

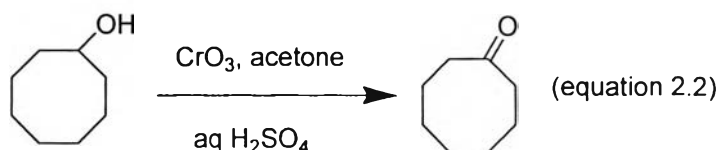
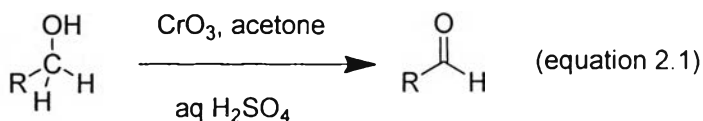
CHAPTER II

OXIDATION OF ALCOHOLS AND SULFUR CONTAINING COMPOUNDS BY CHROMIUM COMPLEXES

2.1 Introduction

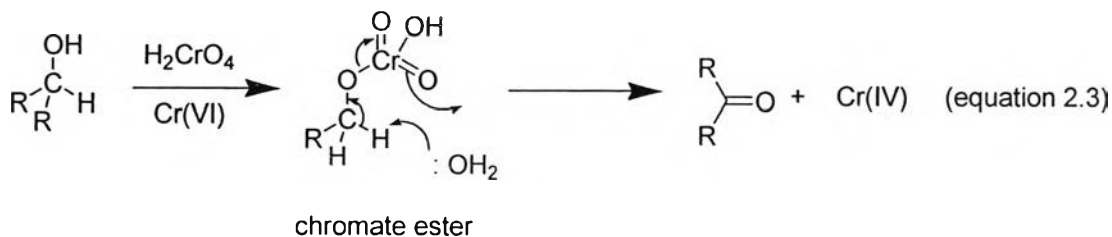
The oxidation of primary and secondary alcohols to the corresponding carbonyl compounds plays a central role in organic synthesis both at the laboratory and industry level. Traditional methods for performing such transformations generally involve the use of stoichiometric quantities of inorganic oxidants such as sodium dichromate dihydrate ($\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$), CrO_3 in aqueous acetic acid (Jones' reagent), Corey's reagent (PCC in CH_2Cl_2), Collins reagent (CrO_3 /pyridine complex). These reagents invariably generate large quantities of waste [23].

Chromic acid (H_2CrO_4) which is *in situ* made by the reaction of H_2O and CrO_3 , is normally used in the oxidation of primary and secondary alcohols to aldehydes and ketones, respectively. This reagent is generally used in conjunction with sulfuric acid and as such this mixture is a powerful oxidant. Jones' reagent, the combination of CrO_3 , sulfuric acid and acetone, is used for the oxidation of primary and secondary alcohols affording the corresponding carbonyl compounds (equations 2.1, 2.2) [24].



The mechanism of this oxidation occurs *via* the formation of a complex between the alcohol and chromate(VI) reagent, known as chromate ester. The

breakdown of this complex liberates a carbonyl compound and a reduced chromium(IV) complex (equation 2.3).

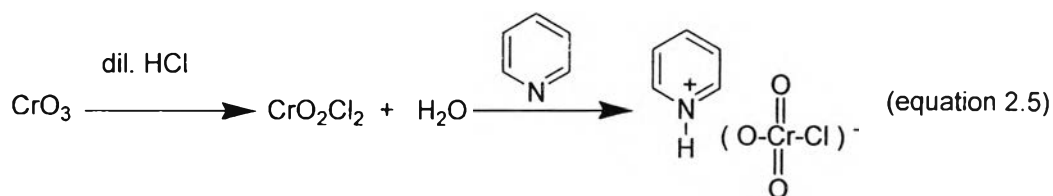


Upon oxidation by Jones' reagent, primary alcohols may transform directly into carboxylic acids due to overoxidation. The oxidation of primary alcohols with sodium dichromate ($\text{Na}_2\text{Cr}_2\text{O}_7$) under solvent free conditions at ambient temperature by shaking is a new system to solve the problem of overoxidation (equation 2.4) [25]. It is a new and efficient method for the preparation of the corresponding aldehyde and ketone from primary and secondary alcohols in high yield. However, this method should certainly never be run on large scale because it is an exothermic oxidation.

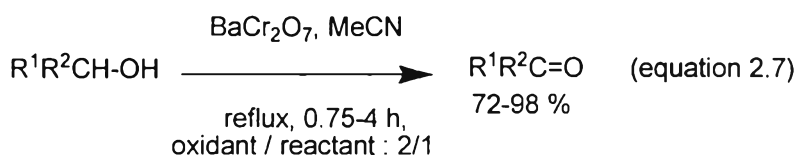
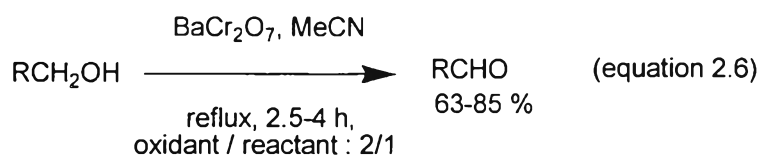


In addition, the use of a non-aqueous complex, for instance, Collins reagent $[(\text{C}_5\text{H}_5\text{N})_2\text{CrO}_3]$ [26], pyridinium chlorochromate (PCC) $[(\text{C}_5\text{H}_5\text{NH})\text{ClCrO}_3]$ [27] and pyridinium dichromate (PDC) $[(\text{C}_5\text{H}_5\text{NH})_2^+\text{Cr}_2\text{O}_7^{2-}]$ has been addressed [28]. These reagents are simply prepared in quantity by mixing CrO_3 and pyridine to furnish excellent yields of aldehydes while secondary alcohol oxidation gives the corresponding ketones. The main disadvantage of this method is the formation of chromyl chloride which is a very toxic and hazardous compound during the first step of the PCC synthesis.

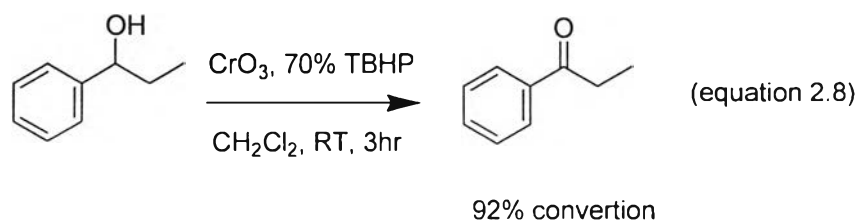
In 1990 Agarwal and colleagues proposed the use of anhydrous acetic acid for the first time as catalyst to get rid of chromyl chloride and improved yield with no side effect. The first step of this oxidation method involves the formation of pyridinium chloride which is much less toxic than chromyl chloride (equation 2.5) [29].



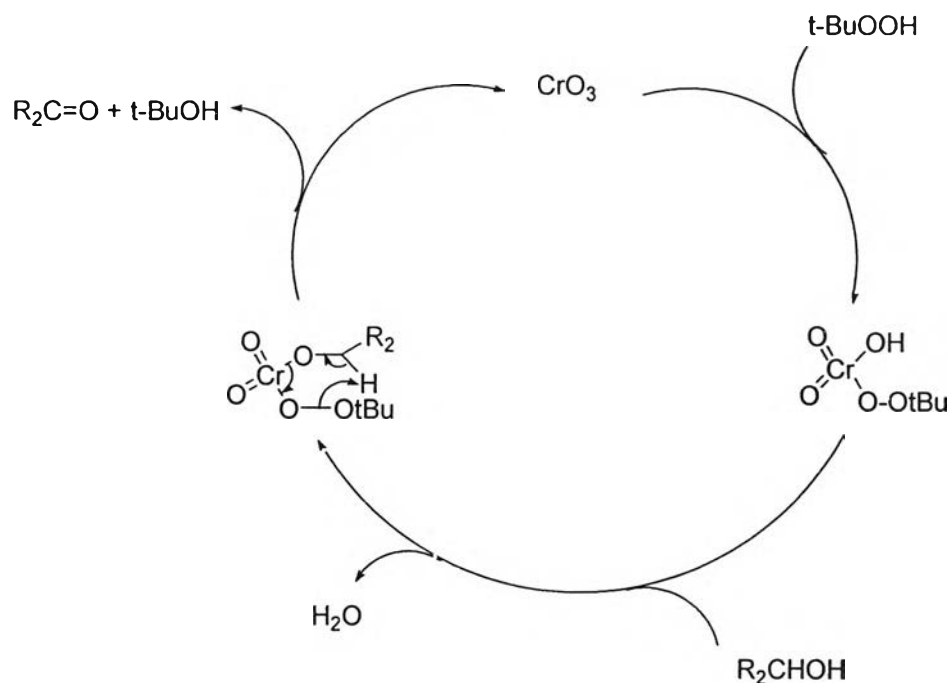
Moreover, Mottaghinejad and colleagues demonstrated barium dichromate as an oxidizing agent for the conversion of alcohols to their corresponding carbonyl compounds [30]. The oxidation reaction was attempted with aliphatic and benzylic alcohols in boiling acetonitrile. Primary alcohols undergo oxidation to produce aldehydes in moderate to good yield (63-85%) while secondary alcohols gave ketones in good to excellent yield (72-98%) (equations 2.6, 2.7). However, the use of Cr(VI) reagents in quantities ranging from stoichiometric to a large excess provide some trouble in carrying out the work-up and expelling chromium residues. Hence, in terms of economical and environmental concerns, catalytic oxidation process with inexpensive and clean oxidants are extremely valuable.



