene yielded 1-dodecene oxide and 1-methylcyclohexene oxide 72% and 86% (entries 4, 6), respectively. The quantity of oxidizing agent that provided the best yield of epoxide was selected for further investigation.

3.3 Comparative study on the epoxidation reaction catalyzed by cobalt(II) complexes of 10, 12, 13 and 14

To extend the scope of the epoxidation of alkenes catalyzed by Co(II) complexes, various alkenes included cyclohexene, 1-dodecene and 1-methylcyclohexene and cobalt(II) complexes of **10**, **12**, **13** and **14** were investigated. The results are presented in Table 3.3 and Figure 3.4.

Table 3.3 Comparative study of the epoxidation reaction catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

Entry	Substrate	Catalyst	Oxidant (mmol)	% epoxide
1	 Cyclohexene	10	10	71.90
2		12		52.40
3		13		52.39
4		14		52.52
5	 1-dodecene	10	20	72.32
6		12		80.62
7		13		3.93
8		14		20.12
9	 1-methylcyclohexene	10	20	86.33
10		12		67.14
11		13		53.78
12		14		53.85

reaction conditions: substrate (5 mmol), catalyst (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

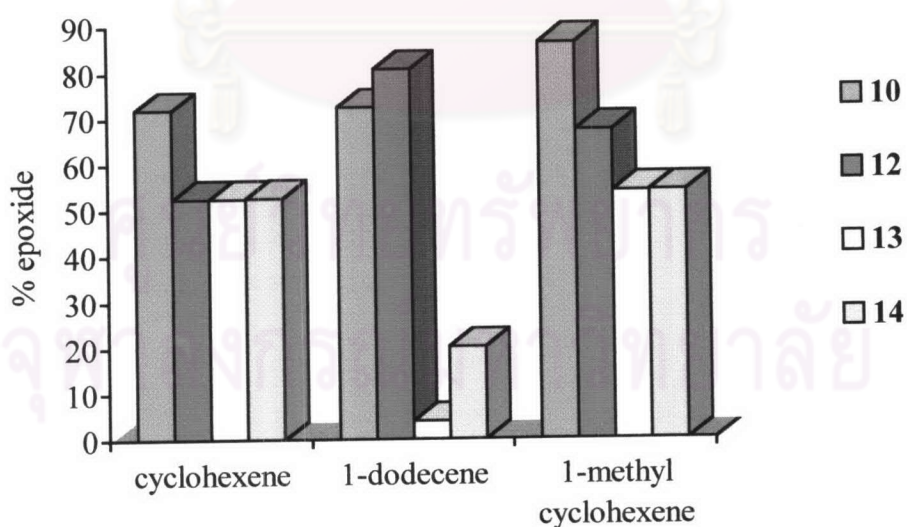


Figure 3.4 The epoxidation reaction of selected alkenes catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

According to the results presented in Table 3.3 and Figure 3.4, the epoxidation reaction of cyclohexene gave the best yield of epoxide product, 72%, with cobalt(II) complex of **10** (entry 1). With other catalysts, moderate yield (~50%) was attained (entries 2-4). For another substrate, 1-dodecene, cobalt(II) complex of **10** (entry 5) and cobalt(II) complex of **12** (entry 6) complexes produced the corresponding 72% and 81%, respectively. Other catalysts (entries 7, 8) gave lower yield (~20%). For 1-methylcyclohexene (entries 9-12), it was found that all catalysts furnished moderate yield of epoxide.

As a result above, the yield of the epoxide product seemed to be depend on the structure of catalyst and substrate. This supported the concept of metal dependence in functionalization reaction. The epoxidation reaction of cyclohexene and 1-methyl cyclohexene provided the promising yield with cobalt(II) complex of **10** as a catalyst, whereas that of 1-dodecene gave the best yield with cobalt(II) complex of **12**.

3.4 Comparative kinetic study of cyclohexene epoxidation catalyzed by cobalt(II) complexes of 10, 12, 13 and 14

The kinetic study of the epoxidation of cyclohexene by various catalysts: cobalt(II) complexes of **10**, **12**, **13** and **14** was conducted at room temperature. The results are shown in Table 3.4 and Figure 3.5.

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Table 3.4 Comparative kinetic study of cyclohexene epoxidation catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

Entry	Catalyst	Time (min)	% epoxide
1	10	30	0
2		90	0
3		180	21.13
4		300	55.09
5		420	52.43
6	12	30	10.11
7		90	30.74
8		180	47.27
9		300	60.38
10		420	55.34
11	13	30	14.80
12		90	24.89
13		180	27.87
14		300	39.59
15		420	46.07
16	14	30	11.73
17		90	24.42
18		180	24.01
19		300	32.54
20		420	36.08

reaction conditions: cyclohexene (5 mmol), catalyst (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 mmol), reaction time (24 hr)

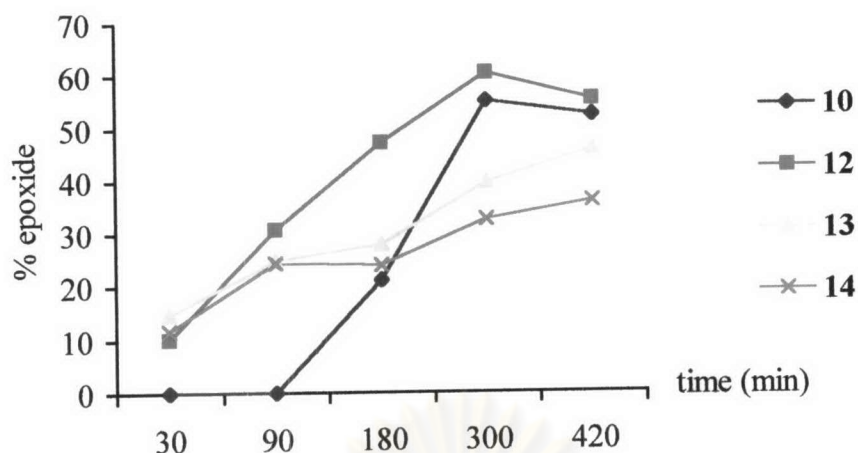





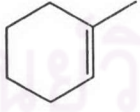
Figure 3.5 Comparative kinetic study of cyclohexene epoxidation catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

From Table 3.4 and Figure 3.5, it was found that the rate of the epoxidation reaction of cyclohexene catalyzed by cobalt(II) complex of **12** was faster than other Co(II) complexes studied. However, the best final yield of cyclohexene oxide was obtained when cobalt(II) complex of **10** was utilized. The half-life of the epoxidation reaction catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14** was approximately 230, 100, 260 and 420 minutes, respectively.