In 1987, Muzart reported the cheap and readily available oxidizing catalytic system constituted of CrO_3 and 70% TBHP [31]. This method was mainly efficient in case of α , β -unsaturated secondary alcohols particularly at benzylic positions (equation 2.8).

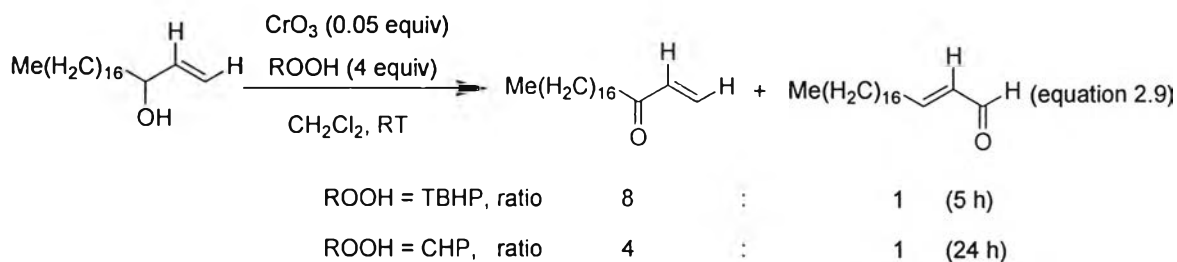


These oxidations seem to involve alkoxy-*tert*-butylperoxy-chromium intermediate in recycling chromium oxide. In this sequence, the formal oxidation state of the Cr^{VI} would be maintained during the whole cycle (Scheme 2.1).

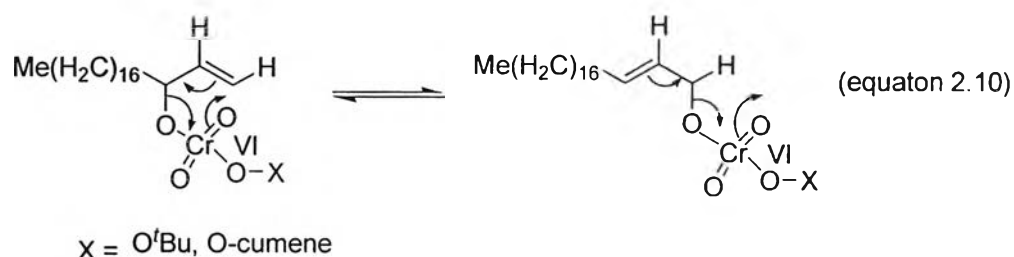


Scheme 2.1 Catalytic cycle of Cr^{VI} for alcohol oxidation

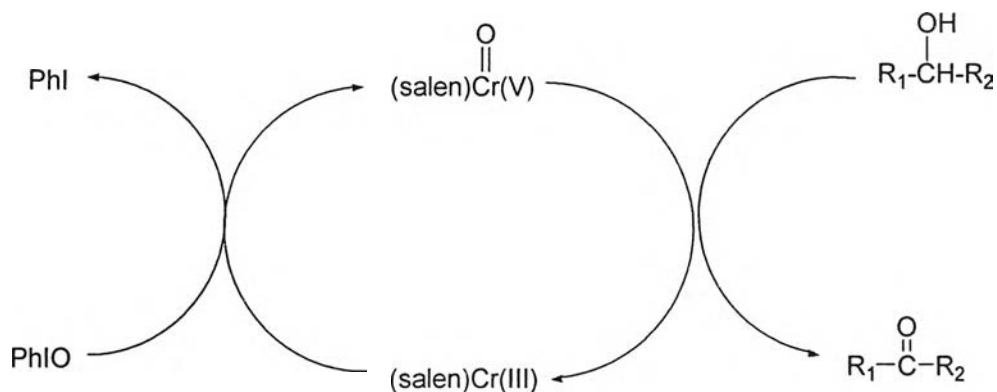
Moreover, the oxidation of allylic alcohols ($R_1\text{CHOH-CR}_2=\text{CHR}_3$) under these conditions generally affords a mixture of ($R_1\text{COCR}_2=\text{CHR}_3$) and ($R_1\text{CH}=\text{CR}_2\text{COR}_3$) (equation 2.9) [32].



A comparative experiment using cumene hydroperoxide (CHP) instead of TBHP revealed the influence of the nature of peroxide on both the rate of the oxidation of alcohol and product distribution. These observations indicated that steric interactions between the alkyl chain of alcohol and *tert*-butyl or cumyl substituent of the hydroperoxide intervene in the course of the process. The CrO₃ catalyzed oxidation of alcohols by ROOH implied a hydrogen elimination from an allyloxychromium intermediate whose the coordination sphere contained the R group (equation 2.10).

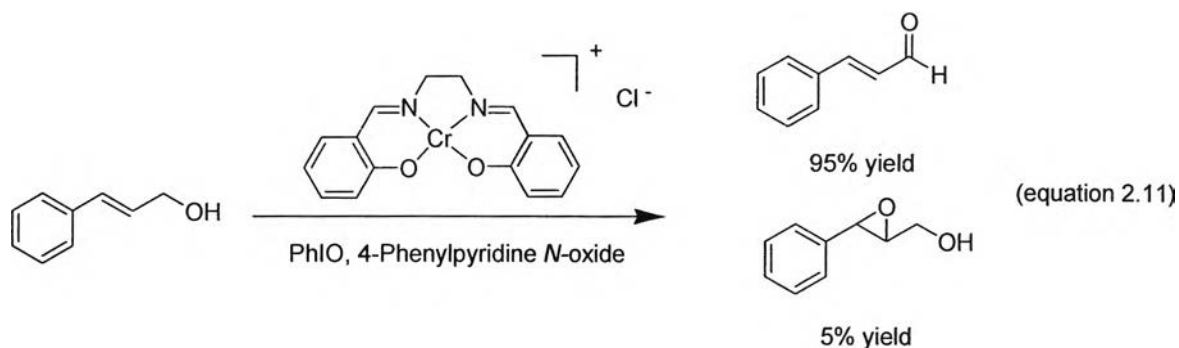


Furthermore, the development of chromium-based catalytic oxidation methods has been studied in recent years. The selective oxidation of alcohols catalyzed by chromium(III) salen with iodozobenzene as the oxygen source was considered. The *in-situ* generated (salen)oxochromium(V) complex is proposed as the actual oxidation (Scheme 2.2) [33,34].



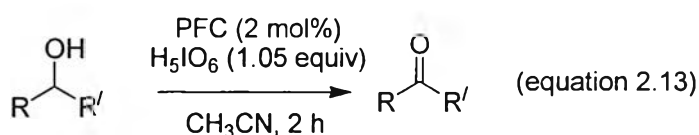
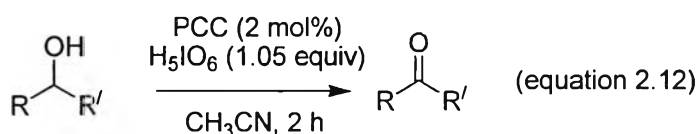
Scheme 2.2 Catalytic cycle for the oxidation of alcohols to carbonyl compounds by (salen)Cr(III)/ PhIO

The oxidation of primary and secondary alcohols with C-H bonds in an activated benzylic position under these conditions was chemoselective to the corresponding carbonyl compounds with high yields. Allylic alcohols with fully substituted double bonds give appreciable amounts of epoxides besides the C-H oxidation products, enones while saturated alcohols are less readily oxidized (equation 2.11).

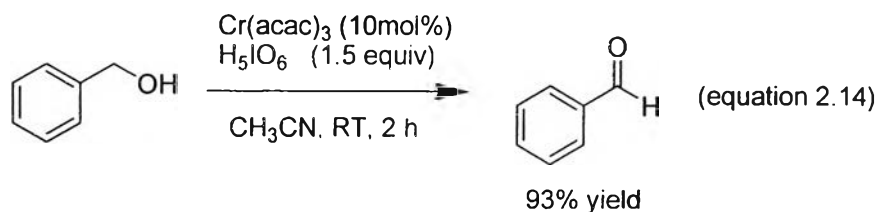


In 2000, chromium(VI) oxide was used as catalyst in oxidation of alcohols and activated methylenes by aqueous TBHP using benzotrifluoride (BTF) as solvent. This method gave a high yield however BTF is not convenient as a solvent for the oxidation of volatile compounds because of its relative high boiling point which precludes an easy and quantitative recovery of the products [35].

The oxidation of alcohols under slightly acidic conditions at room temperature using periodic acid was studied. A facile PCC and fluorochromate catalyzed oxidation of alcohols to ketones and aldehydes using H_5IO_6 as the co-oxidant in acetonitrile is attractive. Both procedures gave the carbonyl compounds in high yield in a short period of time (equations 2.12, 2.13) [36, 37].



Moreover, the use of chromium complex such chromium(III) acetylacetonate as the catalyst with H_5IO_6 to improve the yield of oxidations has been recently addressed. The oxidation of alcohols in acetonitrile at room temperature afforded the corresponding aldehydes and ketones in high yield (equation 2.14) [38].



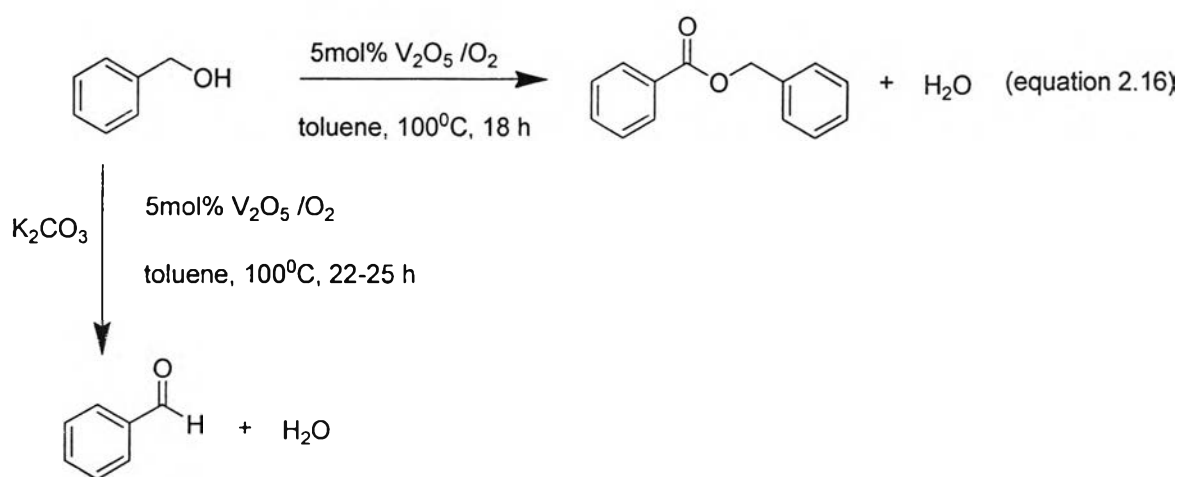
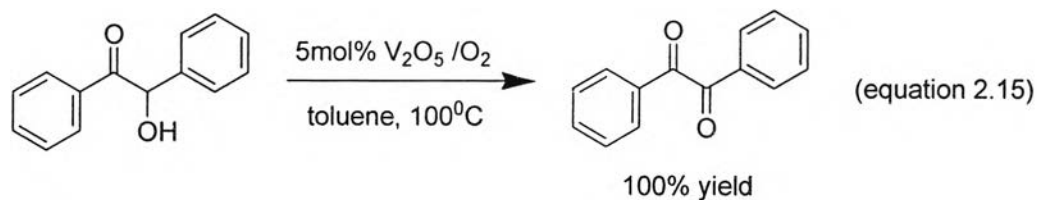
Nevertheless, the oxidation of alcohols containing several functional groups such as sulfide or sulfone was unsuccessful with $\text{Cr(acac)}_2/\text{H}_5\text{IO}_6$ system. These alcohols suffer from competitive oxidation at sulfur to give mixtures of sulfoxides and sulfones. In addition, alcohols that contained silyl ethers (OTMS and OTBS), *N*-tert-butoxy-carbonyl (*N*-Boc) and phenolic groups gave poor yields or intractable product mixtures.

Besides chromium complexes, other transition metal complexes such as manganese(III) complex were reported to use for alcohols oxidation by H_2O_2 [39]. For oxo complexes of Ru(IV), a series of reaction pathways have been identified including the oxidation of alcohols to carbonyl compounds [40]. In the case of cobalt complexes, cobalt(II) acetylacetonate, Co(acac)_2 , has been studied both in homogeneous and heterogeneous catalytic oxidation of benzylic and secondary alcohols in the presence of excess 2-methylpropanal. Under homogeneous conditions the reaction was achieved at 40°C by using molecular oxygen as the oxidant while the analogue of Co(acac)_2 supported cobalt polymer acts as an active and reusable catalyst in heterogeneous condition [41]. The results from using both conditions for the alcohol oxidation are not different but the supported catalyst was easily separated from the reaction mixture and it was recycled at least once without appreciable loss of activity and selectivity.

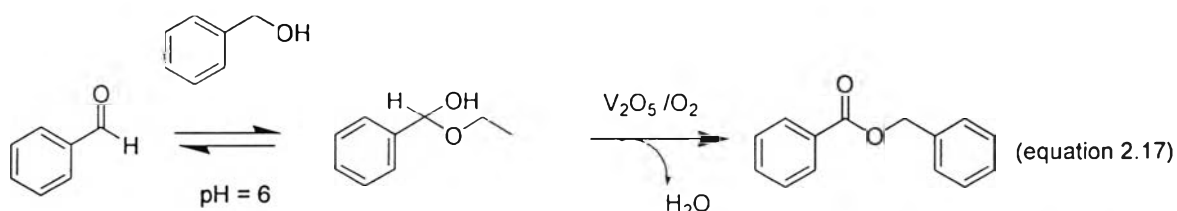
The study of dirhodium(II) tetraacetate as catalyst was addressed for allylic and benzylic alcohol oxidation to the corresponding carbonyl compounds by TBHP, preferably in stoichiometric amounts, in CH_2Cl_2 at ambient temperature. Secondary alcohols such as 2-cyclohexenol gave a high yield of cyclohexenone. However, primary allylic and benzylic alcohols could be oxidized under these reaction conditions, although the yields of the corresponding ketones are considerably lower, due to by-product formation [42].

Oxidation of alcohols to aldehydes and ketones could be achieved in high yield using atmospheric oxygen and a catalytic amount of V_2O_5 in toluene with

heating (100 °C) [43]. Secondary alcohols were oxidized to the corresponding ketones in high yields (equation 2.15). However, the oxidation of primary alcohols to aldehydes required 0.5 equiv of K_2CO_3 , and in its absence, the corresponding esters were obtained (equation 2.16).

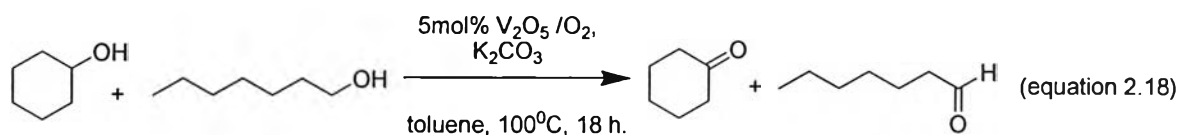


The ester formation from the oxidation of primary alcohols in the absence of K_2CO_3 may be due to the formation of a hemiacetal and its subsequent oxidation to ester as shown in equation 2.17. This is due to the weakly acidic nature of the reaction media (pH = 6). The addition of K_2CO_3 in the reaction increase the pH to 9 inhibiting the hemiacetal formation.



To study the chemoselectivity oxidation of alcohols, a mixture of cyclohexanol and heptyl alcohol was allowed to react. The former was oxidized to cyclohexanone 87% yield while the latter gave heptanal in less than 5% yield (equation 2.18). These studies clearly reveal that this method can be applied for the

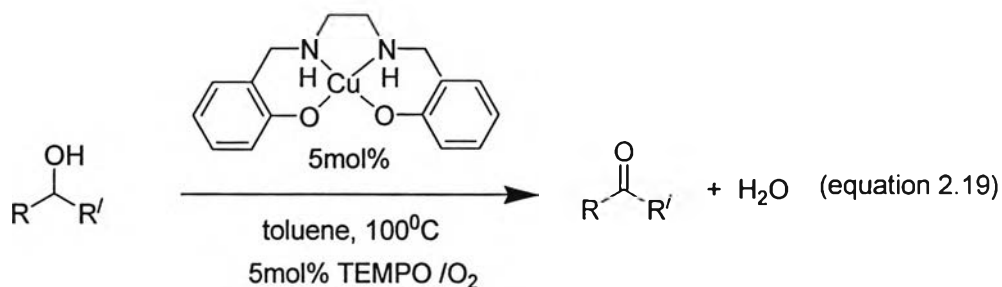
chemoselective oxidation of secondary alcohols in the presence of primary hydroxy groups.