3.5 Comparative kinetic study of the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of 10

The kinetic study of the epoxidation reaction was performed in order to observe the progress of the reaction vs time. The rate of these reactions was generally slow and needed more time to complete. The rate of the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10** was compared. The results are shown in Table 3.5 and Figure 3.6.

Table 3.5 Comparative kinetic study on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10**

Entry	Substrate	Oxidant (mmol)	Time (min)	% epoxide
1	 Cyclohexene	10	30	0
			90	0
			180	21.13
			300	55.09
			420	52.43
2	 Cyclohexene	20	30	7.44
			90	29.23
			180	44.21
			300	45.87
			420	47.32
3	 1-dodecene	20	30	14.34
			90	18.42
			180	19.76
			300	19.91
			420	22.52
4	 1-methylcyclohexene	20	30	6.19
			90	13.73
			180	29.01
			300	50.87
			420	59.86

reaction conditions: substrate (5 mmol), Cobalt(II) complex of **10** (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

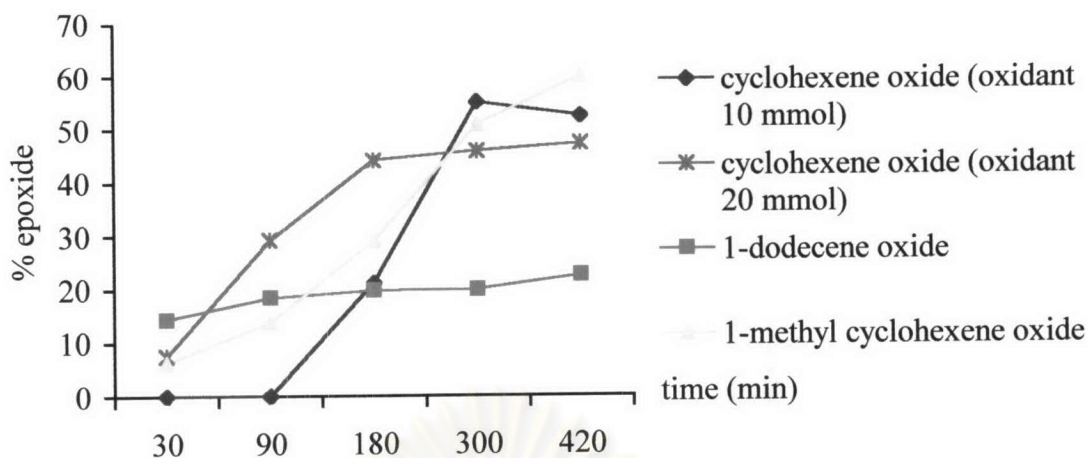




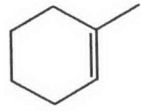
Figure 3.6 Comparative kinetic study on the reaction rate of the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt (II) complex of **10**

From Table 3.5 and Figure 3.6, it was found that the rate of the epoxidation of 1-methylcyclohexene was faster than those of cyclohexene and 1-dodecene, respectively. These could be explained that 1-methylcyclohexene was trisubstituted alkene whose the electron density was more prevailed than other substrates tested. This observation also implied that the active site of catalyst should be electrophilic in character. The half-life of the epoxidation reaction of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10** was approximately 100, > 420 and 250 min (entries 2-4), respectively.

3.6 The effect of solvent on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complexes of **10** and **12**

From the experiment described above, acetonitrile was the first solvent chosen as a reaction medium because it could dissolve both cobalt complex catalyst and substrate. From previous studies⁴³, toluene was also claimed to be appropriate for performing the epoxidation. The high yield of the desired product epoxide was received. Therefore, acetonitrile, toluene and a mixture of acetonitrile and toluene of various ratios as 2:13, 5:10 and 10:5 were experimented. The results shown in Table 3.6 and Figure 3.7 were derived from the use of cobalt(II) complex of **10** as a catalyst.

Table 3.6 The effect of acetonitrile and toluene on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10**

Entry	Substrate	Oxidant (mmol)	acetonitrile : toluene	% epoxide
1	 Cyclohexene	10	0 : 15	73.87
2			2 : 13	97.89
3			5 : 10	98.26
4			10 : 5	95.43
5			15 : 0	71.90
6	 1-dodecene	20	0 : 15	36.28
7			2 : 13	3.53
8			5 : 10	5.52
9			10 : 5	6.59
10			15 : 0	72.32
11	 1- methyl cyclohexene	20	0 : 15	99.45
12			2 : 13	88.89
13			5 : 10	75.15
14			10 : 5	79.22
15			15 : 0	86.34

reaction conditions: substrate (5 mmol), cobalt(II) complex of **10** (0.05 mmol), acetonitrile:toluene (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

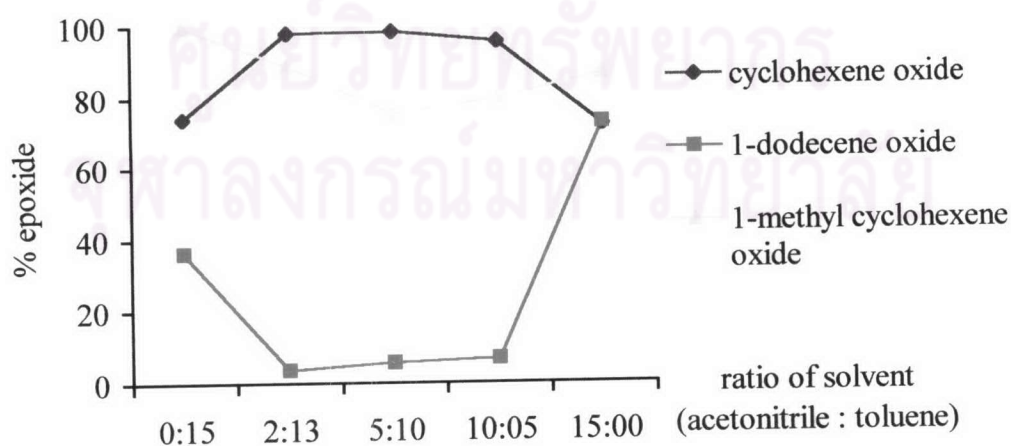


Figure 3.7 The effect of solvent on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10**



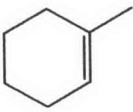
From Table 3.6 and Figure 3.7, the use of acetonitrile or toluene for cyclohexene epoxidation gave good yield of epoxide 72% and 74%, respectively. It should be noted that when a mixture of acetonitrile and toluene at any ratio was employed, the higher yield of the desired product 95-98% (entries 2-4) was obtained. On the contrary, the epoxide product from the epoxidation of 1-dodecene in acetonitrile was 72% (entry 10) whereas the amount of desired product was decreased when toluene was used 36% (entry 6). In addition, a mixture of solvent between acetonitrile and toluene gave only 3-6% (entries 7-9). The type of solvent for the epoxidation of 1-methylcyclohexene was however not affected to the yield of 1-methylcyclohexene oxide as epoxide product (entries 11-15).