In the case of efficient iron complexes, selective oxidation of secondary and benzylic alcohols was accomplished by H_2O_2 under solvent-free condition catalyzed by FeBr_3 . Secondary alcohols are selectively oxidized even in the presence of primary ones and also work well with sterically hindered alcohols such as menthol or 2-adamantanol. An important advantage of this method aside from the solvent-free conditions is that it does not require a phase-transfer catalyst [44].

The use of dinuclear iron complexes such as $[\text{Fe}(\text{ind})\text{Cl}]_2\text{O}$; (ind = 1,3-bis(2'-pyridylimino)isoindoline) as catalyst with H_2O_2 as a primary oxidant was carried out at room temperature. It was shown that alcohols are oxidized rapidly to the corresponding aldehydes or ketones with good selectivity [45].

The selective oxidation of primary alcohols to aldehydes with 2,2,6,6-tetramethylpiperidinoxy (TEMPO) in toluene under atmospheric oxygen catalyzed by copper(II) complex was studied (equation 2.19) [46].



$\text{R} = \text{alkyl, aryl, ally}; \text{R}' = \text{H}, 50\text{-}99\% \text{ yield}$

$\text{R} = \text{alkyl, aryl}; \text{R}' = \text{alkyl, aryl}, 2\% \text{ yield}$

Aliphatic and aromatic primary alcohols can be oxidized to the corresponding aldehydes in high yield without overoxidation to the carboxylic acid. This procedure does not require additive and the catalyst is recyclable without loss of activity.

2.2 Scope of this study

The aforementioned literature revealed good evidence that metal complexes could be employed as a good catalyst for the oxidation of alcohols. However, the disadvantage of some catalyst is the poor solubility of the catalysts in reaction media. Some catalysts such as chromium(III)salen is very complicated to prepare. Several methods still needed the use of stoichiometric amounts of toxic reagents. From our understanding, chromium(III) complexes have hitherto used as a catalyst in the oxidation of substrates with TBHP. Thus, this chapter devoted for detailed investigation of the oxidation of alcohols and sulfur containing compounds using chromium(III) complexes as a catalyst and TBHP as an oxidant.

2.3 Experimental

2.3.1 General procedure:

This section provides general information of general and/or specific reaction conditions and spectral data for compounds along with a representative ^1H NMR and ^{13}C NMR spectra. The reactions were monitored by analytical TLC on aluminium sheets precoated with silica gel (Merck's, Kieselgel 60 PF254). Visualization was observed by UV light (254 nm), followed by dipping the plate into the appropriate stain. All reactions were stirred with Teflon-coated magnetic bars in condenser fitted round bottom flask. Removal of solvents was normally accomplished using a *Buchi* rotary evaporator connected to a vacuum pump.

Chromatography: Gas chromatography analysis was carried out on Shimadzu Gas Chromatography 9A instrument equipped with flame ionization with N_2 as a carrier gas. The columns used for analysis were HP5 20M. Column chromatography was performed on silica gel (Merck's, Kieselgel 60 G Art 7734 (70-230 mesh)).

^1H and ^{13}C -NMR spectra were recorded at 400 MHz on a Varian spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance of CDCl_3 (7.26 ppm).

Infrared spectra: Infrared spectra were recorded on a Shimadzu Fourier transform infrared spectrometer with 2 cm^{-1} resolution in a solution cell. Infrared frequencies are reported in reciprocal centimeters (cm^{-1}).

Melting points: Melting points were measured on a Fisher-Johns melting point apparatus and are uncorrected.

Elemental analysis (EA) was carried out on CHNS/O ANALYSER (Perkin Elmer PE2400 Series II) at Scientific and Technological Research Equipment Center Chulalongkorn University. Gaseous products freed by pyrolysis in high-purity oxygen 15 and were chromatographically separated by frontal analysis and quantitatively detected by thermal conductivity detector.

Chemicals: All solvents in this research were purified according to the procedures described in the standard methodology except for reagents and solvents that are reagent grade. The reagents for the preparation of Cr(str)₃ and for synthesizing some substrates as well as commercial available substrates, *e.g.* cyclohexanol, benzyl alcohol, cinnamyl alcohol, menthol *etc.*, were purchased from Fluka chemical company and were used without further purification.

2.3.2 Syntheses

2.3.2.1 Preparation of Cr(str)₃

Stearic acid (6.26 g, 22 mmol) was dissolved in the solution of NaOH (0.88 g NaOH in 20 mL) at 80 °C to give a 2 M solution. The solution was stirred until clear and homogenous. Chromium trichloride hexahydrate (1.95 g, 7.3 mmol) dissolved in 10 mL of distilled water was added giving a light purple precipitate. The reaction mixture was allowed to stir at the same temperature until the complex was fully formed, then the precipitate was collected and dried *in vacuo* (75% yield), m.p. 100-103°C. IR (KBr, cm⁻¹) 2850-2900(s), 1600-1700 (w). 1400-1450 (m). EA, %C = 69.52 and %H = 11.74.

2.3.2.2 Preparation of Cr(pic)₃1.5H₂O

The catalyst was prepared by dissolving 5.12 g (19.21 mmol) of CrCl₃.6H₂O and 7.50 g (60.98 mmol) of picolinic acid in 40 mL of deionized water. Crystals of Cr(pic)₃ formed after stirred the solution mixture for 24 h (70% yield), m.p. 100-103°C. IR (KBr, cm⁻¹): 1750 (s), 1607 (s), 1473 (m), 1327 (s), 1287 (s), 1051 (m), 864 (m), 767 (m), 475 (s). (EA), %C = 48.35, %H = 3.27 and %N = 9.44.

2.3.2.3 The general procedure for the oxidation of alcohols.

To a solution of alcohol (5 mmol) in isooctane (5 mL) containing the catalyst (0.2 mmol) in a round bottom flask was added TBHP giving a purple suspension. The reaction mixture was heated and kept constant at 70⁰C. After the specified time or completion of the reaction (monitored by TLC), 1 mL of the reaction mixture was taken and extracted twice with Et₂O. The combined extracts were washed with 30% H₂SO₄ to get rid of catalyst from oxidation reaction and saturated NaHCO₃, respectively. The organic layer was dried over anhydrous Na₂SO₄ and analyzed by GC with the addition of an exact amount of an appropriate internal standard.

2.3.2.4 Optimum conditions for oxidation of alcohols

Effect of type of chromium complexes

The oxidation reaction was conducted as described in general procedure but the using Cr(III) palmitate, Cr(III) stearate, Cr(III) behenate, Cr(III) acetyl acetonate, Cr(III) salenCl as catalysts.

Effect of the amount of oxidant

The oxidation reaction was conducted as described in general procedure but the amount of oxidant was varied (9, 12, 18, 20 and 27 mmol).

Effect of temperature

The oxidation reaction was conducted as described in general procedure but the temperature was varied (RT, 50, 70 and 99 ⁰C).

Effect of the amount of catalyst

The oxidation reaction was conducted as described in general procedure but the amount of catalyst was varied (0.01, 0.05, 0.10, 0.20, 0.25 and 0.50 mmol).

Effect of reaction time for Cr(str)₃ catalyzed oxidation of cyclohexanol

The oxidation reaction was conducted as described in general procedure but the reaction time was varied (1, 3, 5 and 24 h).

Effect of metal stearate catalyzed

The oxidation reaction was conducted as described in general procedure using Ni(II) stearate, Co(II) stearate, Cu(II) stearate, Fe(III) stearate, Mn(III) stearate and Cr(III) stearate as catalysts.

2.3.2.5 Oxidation of secondary alcohols catalyzed by Cr(str)₃

The oxidation reaction was carried out as described in general procedure, with Cr(str)₃ employed as catalyst, but the substrate was varied (cyclohexanol, 2-octanol, menthol, chloesterol, benzoin, 1,4-cyclohexadiol).

benzil: yellow solid (24%), m.p. 93-95°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 7.52 (2H, t, *J* = 15.6 Hz), 7.66 (1H, t, *J* = 14.8 Hz), 7.97 (2H, d, *J* = 7.2 Hz)

2.3.2.6 Oxidation of primary alcohols catalyzed by Cr(str)₃

The oxidation reaction was carried out as described in general procedure with Cr(str)₃ employed as catalyst, but the substrate was varied (1-octanol, benzyl alcohol, *trans*-2-hexene-1-ol, cinnamyl alcohol, furfural alcohol, 3-phenoxy benzyl alcohol).

octanoic acid: yellow oily liquid (50%); ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 0.95 (3H, t, *J* = 1.40 Hz), 1.29 (4H, m), 1.33 (2H, m), 2.40 (2H, q, *J* = 2.80 Hz).

benzoic acid: colorless solid (80%), m.p. 120-122°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 7.48 (2H, t, *J* = 7.1 Hz), 7.62 (1H, t, *J* = 6.1 Hz), 8.12 (2H, d, *J* = 7.1 Hz)

***trans*-cinnamic acid:** colorless solid (37%), m.p. 132-134°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 6.46 (1H, d, *J* = 16 Hz), 7.40-7.61 (5H, m), 7.80 (1H, d, *J* = 16 Hz)

3-phenoxybenzoic acid: white solid (24%), m.p. 149-150°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 7.10 (2H, d, *J* = 8.40 Hz), 7.15-7.50 (5H, m), 7.79 (1H, s), 7.85 (1H, d, 8.80 Hz)

2.3.2.7 Reactivity and selectivity study on the oxidation of primary alcohols catalyzed by Cr(str)₃

The selective oxidation reaction of 1-phenylethanol in the presence of 1-hexanol and benzyl alcohol, and 1-phenylethane-1,2-diol were conducted as described in general procedure using Cr(III)stearate as catalyst but the different amounts of oxidant (3 mmol and/or 9 mmol) was varied.

2-Hydroxy-1-phenylethanone: pale yellow solid (52%), m.p. 78-81°C; R_f 0.50 (1:1, EtOAc : Hexane); ¹H-NMR (CDCl₃, δ (ppm)): 7.95 (1H, d, *J* = 7.2 Hz), 7.66 (2H, t, *J* = 7.5 Hz), 7.53 (2H, t, *J* = 7.7 Hz), 4.95 (2H, s), 3.40 (1H, br s); ¹³C-NMR (CDCl₃, δ (ppm)): 198.4 (C=O), 134.3 (aromatic C), 129.0 (aromatic C), 127.7 (aromatic C), 65.4 (-CH₂-).

Synthesis of 1-phenylethane-1,2-diol [51]

Into a rounded-bottom flask was placed styrene oxide 20 mmol (2.403 g) in a mixture of 10 mL of deionized water and 10 mL of diethyl ether. A mixture was stirred at room temperature for 48 hours. When the reaction was completed, the mixture was extracted with diethyl ether and dried over Na_2SO_4 and evaporated *in vacuo*. To the residue was precipitated by adding hexane. The solid was collected upon filtration, washed with cooled hexane and air-dried. Recrystallization from hexane to obtain white crystal (80%), m.p. 66-68°C, R_f 0.26 (1 : 1 EtOAc : Hexane); $^1\text{H-NMR}$ (CDCl_3) δ (ppm): 7.35 (5H, s, Ar-H), 4.81 (1H, d, $J = 7.8$ Hz), 3.73 (1H, dd, $J = 6.5$ Hz), 3.63 (1H, dd, $J = 6.7$ Hz), 3.28 (1H, s, -OH).

2.3.2.8 Optimum conditions for the oxidation of alcohols by $\text{Cr}(\text{pic})_3$

Effect of the amounts of the amount of catalyzed

The oxidation reaction was carried out as described in general procedure with $\text{Cr}(\text{pic})_3$ employed as catalyst, however varying amounts of chromium(III) picolinate were used (0.1, 0.2, 0.3, 0.4 mmol).

Effect of solvents

The oxidation reaction was carried out as described in general procedure with $\text{Cr}(\text{pic})_3$ employed as catalyst, with varied solvents (CHCl_3 , CH_3CN , isooctane, THF, pyridine: acetic acid (3:1)).

2.3.2.9 Oxidation of secondary alcohols catalyzed by $\text{Cr}(\text{pic})_3$

The oxidation reaction was carried out as described in general procedure with $\text{Cr}(\text{pic})_3$ employed as catalyst, however the concentration of substrate was varied (cyclohexanol, 2-octanol, menthol, benzoin, 1,4-cyclohexadiol).

2.3.2.10 Oxidation of primary alcohols catalyzed by $\text{Cr}(\text{pic})_3$

The oxidation reaction was carried out as described in general procedure with $\text{Cr}(\text{pic})_3$ employed as catalyst, but different substrate concentrations were used (1-octanol, benzyl alcohol, *trans*-2-hexene-1-ol, cinnamyl alcohol, furfural alcohol, 3-phenoxy benzyl alcohol).

2.3.2.11 Oxidation of selected aldehydes catalyzed by Cr(pic)₃

The oxidation reaction was carried out as described in general procedure with Cr(pic)₃ employed as catalyst, however different substrates were used (octylaldehyde, benzaldehyde, cinnamylaldehyde, *p*-fluorobenzaldehyde, *p*-hydroxybenzaldehyde, *p*-methoxybenzaldehyde, *p*-nitrobenzaldehyde, *m*-nitrobenzaldehyde).

***p*-fluorobenzoic acid:** colorless solid (97%), m.p. 183-185°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 8.25 (2H, d, *J* = 8.0 Hz), 8.47 (2H, d, *J* = 8.8 Hz).

***p*-methoxybenzoic acid:** colorless solid (30%), m.p. 183-186°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 3.92 (3H, s), 6.98 (2H, d, *J* = 8.8 Hz), 8.04 (2H, d, *J* = 8.8 Hz)

***p*-nitrobenzoic acid:** yellow solid (85%), m.p. 239-242°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 8.20 (2H, d, *J* = 8.8 Hz), 8.34 (2H, d, *J* = 8.8 Hz)

***m*-nitrobenzoic acid:** yellow solid (81%), m.p. 139-142°C; ¹H-NMR (CDCl₃, 400MHz, δ (ppm)): 7.65 (1H, t, *J* = 16.8 Hz), 8.36 (1H, d, *J* = 8.0 Hz), 8.45 (1H, d, *J* = 7.0 Hz), 8.89 (1H, s).

2.3.2.12 Oxidation of alcohols catalyzed by Cr(str)₃ and Cr(pic)₃ with various oxidants.

with H₂O₂.

The selective oxidation reaction of cyclohexanol was conducted as described in general procedure using Cr(str)₃ and Cr(pic)₃ as catalyst but using H₂O₂ as an oxidant.

with sodiumhypochlorite (NaOCl).

The selective oxidation reaction of cyclohexanol was conducted as described in general procedure using Cr(str)₃ and Cr(pic)₃ as a catalyst but using NaOCl as the oxidant. For the suitable condition, the reaction was stirred at 0°C.

2.3.2.13 Study on the oxidation of sulfur containing compounds by Cr(str)₃

Optimum conditions for the oxidation of cyclohexyldisulfide

The general oxidation procedure of alcohols was applied to study the oxidation of thiols but the reaction time was varied (1, 3, 5 and 24 h) and using isooctane and acetonitrile as solvent

Oxidation of saturated thiols

The selective oxidation reaction of saturated thiols were conducted as described in general procedure using n-butylthiol and 2-butylthiol as substrate catalyzed by $\text{Cr}(\text{str})_3$.

Effect of amounts of oxidants

The selective oxidation was conducted as described in general procedure using thiols as substrate catalyzed by $\text{Cr}(\text{str})_3$ but the amounts of oxidants was varied. (4.5 and 9 mmol)

Effect of time

The selective oxidation was conducted as described in general procedure using cyclohexyldisulfide as substrate catalyzed by $\text{Cr}(\text{str})_3$ but the time was varied. (1, 3, 4, 6 and 18 h) with 2.0 mmol of TBHP.

2.4 Results and discussion

2.4.1 The oxidation of alcohols catalyzed by $\text{Cr}(\text{str})_3$

$\text{Cr}(\text{str})_3$ is very active catalyst for the oxidation of secondary alcohols to the corresponding ketones by organic hydroperoxides [47]. Reaction of organic hydroperoxides and chromium(III) compounds would generate chromium(VI) compounds which are probably the active agents capable of oxidizing secondary alcohols to ketones.

2.4.1.1 Synthesis and characterization of $\text{Cr}(\text{str})_3$

$\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ was prepared by the mixing stearic acid in NaOH solution with chromium trichloride hexahydrate at 80 °C. A light purple precipitate was formed in 75% yield and the melting point was around 100-103°C. The identity of synthesized chromium(III) stearate was confirmed by comparison of physical properties, elemental analysis (EA), and IR spectroscopic data with those reported [48].

Elemental analysis (EA)

Percent composition of carbon and hydrogen in $\text{Cr}(\text{str})_3$ was analyzed by elemental analysis technique (EA). The result is presented in Table 2.1.