Furthermore, the effect of acetonitrile and toluene was further investigated in the epoxidation system utilizing cobalt(II) complex of **12** as a catalyst. The results are tabulated as shown in Table 3.7 and Figure 3.8.



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Table 3.7 The effect of acetonitrile and toluene on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **12**

Entry	Substrate	Oxidant (mmol)	acetonitrile : toluene	% epoxide
1	 Cyclohexene	10	0 : 15	64.02
2			2 : 13	98.34
3			5 : 10	96.40
4			10 : 5	93.23
5			15 : 0	52.40
6	 1-dodecene	20	0 : 15	28.07
7			2 : 13	15.08
8			5 : 10	38.93
9			10 : 5	43.03
10			15 : 0	80.62
11	 1- methyl cyclohexene	20	0 : 15	79.15
12			2 : 13	86.37
13			5 : 10	79.00
14			10 : 5	71.96
15			15 : 0	67.14

reaction conditions: substrate (5 mmol), cobalt(II) complex of **12** (0.05 mmol), acetonitrile:toluene (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

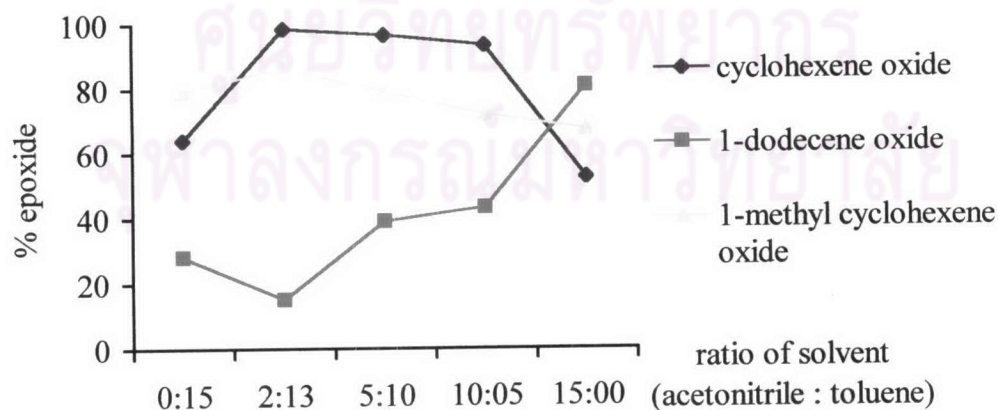


Figure 3.8 The effect of solvent on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **12**

From the results demonstrated in Table 3.7 and Figure 3.8, when the solely acetonitrile or toluene were chosen as a solvent, the moderate yield of the desired product as epoxide was received 64% and 52% (entries 1 and 5), respectively. Nevertheless, a mixture of acetonitrile and toluene at any ratios studied provided superb results to lift up the yield of the desired products. Interestingly, in the case of 1-dodecene, the percentage of epoxide product was related to the ratio of acetonitrile and toluene (entries 7-9). The use of only acetonitrile gave the most epoxide product about 81 % (entry 10). While a type of solvent for the epoxidation of 1-methylcyclohexene had no effect on the yield of 1-methylcyclohexene oxide (entries 11-15).

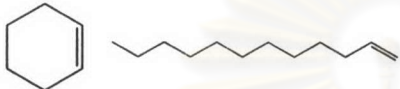
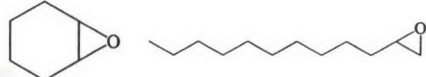
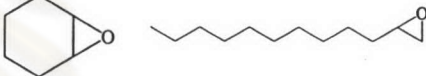

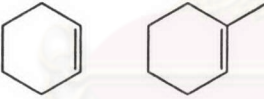
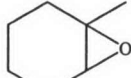

According to the above data, the epoxidation reaction of cyclohexene that exerted cobalt(II) complex of **10** and **12** as a catalysts and a mixture of acetonitrile and toluene as solvent furnished prominent percentage yield of cyclohexene oxide product 93-98%. The epoxidation of 1-methylcyclohexene as substrate showed the same result like case study of cyclohexene (percentage yield of 1-methylcyclohexene oxide in 67-99%). Nevertheless, when the substrate was 1-dodecene, the percentage yield of 1-dodecene oxide was depended on the the catalyst. The difference of catalyst activity of cobalt(II) complex of **10** and **12** for the epoxidation of 1-dodecene was investigated. In summary, the catalytic activity of cobalt(II) complex **12** was increased when the amount of acetonitrile was increased, whereas the desired product from the epoxidation was lower when a mixture of solvent as acetonitrile and toluene was employed. Cobalt(II) complex of **10** and **12** exhibited the same result in terms of catalytic activity for cyclohexene and 1-methylcyclohexene.

This finding also displayed the necessity of condition optimization. An optimized condition for one substrate or one catalyst did not absolutely mean the optimization conditions for others.

3.7 Competition study on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of 10

In order to examine the unique characteristics of this developed catalytic system, the competitive studies on the epoxidation between cyclohexene and 1-dodecene, and 1-methylcyclohexene were investigated. The results are presented in Table 3.8.

Table 3.8 Competition study on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene catalyzed by cobalt(II) complex of **10**

Entry	Substrate	Time (hr)	% epoxide (s)
1		1.0	no reaction
2		5.5	 42.57 4.39
3		24.0	 66.12 17.01
4		1.0	 3.84
5		5.5	 3.32
6		24.0	 4.98 32.41

reaction conditions: substrate (5 mmol), cobalt(II) complex of **10** (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 mmol), reaction time (24 hr)

From Table 3.8, the competition reaction between cyclohexene and 1-dodecene in the period of 24 hr was carried out. It was observed that the epoxidation of cyclohexene took place more prevail than that of 1-dodecene. This could be explained that the more electron rich substrate possessed, the faster the epoxidation occurred. The following experiment between cyclohexene and 1-methylcyclohexene revealed the same trend. The product derived from the epoxidation of 1-

methylcyclohexene was obviously detected more than that from cyclohexene. Therefore, it could be summarized that more substituted alkenes could undergo the epoxidation reaction more effectively. This also implied that the active species responsible for the epoxidation should be an electrophilic species.

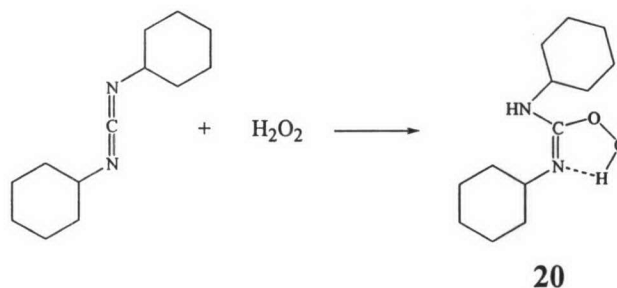
3.8 Epoxidation of selected alkenes catalyzed by cobalt complexes

With the aim to extend this developed epoxidation systems, various alkenes, namely 4-vinylcyclohexene, *cis*-4-hexen-1-ol, *trans*-2-hexen-1-ol, α -pinene, β -pinene, *trans*-ethyl cinnamate, *trans*-ethyl 4-methoxycinnamate, α -methylstyrene and 1,2-dihydronaphthalene were selected for exploring the selectivity of the reaction compared with those addressed in the literature. The regioselectivity of the reaction was mainly focused on the epoxidation of 4-vinylcyclohexene whose structure contained two different olefinic site for the epoxidation to take place, whereas *cis*- and *trans*-stilbenes were chosen for studying the stereoselectivity of the system.

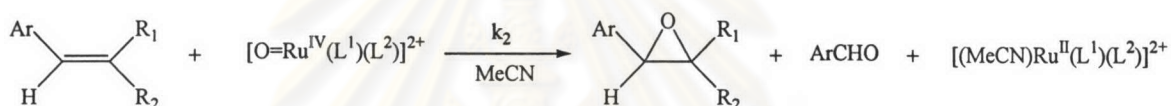
3.8.1 Stereoselectivity study

Stereoselectivity study, one of three selectivity studies in organic reaction is important criterion for the developed reaction that needed to be carefully examined. Two isomeric, *cis*- and *trans*-stilbenes are selected as chemical models to perform this selectivity study.

Taking into an account for the stereoselectivity of the epoxidation exploiting *m*-CPBA, it was reported that the use of *m*-CPBA yielded the epoxide with retention of configuration of alkenes. For instance, the epoxidation of *cis*-2-pentene by *m*-CPBA yielded *cis*-2-pentene oxide as a sole product. The mechanistic pathway was thus believed to take place *via* a concerted reaction.⁵⁰ Other epoxidized systems, for example, the epoxidation reaction of α -methylstyrene,⁵¹ with dicyclohexylcarbodiimide-H₂O₂ as oxidant, giving α -methylstyrene oxide. The reaction presumably occurs *via* an adduct **20** derived from the interaction of DCC and H₂O₂. Intramolecular H-bonding in adduct **20** is probably necessary for the epoxidation to occur in a manner similar to that shown in peracids.⁵² In peracid, epoxidation rates decrease as the Lewis basicity of the solvent increases. This could interpret⁵² that the increased basicity of the solvent led to greater disruption of the intramolecular H-bond in the peracid.



The utilization of monooxoruthenium complex as a catalyst for epoxidation reaction of *cis*- and *trans*- alkenes,⁵³ exhibited that the obtained product possessed the same configuration as of parent compounds. The mechanism postulated for this epoxidation involved the generation of a benzylic radical intermediate at the rate-determining step, possibly proceeded by a rapid and reversible charge-transfer complex formation as shown below.



For this developed epoxidized system, the results of the epoxidation of *cis*- and *trans*-stilbenes catalyzed by cobalt(II) complexes of **10** and **12** are expressed as shown in Table 3.9.

Table 3.9 Stereoselectivity study on the epoxidation of *cis*- and *trans*-stilbenes catalyzed by cobalt(II) complexes of **10** and **12**

Entry	Substrate	Catalyst	Oxidant (mmol)	% epoxide	
				<i>cis</i> -stilbene oxide	<i>trans</i> -stilbene oxide
1	<i>cis</i> -stilbene	10	20	6.30	7.31
2			10	4.20	6.22
3		12	20	4.20	7.00
4			10	-	2.34
5	<i>trans</i> -stilbene	10	20	-	3.98
6			10	-	7.56
7		12	20	-	13.26
8			10	-	-

reaction conditions: substrate (5 mmol), catalyst (0.05 mmol), toluene (15 mL), O₂ and 2-ethylbutyraldehyde (10 or 20 mmol), reaction time (24 hr)

From Table 3.9, it was observed that in the case of *cis*-stilbene, the use of either cobalt(II) complexes of **10** and **12** yielded comparable isolated yield of the desired products, a mixture of *cis*- and *trans*-stilbene oxide, even more oxidant was used (20 mmol). The detection of *cis*-epoxide could be accomplished by ¹H-NMR spectroscopy. In the ¹H-NMR spectra (Figures 3.9 and 3.10), the aromatic protons were observed around δ 7.16-7.42 ppm. Fortunately, the most characteristic peaks for *cis*- and *trans*-stilbene oxide distinguishably appeared at different chemical shifts. To illustrate this, the protons on the carbon connected to the oxygen of an oxirane ring of *cis*-stilbene oxide could be detected at δ 4.39 ppm while those belonged to *trans*-stilbene oxide was clearly observed at δ 3.91 ppm. These observed chemical shifts of the epoxidized products were in good agreement with those obtained from authentic samples synthesized. The quantitative analysis could be accomplished by comparison with the intensity of methyl protons of the known amount of an internal standard, toluene added. Under this condition, the yield of the epoxide was quite low; perhaps because the large size of both substrate and the catalyst involved. That made the steric hindrance occurred. Similar observation was noticed from the oxidation of *trans*-stilbene. In the latter case it was observed that cobalt(II) complex of **10** could be employed as a better catalyst than cobalt(II) complex of **12**. The best isolated yield was attained in the case of employing 20 mmol of the oxidant.

The more important point derived from this experimental fact was that the epoxidation of *trans*-stilbene provided solely *trans*-epoxide whereas the products achieved from the epoxidation of *cis*-stilbene was a mixture of *cis*- and *trans*-stilbene oxides in comparable amount (1:1). This informative data could be used for mechanistic interpretation. The explanation for this observation should derive from the consideration of the intermediate of the reaction formed. The more stable radical intermediate should be a *trans*-form more than the *cis*-one due to their stability. Thus, in the case of *cis*-stilbene, in an equilibrium stage, the formation of *trans*- radical intermediate derived from the free rotation around C-C single bond from *cis*-one should be occurred simultaneously with the *cis*-radical. This will lead to the observation of a mixture of *cis*- and *trans*-stilbene oxides occurred equally. Whereas the epoxidation of *trans*-stilbene took place *via* more stable *trans*-radical intermediate and produced the *trans*-epoxide as the sole product.