Table 2.1 Elemental analysis of prepared Cr(str)₃

Value	%C	%H
Theoretical	71.87	11.73
Experimental	69.52	11.74

Table 2.1 presents the composition of prepared Cr(III)stearate and the theoretical values. The result indicated that the complex contains 69.52% and 11.74% of carbon and hydrogen, respectively vs the theoretical value of 71.87% carbon and 11.73% hydrogen. The theoretical and experimental values for both carbon and hydrogen were acceptable to claim that the synthesis of Cr(str)₃ was successful.

Infrared spectroscopy (IR)

From the IR spectrum, this chromium complex presents a significant absorption band of carbonyl C=O around 1710 cm⁻¹; in addition, the C-O band of carboxylate group was observed around 1400-1450 cm⁻¹. The C-H stretching vibration was detected around 2850-2900 cm⁻¹. Furthermore, the absorption peak around 3500 cm⁻¹ corresponded to the -OH stretching was not observed. The C=O stretching vibration of chromium complex was found to absorb at higher frequency than that of free carboxylic acid (appeared at 1700 cm⁻¹), due to increasing of bond strength. The IR spectrum of Cr(str)₃ is presented in Figure 2.1.

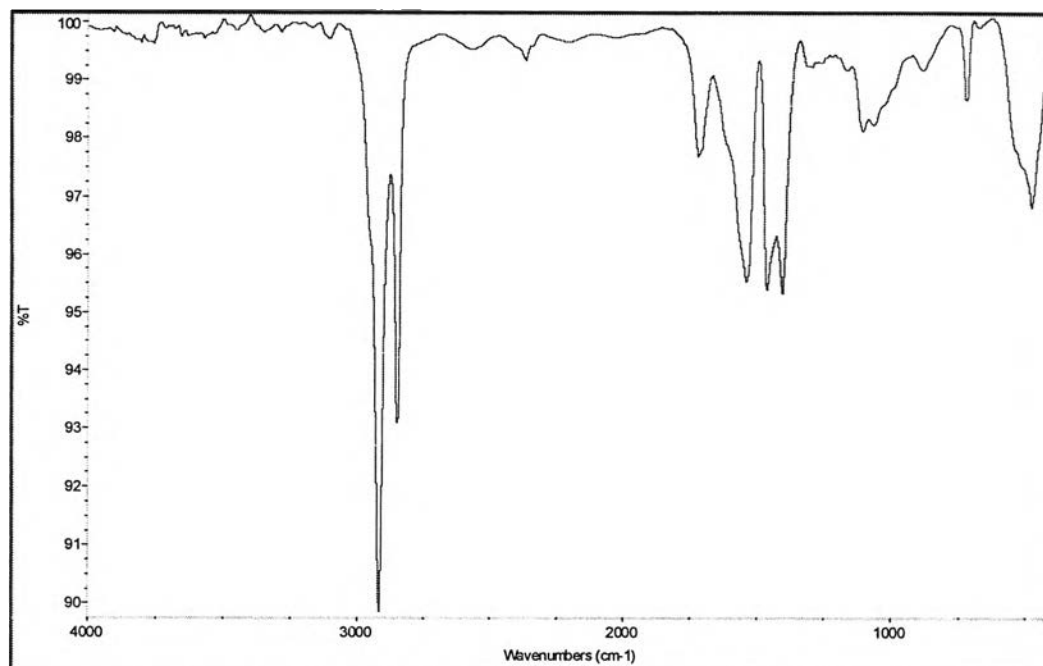


Figure 2.1 IR spectrum of Cr(str)₃.

2.4.1.2 Optimum conditions for oxidation of alcohols

Cyclohexanol, a structurally simple secondary alcohol, provides the opportunity to optimize conditions for oxidation of alcohols. Various factors were evaluated prior to reach the optimal conditions for the oxidation of cyclohexanol.

Effects of type of chromium complexes

The goal of this study was to screen for suitable catalysts that could mediate the transformation of cyclohexanol to the corresponding carbonyl function in high yield with good selectivity. The results of the oxidation of cyclohexanol catalyzed by different chromium complexes are presented in Table 2.2.

Table 2.2 Effect of type of chromium complexes on the oxidation of cyclohexanol

entry	catalysts	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance
1	none	92	8	100
2	Cr(III)palmitate	20	80	100
3	Cr(III)stearate	14	83	97
4	Cr(III)behenate	25	74	99
5	Cr(III)acetylacetonate	31	69	100
6	Cr(III)SalenCl	18	76	94

Reaction conditions: cyclohexanol (5 mmol), catalyst (0.2 mmol), isoctane (5 mL), TBHP (9 mmol), at 70⁰C for 24 h

Five chromium complexes were screened to observe their potentially catalytic oxidation ability. It was disclosed that all chromium complexes afforded good yield for transformation of cyclohexanol to cyclohexanone without contamination of undesired products. Among those chromium complexes examined, Cr(str)₃ provided the highest yield of cyclohexanone. In the absence of chromium complex, the oxidation of cyclohexanol to cyclohexanone was scarcely occurred (entry 1). Therefore, in this work Cr(str)₃ was selected to further utilize as a catalyst for the oxidation of secondary alcohols.

Effects of the amount of oxidant

With the suitable catalyst in hand, the amount of oxidant was the next parameter to examine. The amount of TBHP in the reaction was varied from 9-27 mmol. The results are summarized as shown in Table 2.3.

Table 2.3 Effect of the amount of oxidant on the oxidation of cyclohexanol catalyzed by $\text{Cr}(\text{str})_3$

Entry	amount of oxidant (mmol)	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance
1	9	29	71	100
2	12	30	76	106
3	18	9	91	100
4	20	16	81	97
5	27	13	86	99

Reaction conditions: cyclohexanol (5 mmol), $\text{Cr}(\text{str})_3$ (0.2 mmol), isooctane (5 mL), at 70°C for 24 h

From Table 2.3, the large excess amount of oxidant is required in order to generate oxo-chromium species for cyclohexanol oxidation. When TBHP 18 mmol was used, the reaction gave the highest yield of desired product 91% (entry 3). In addition, when the amount of TBHP was decreased from 18 mmol, the yield was declined, possibly due to the less amount of active species present. On the other hand, when the amount of TBHP was increased (entries 4 and 5), the yield of cyclohexanone was similar to the use of 18 mmol of TBHP. This implied that the reaction was carried out with 20 or higher mmol of oxidant was not required.

Effects of temperature

Temperature is one of the important parameters for conditions optimization. The temperature examined was room temperature (30°C), 50°C, 70°C and at refluxing isooctane temperature (99°C). The results are pointed out in Table 2.4.

Table 2.4 Effect of temperature on the oxidation of cyclohexanol catalyzed by Cr(str)₃

entry	temperature °C	time (h)	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance
1	RT (30)	24	80	20	100
2	50	24	27	68	95
3	70	6	24	75	99
4	70	24	14	83	97
5	70	48	20	80	100
6	reflux isooctane	6	28	68	96
7	(99) reflux isooctane (99)	24	25	75	100

Reaction conditions: cyclohexanol (5 mmol), Cr(str)₃ (0.2 mmol), isooctane (5 mL), TBHP (9 mmol)

From Table 2.4, it was observed that at 70°C for 24 h, the highest yield of cyclohexanone could be accomplished. This might be suggested that TBHP could be homolytically cleaved forming a radical to initiate the oxidation reaction (entry 4). At 70 °C for 6 h (entry 3), it was found that the yield of the desired product was formed only 75%. Likewise, when the reaction time was prolonged to 48 h, the yield of cyclohexanone was decreased. Whereas the reaction carried out at lower temperature was not successful. It might be explained that TBHP did not probably expose well to form a radical to initiate the oxidation reaction (entries 1 and 2). At refluxing temperature of isooctane (99 °C), the conversion of cyclohexanol and the formation of cyclohexanone were slightly decreased due to plausibly the rapid decomposition of TBHP at high temperature (entries 6 and 7). According to the previous report on the first use of Cr(str)₃ for the oxidation of secondary alcohols into carbonyl using TBHP as an oxidant, it was declared that the ratio of substrate/oxidant/catalyst was 2/1/0.02 in benzene at 80 °C for 6 h affording only lower yield (26%) [49].

Effects of the amount of catalyst

Variable amounts of chromium complexes: 0.01 (0.2 % mol), 0.05 (1% mol), 0.10 (2% mol), 0.20 (4% mol), 0.25 (5% mol) and 0.50 mmol (10% mol) were used to search for the appropriate amount of catalyst in this oxidation reaction. The results are shown in Table 2.5.