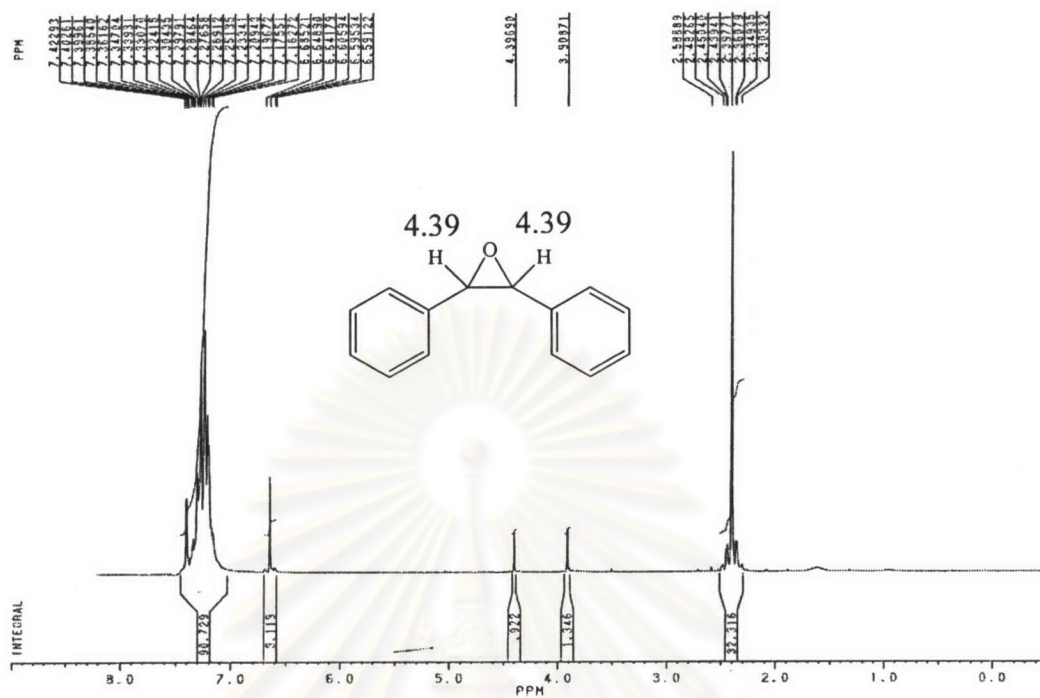


Figure 3.9 The $^1\text{H-NMR}$ spectrum of a mixture of *cis*- and *trans*-stilbene oxide

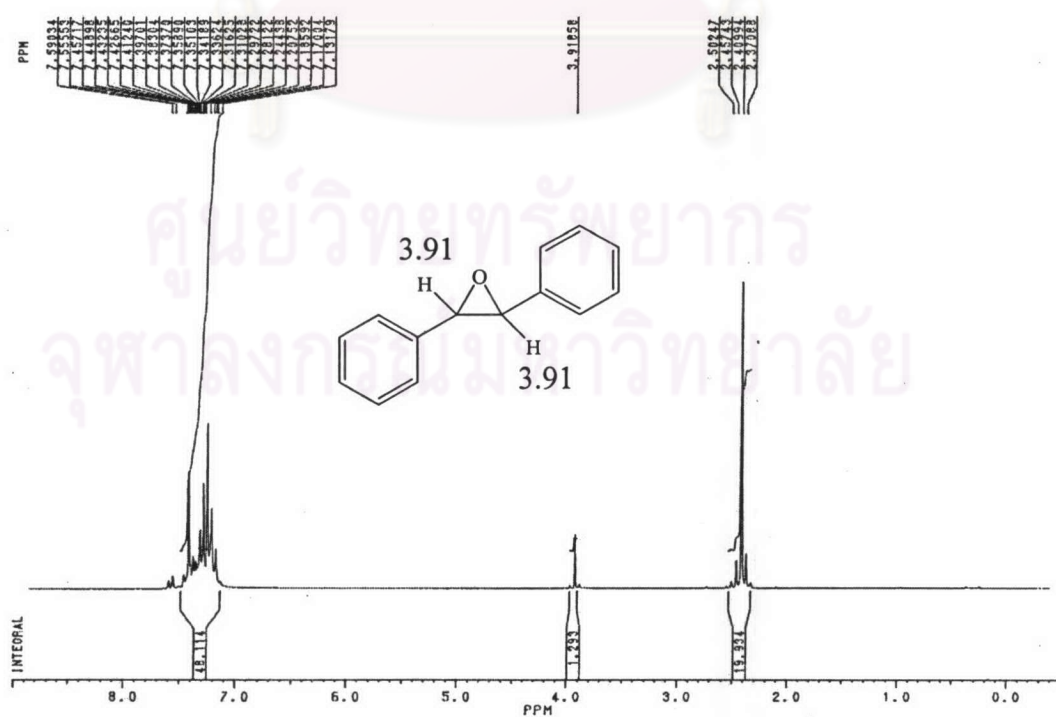



Figure 3.10 The $^1\text{H-NMR}$ spectrum of *trans*-stilbene oxide

3.8.2 Regioselectivity study

A concern of the direction of chemical reaction to take place involved in the regioselectivity study. Catalyst plays an important role in this regard. 4-Vinylcyclohexene was selected as a model for studying this purpose. Comparative studies were carried out utilizing cobalt(II) complexes of **10**, **12**, **13** and **14** as catalysts in three different media. The results are presented in Table 3.10 and Figure 3.11.

Table 3.10 Regioselectivity study on the epoxidation of 4-vinylcyclohexene catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

Entry	Substrate	Catalyst	Solvent	% epoxide(s)
1	 4-vinylcyclohexene	10	acetonitrile	63.52
2			acetonitrile : toluene	80.66
3			toluene	70.92
4		12	acetonitrile	73.31
5			acetonitrile : toluene	84.92
6			toluene	79.28
7		13	acetonitrile	25.49
8			acetonitrile : toluene	23.98
9			toluene	22.25
10		14	acetonitrile	34.64
11			acetonitrile : toluene	19.47
12			toluene	20.25

reaction conditions: 4-vinylcyclohexene (5 mmol), catalyst (0.05 mmol), solvent (15 mL) acetonitrile 2 mL:toluene 13 mL, O₂ and 2-ethylbutyraldehyde (10 mmol), reaction time (24 hr)