Table 2.5 Effect of the amount of Cr(str)₃ on the oxidation of cyclohexanol catalyzed by Cr(str)₃

Entry	catalyst (mmol)	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance	TON
1	0.01	64	35	99	153
2	0.05	26	74	100	73
3	0.10	16	80	96	39
4	0.20	9	91	100	23
5	0.25	20	87	97	18
6	0.50	20	77	97	8

Reaction conditions: cyclohexanol (5 mmol), isooctane (5 mL), at 70⁰C for 24 h

From Table 2.5, it was disclosed that 0.20 mmol of varied Cr(str)₃ was the optimal amount of catalyst (entry 4). In addition, when the amount of catalyst was increased or decreased from 0.20 mmol, the lower yield was detected. When 0.50 mmol of catalyst was used, the yield of product was decreased. This might be explained by increasing agglomeration of catalyst when large amount of catalyst was loaded as well as the rapid decomposition of TBHP boosted by the overloaded catalyst [50]. The use of lower amounts of catalyst led to lower yields; on the other hand, turnover numbers (TON) was increased.

Effect of reaction time for Cr(str)₃ catalyzed oxidation of cyclohexanol

The effect of reaction time on the oxidation of cyclohexanol was examined. The reaction time was varied from 1 h to 24 h. The results are presented in Table 2.6.

Table 2.6 Effect of reaction time on the oxidation of cyclohexanol catalyzed by $\text{Cr}(\text{str})_3$

entry	time (h)	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance
1	1	56	44	100
2	3	40	55	95
3	5	17	80	97
4	24	8	91	99

Reaction conditions: cyclohexanol (5 mmol), $\text{Cr}(\text{str})_3$ (0.2 mmol), isooctane (5 mL), TBHP (9 mmol), at 70°C

As noticed from Table 2.6, the oxidation of cyclohexanol gave cyclohexanone in high yield within 24 h. The half-life of the reaction was about 3 h. However, the yield of cyclohexanone within 5 h was slightly different from that obtained for 24 h. It could thus be summarized that the suitable reaction time for cyclohexanol oxidation is 5 h.

Effect of metal stearates catalyzed oxidation of cyclohexanol

Some metal stearate catalysts have been documented to be effective in oxidation reaction. In this research, six synthesized metal stearate complexes were explored for their capability on cyclohexanol oxidation and the results are presented in Table 2.7.

Table 2.7 Effect of metal stearates on the catalytic oxidation of cyclohexanol

entry	metal(III) stearate	% recovery (cyclohexanol)	%yield (cyclohexanone)	mass balance
1	Ni(II) stearate	52	45	97
2	Co(II) stearate	75	22	97
3	Cu(II) stearate	66	32	98
4	Fe(III) stearate	70	28	98
5	Mn(II) stearate	65	31	96
6	Cr(III) stearate	17	80	97

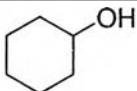
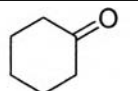


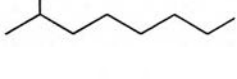
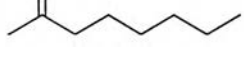
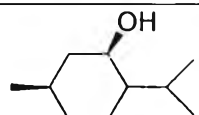
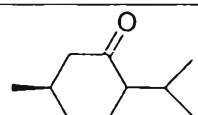
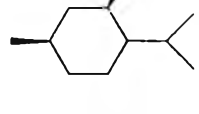
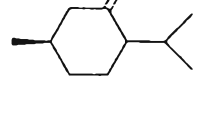
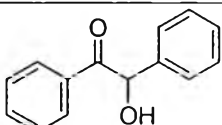
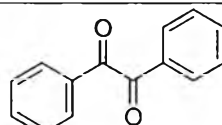
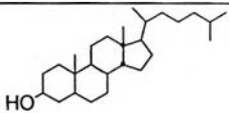
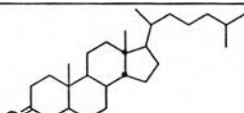
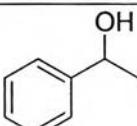
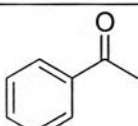

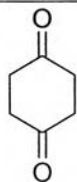
Reaction conditions: cyclohexanol (5 mmol), metal stearate (0.2 mmol),
isooctane (5 mL), TBHP (9 mmol), at 70⁰C, for 5 h

It was clearly seen from Table 2.7 that among appropriate six transition metal stearate complexes, Cr(str)₃ (entry 6) was the most effective catalyst for cyclohexanol oxidation. This observation strongly supported the concept of metal-dependence in the oxidation reaction [51a,b]. The role of metal stearate complexes in catalyzing the oxidation reaction was believed to involve two aspects [51c]. The first involved the acceleration step for the production of alkyl hydroperoxide intermediate *via* free radical process. The second important role concerned with the decomposition of the active intermediate to the oxidizing product. However, some limitations for the substrate to be oxidized still exist. Because of the instability of the intermediate produced, the yield of desired product was decreased. Product yield was decreased because the catalyst deactivation may occur by the formation of metallic polymer or formation of stable complexes between metal salts and some electron donor [51d]. Related researches concerning the transformation of ethylbenzene to acetophenone with the various transition metal (Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II)) stearate complexes as the catalysts were cited in literature. It was found the same result that Cr(str)₃ provided the best results among six metal stearate complexes (95% yield) for the oxidation of ethylbenzene with TBHP in the terms of acetophenone as the desired product [51e].

2.4.1.3 Oxidation of secondary alcohols catalyzed by Cr(str)₃

Utilizing the optimized conditions for cyclohexanol oxidation, it can be possible to apply the conditions to oxidize various selected secondary alcohols. The outcomes are accumulated in Table 2.8.

Table 2.8 The catalytic oxidation of secondary alcohols catalyzed by Cr(str)₃

entry	substrates	products	time (h)	%recovery of alcohol	%yield of product	mass balance
1			5	17	80	97
2			5	30	70	100
3 ^a			5	18	74	92
4 ^a			24	20	80	100
5			5	28	54	82
6			24	33	67	100
7 ^a			24	22	78	100
8			24	60	24 ^b	84
9			24	30	58 ^b	88
10			24	-	82 ^b	82
11			24	63	25	88

Reaction conditions: alcohol (5 mmol), Cr(str)₃ (0.2 mmol), isooctane (5 mL), TBHP (9 mmol), at 70°C for 5 h, ^a 18 mmol TBHP, ^b isolated yield

From Table 2.8, the oxidation of secondary alcohols could provide a good yield of the corresponding ketone such as the oxidation of cyclohexanol to cyclohexanone (80% yield) within 5 h. The oxidation of saturated secondary alcohol, 2-octanol (entry 2), was also cleanly oxidized to 2-octanone in high yield when 18 mmol of TBHP was used (entry 4). In case of menthol (entry 5), the yield of menthone under standard condition was 54%. Nevertheless, when the reaction time or the amount of TBHP was altered by increasing to 24 h and 18 mmol, respectively, menthone could be attained in 78%. The low conversion and yield of the sterically hindered isopropyl-substituent in menthol compared to that of cyclohexanol implied that the oxidation catalyzed by $\text{Cr}(\text{str})_3$ was sensitive to steric effects. From previous report, Adam and his colleagues carried out the oxidation of menthol mediated by chromium(III)salen complex using iodozobenzene as oxidant to furnish low conversion of menthone (21% conversion) [33,34].

Moreover, under these present standard conditions, benzoin could be transformed into benzil in low yield (24% isolated yield) because of steric effect of aromatic bulky group. On the other hand, the use of V_2O_5 as previously addressed to the catalyzed oxidation of benzoin to benzil under atmospheric oxygen in toluene afforded good yield (95%) within 8 h [43]. However, the reaction required high temperature (150°C) to perform the reaction. The identity of benzil obtained was confirmed by IR (Figure 2.2) and $^1\text{H-NMR}$ (Figure 2.3). From the IR spectrum, the presence of a signal belonging to $\text{C}=\text{O}$ stretching around 1700 cm^{-1} was observed while O-H stretching of alcohol was not detected.

The $^1\text{H-NMR}$ spectrum of isolated benzil (Figure 2.3) shows a characteristic peak around δ 7.40-8.00 (10H) due to aromatic protons while the C-H singlet proton of benzoin at δ 6.01 was not present in the spectrum of the product, indicating successful oxidation to the corresponding ketone.