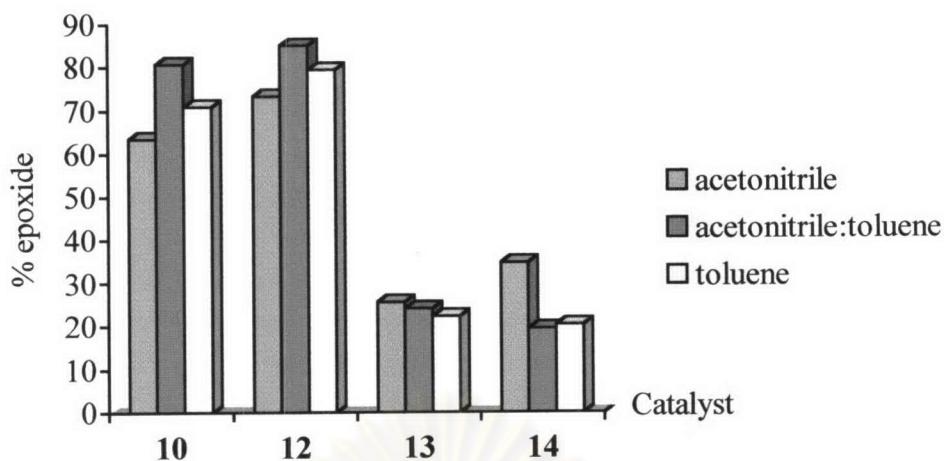


Figure 3.11 Regioselectivity study on the epoxidation of 4-vinylcyclohexene catalyzed by cobalt(II) complexes of **10**, **12**, **13** and **14**

From Table 3.10 and Figure 3.11; cobalt(II) complexes of **10** and **12** emerged as good catalysts for the epoxidation of reaction providing the amount of the desired product about 64-85% (entries 1-6). On the other hand, cobalt(II) complexes of **13** and **14** could moderately catalyze the same reaction, however, yielding the lesser extent of the epoxide 19-35% (entries 7-12), respectively. In addition, it was found that the utilization of a mixture of acetonitrile and toluene did not reveal a major difference in the percentage yield of the epoxide products. Hence, the catalytic epoxidation of 4-vinylcyclohexene was not mainly depended on the medium on the reaction.

In fact, 4-vinylcyclohexene possessed two olefinic bonds in its molecule: one is endocyclic double bond and the other is terminal double bond outside the ring. Therefore, it was possible that two isomeric epoxide products as 1,2-oxide **21** and 7,8-oxide **22** could be formed. The attempt to purify these two epoxides from the crude product from the reaction was accomplished *via* silica gel column chromatography. Those two isolated pure single isomers were well confirmed their structures by spectroscopic evidence as illustrated as follows:

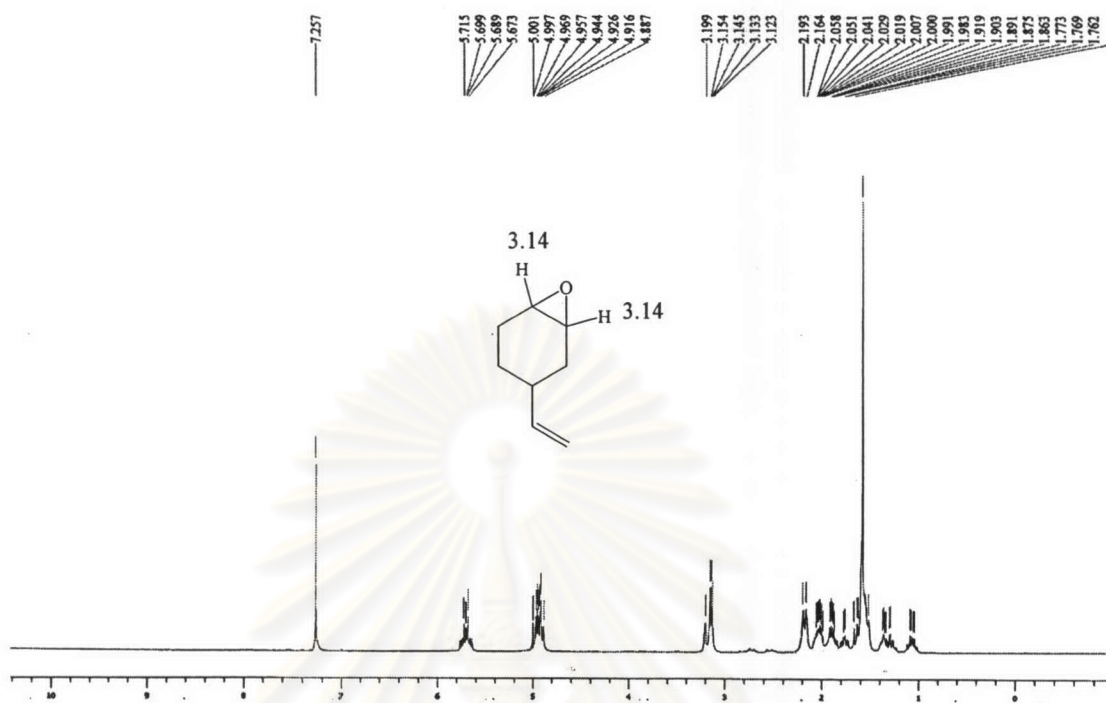


Figure 3.12 The ¹H-NMR spectrum of 21

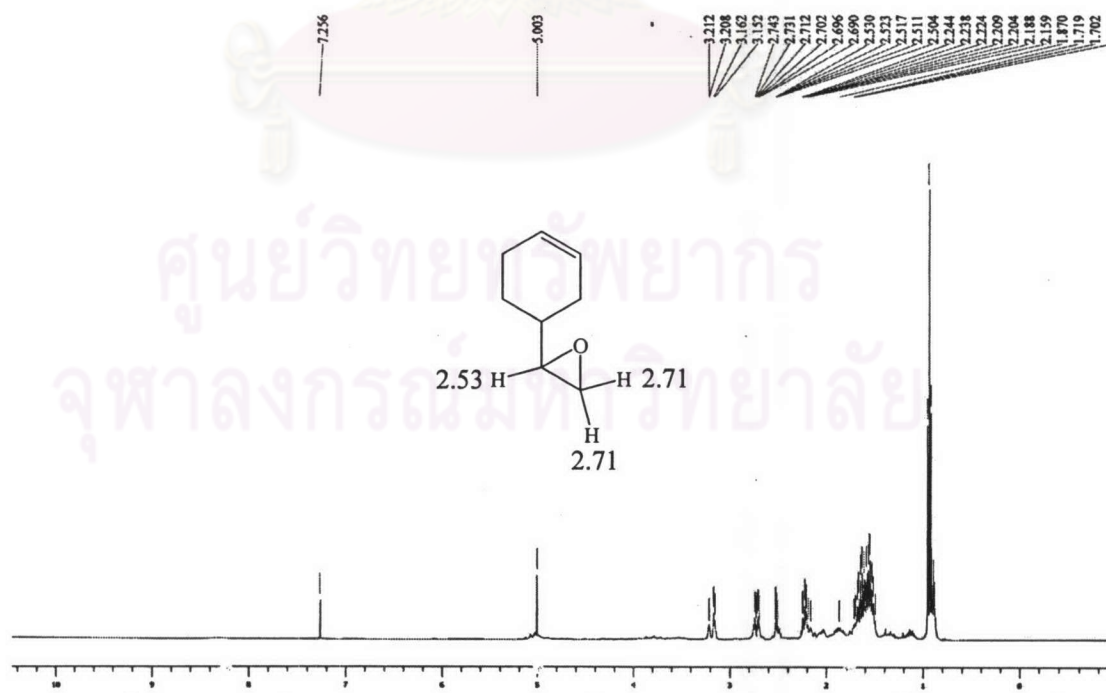


Figure 3.13 The ¹H-NMR spectrum of 22

From Figures 3.12 and 3.13, 1,2-oxide **21** displayed the characteristic chemical shift of the protons of an oxirane ring at δ 3.14 ppm while 7,8-oxide **22** exhibited at δ 2.53 (1H, CH-O-) and 2.71 (2H, CH₂-O-) ppm.

The %composition of each isomer from the epoxidation of 4-vinylcyclohexene catalyzed by cobalt(II) complexes of **10** and **12** are presented in Table 3.11.

Table 3.11 %composition of the products derived from 4-vinylcyclohexene epoxidation

Entry	Catalyst	Total yield	% composition	
			1,2-oxide 21	7,8-oxide 22
1	10	56	86	14
2	12	72	86	14

reaction conditions: 4-vinylcyclohexene (5 mmol), catalyst (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (10 mmol), reaction time (24 hr)

From Table 3.11, 1,2-oxide **21** was detected as a major product. This could be explained by the electron density, the olefinic portion in the ring of cyclohexene has clearly more electron density than that at terminal site; therefore gave more product. According to the isolation of epoxide isomer from the epoxidation reaction of 4-vinylcyclohexene catalyzed by cobalt(II) complexes of **10** and **12**, the major product was 1,2-oxide **21** (86% composition) and 7,8-oxide **22** (14% composition).

The epoxidation reaction of 4-vinylcyclohexene by *m*CPBA was previously reported,¹² it was claimed that two products identified were 1,2-oxide **21** and 7,8-oxide **22** in 97% and 3% composition, respectively. In the same experiment when using peroxybenzimidic acid as an oxidant, 1,2-oxide **21** and 7,8-oxide **22** were obtained in 46% and 53% composition. This present study also exhibited that cobalt(II) complexes of **10** and **12** catalysts illustrated highly stereoselective on the epoxidation reaction of 4-vinylcyclohexene.

3.8.3 Epoxidation of other alkenes

To extend the scope of this developed epoxidation catalyzed by cobalt(II) complexes of **10** and **12**, various alkenes were selected. These included *cis*-4-hexen-1-ol, *trans*-2-hexen-1-ol, *trans*-ethyl cinnamate, *trans*-ethyl 4-methoxycinnamate, α -methylstyrene and 1,2-dihydronaphthalene. The results are presented in Table 3.12.

Table 3.12 Epoxidation of selected alkenes catalyzed by cobalt(II) complexes of **10** and **12**

Entry	Substrate	Catalyst	% epoxide
1	<i>cis</i> -4-hexen-1-ol	10	23.86
2		12	9.33
3	<i>trans</i> -2-hexen-1-ol	10	55.62
4		12	55.73
5	α -pinene	10	68.14
6		12	65.37
7	β -pinene	10	no reaction
8		12	no reaction
9	<i>trans</i> - ethyl cinnamate	10	41.11
10		12	21.61
11	<i>trans</i> - ethyl 4-methoxycinnamate	10	9.15
12		12	5.58
13	α -methylstyrene	10	28.90
14		12	32.64
15	1,2-dihydronaphthalene	10	44.43
16		12	17.45

reaction conditions: substrate (5 mmol), catalyst (0.05 mmol), acetonitrile (15 mL), O₂ and 2-ethylbutyraldehyde (20 mmol), reaction time (24 hr)

As results presented in Table 3.12, it was found that under the standard conditions employed the epoxidation of *cis*-4-hexen-1-ol to the corresponding epoxide could be carried out. The yield obtained from the system utilized cobalt(II) complex of **10** was found to be superior to that using cobalt(II) complex of **12** (entries 1 and 2). When *trans*-2-hexen-1-ol was used as a substrate, moderately yield was obtained for both cases (entries 3 and 4). It is noteworthy at this point that the presence of the hydroxyl group in the molecule did not interfere the epoxidation occurred at the olefinic site. Nevertheless, the conditions for the epoxidation these substrates needed to be a bit change for perhaps gaining a better yield.

The attempt to use both cobalt(II) complexes of **10** and **12** for the epoxidation of natural products were conducted. α -Pinene was found to smoothly transform to α -

pinene oxide as a major product in good yield 68% and 65% (entries 5 and 6), respectively. No other rearranged product was observed. Nonetheless, the epoxidation of β -pinene catalyzed by these two cobalt complexes was not successful under this particular conditions. This was because, as discussed earlier, more substituted alkenes were more reactive than less substituted alkenes towards this reaction.

The epoxidation of *trans*-ethyl cinnamate and *trans*-ethyl 4-methoxy cinnamate catalyzed by cobalt(II) complexes of **10** and **12** were also carried out in order to observe the possibility to employ this methodology to synthesize epoxy acid or its ester derivatives. It was noticed that low to moderate isolated yield of the corresponding epoxide, *trans*-ethyl cinnamate oxide 22-41% (entries 9 and 10) and *trans*-ethyl 4-methoxycinnamate oxide 5-9% (entries 11 and 12) were obtained. The ethyl ester moiety of cinnamate group displayed as electron withdrawing group which therefore decreased the electron density of double bond and therefore rendered the reactivity of the substrate.

Moderate yield of the corresponding epoxides was also obtained from both the epoxidation of α -methylstyrene and 1,2-dihydronaphthalene catalyzed by cobalt(II) complexes of **10** and **12** (entries 13-16).

The moderate yield of the epoxide formation may come from various factors. In order to gain the maximum yield for each substrate, the conditions may need to a bit modify. With the substrate bearing electron withdrawing substituents, more oxidant or longer reaction time may require.

3.9 Proposed mechanism for cobalt(II) complexes of **10** catalyzed epoxidation of alkenes

During the study of cyclohexene epoxidation, it was observed that on the GC chromatogram revealed another distinct peak (besides cyclohexene oxide at retention time 14.02 min as shown in Figure 3.14).

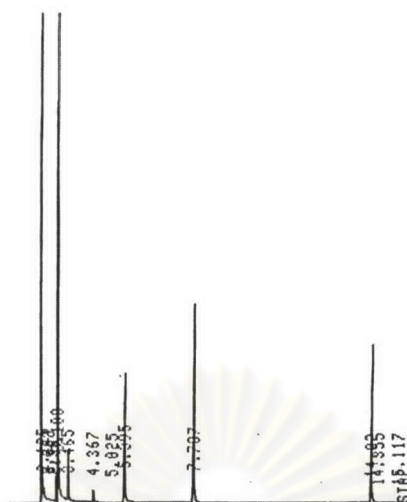


Figure 3.14 Chromatogram of epoxidation of cyclohexene catalyzed by cobalt(II) complexes of **10**

The component with retention time of 14.02 min was successfully isolated from the reaction mixture. It was obtained as yellow liquid, R_f 0.44 (hexane:ethyl acetate, 1:1) The $^1\text{H-NMR}$ (CDCl_3) spectrum of this compound exhibited the significant signal at δ 10.98 (br, 1H) which was compatible with the proton of carboxylic acid. other peaks at 1.87-2.03 (m, 1H, $-\text{CH}(\text{CH}_2\text{CH}_3)_2$), 1.43-1.69 (m, 4H, $-\text{CH}_2-$), and 0.87-0.92 (t, $J = 12$ Hz, 6H, $-\text{CH}_3$). From the $^1\text{H-NMR}$ spectral data, this compound was believed to be 2-ethylbutanoic acid. The GC-MS (column DB-5) (Figure 3.15) gave good spectral information with that obtained from $^1\text{H-NMR}$. It showed the fragmentation ion peak $M+1$ at m/z 117 corresponding to $\text{C}_6\text{H}_{12}\text{O}_2$ (2-ethylbutanoic acid).

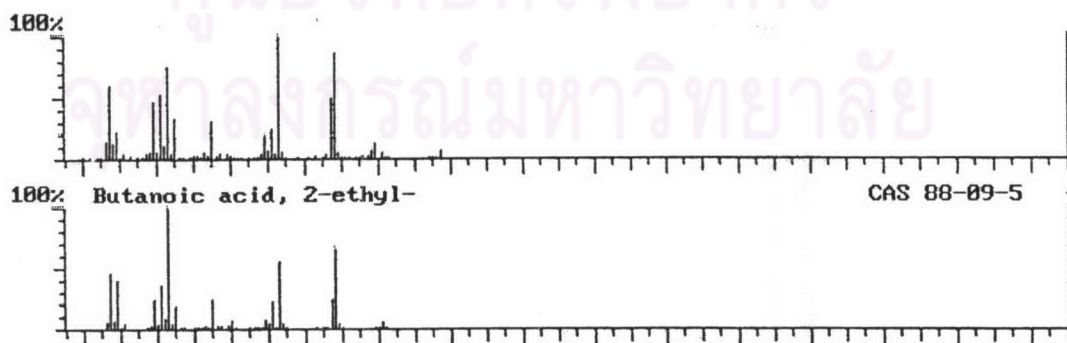
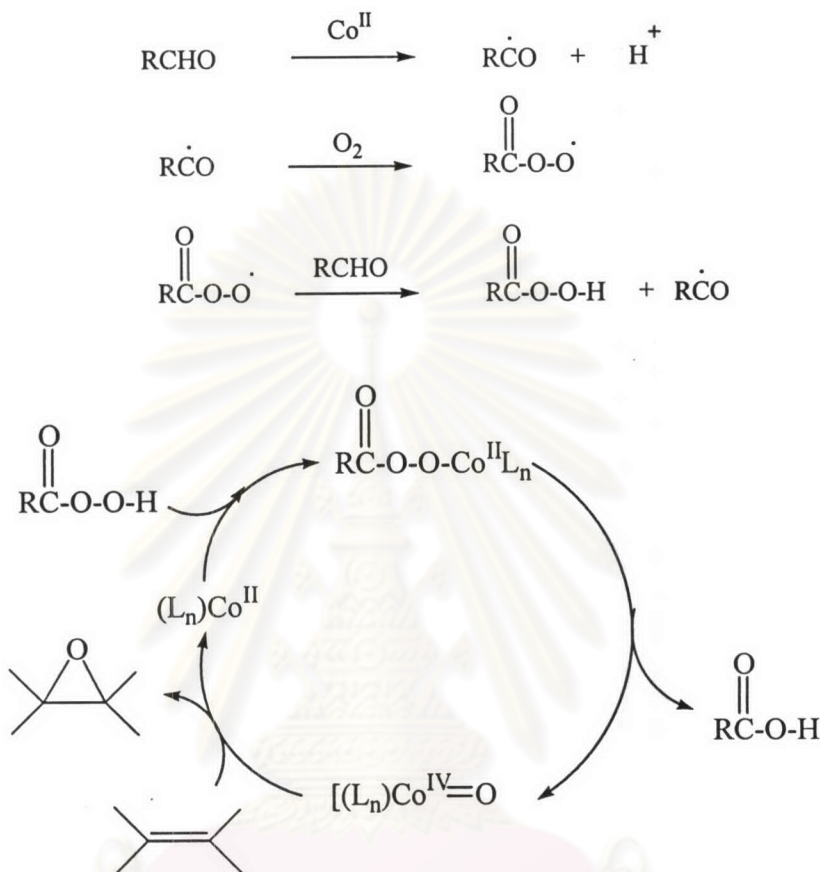


Figure 3.15 Mass spectrum of 2-ethylbutyraldehyde

The separation and identification of 2-ethylbutanoic acid supported the mechanism of reaction to occur through peroxyacid. The mechanism was proposed as shown in Scheme 3.1.



Scheme 3.1 Proposed mechanism for cobalt(II) complexes of **10** catalyzed epoxidation of alkenes

The mechanistic pathway proposed above as that postulated in literature¹⁷ is believed that the cobalt complex played two major roles. First, the cobalt complex reacted with the aldehyde to generate an acyl radical ($\text{RC(O)}\cdot$). The acyl radical then reacted with dioxygen to give an acylperoxy radical ($\text{RC(O)OO}\cdot$). The acylperoxy radical acted as a carrier in a chain mechanism by reacting with another aldehyde molecule to give the peroxyacid, thereby generating another acyl radical. Oxygenation of substrate was assumed to occur *via* reactive high-valent cobalt oxo intermediates, which were produced by the reaction of the peroxyacid with the cobalt catalysts and which then reacted with the olefin in a fashion analogous to that observed previously for metal complex-catalyzed reactions of peroxy acids with olefins.¹⁷