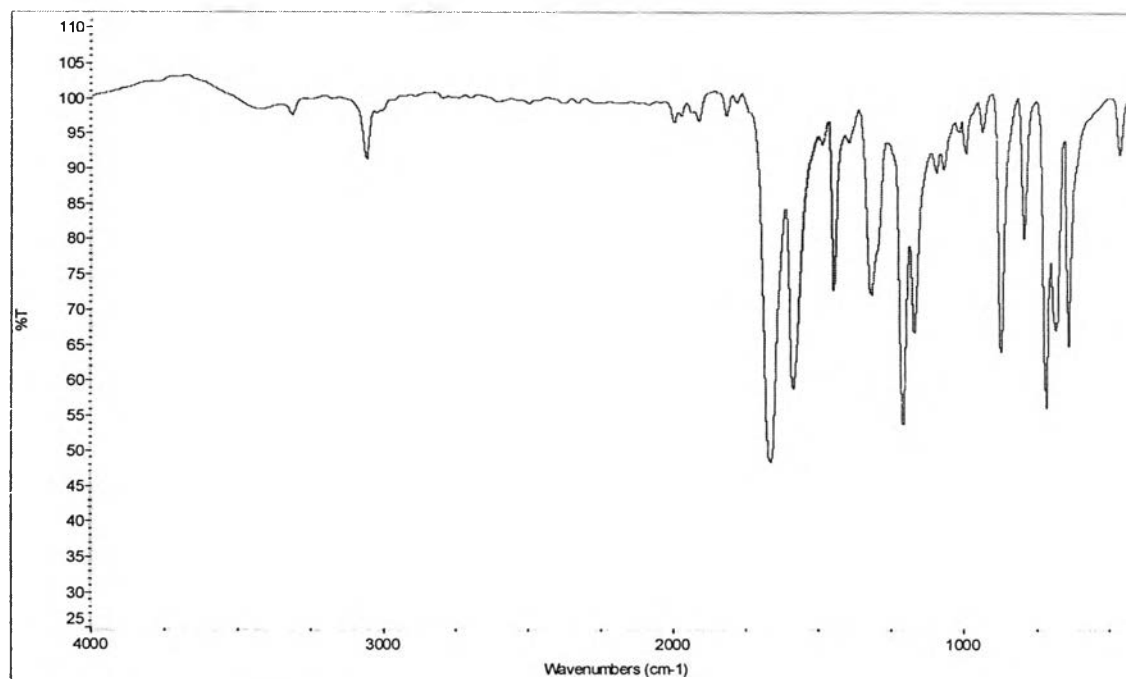


Figure 2.2 IR spectrum of isolated benzil.

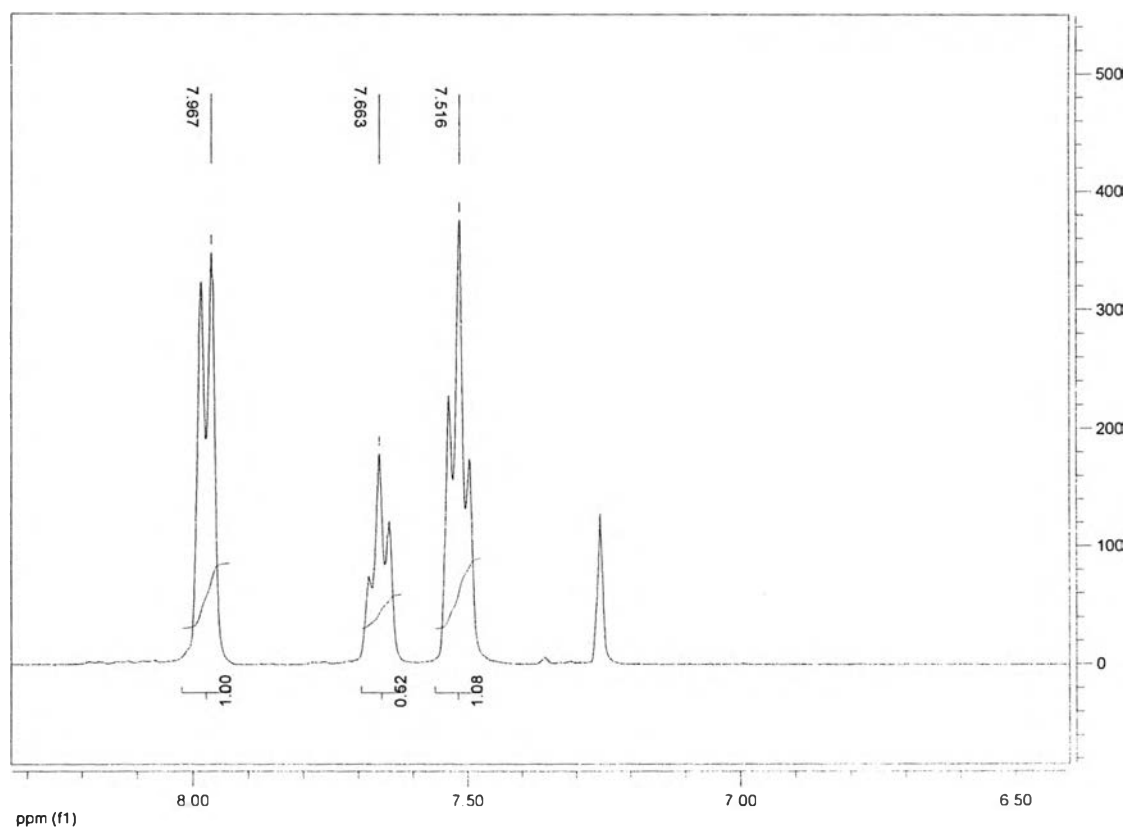


Figure 2.3 ¹H-NMR spectrum of benzil

In the case of a steroidal compound, cholestanol could be transformed into cholestanone in moderate yield. The identity of cholestanone was confirmed by IR spectroscopic data (Figure 2.4). From IR spectrum, the presence of the signal belonging to C=O stretching around 1700 cm^{-1} was visualized while O-H stretching of alcohol could not be observed.

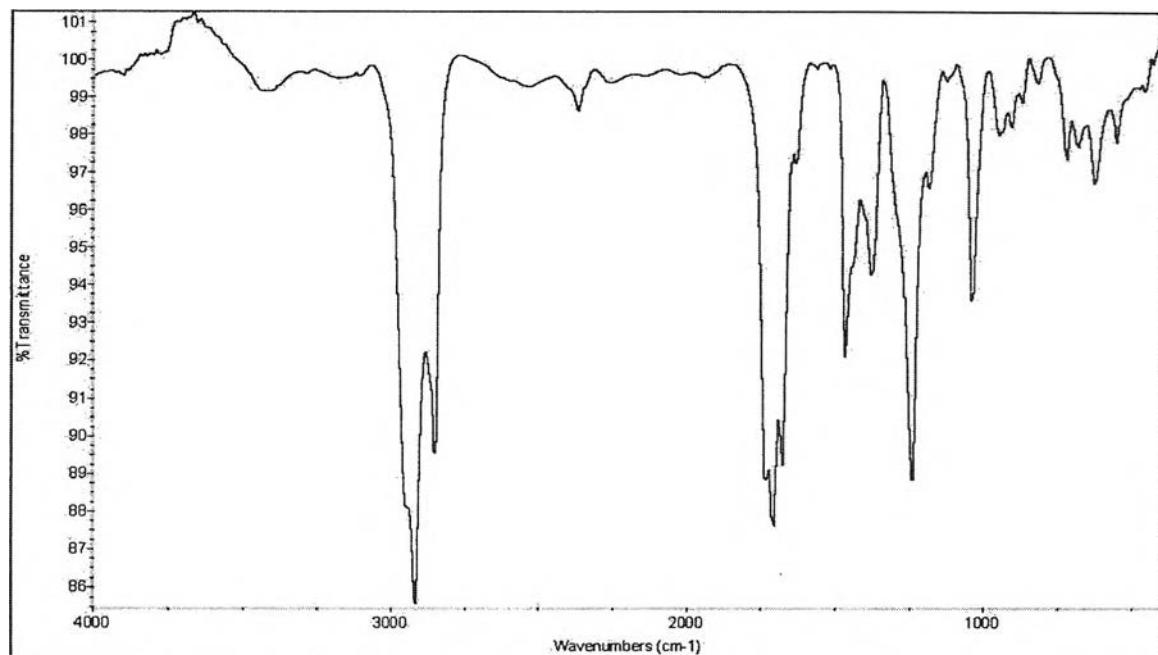


Figure 2.4 IR spectrum of cholestanone

In addition, 1-phenylethanol was easily oxidized to acetophenone in excellent yield (entry 10). The isolated acetophenone from the reaction was further purified and analyzed by ^1H - and ^{13}C -NMR. The ^1H -NMR spectrum of acetophenone (Figure 2.5) shows a characteristic singlet peak with integrations of 3H due to the methyl group, at δ 2.62 and the aromatic proton signals around δ 7.40-8.00. The ^{13}C -NMR spectrum displays a singlet peak of new C=O at δ 198.2 as shown in Figure 2.6.

For the oxidation of 1,4-cyclohexanediol (entry 11), 1,4-cyclohexanedione was only moderate product attained (25%yield).

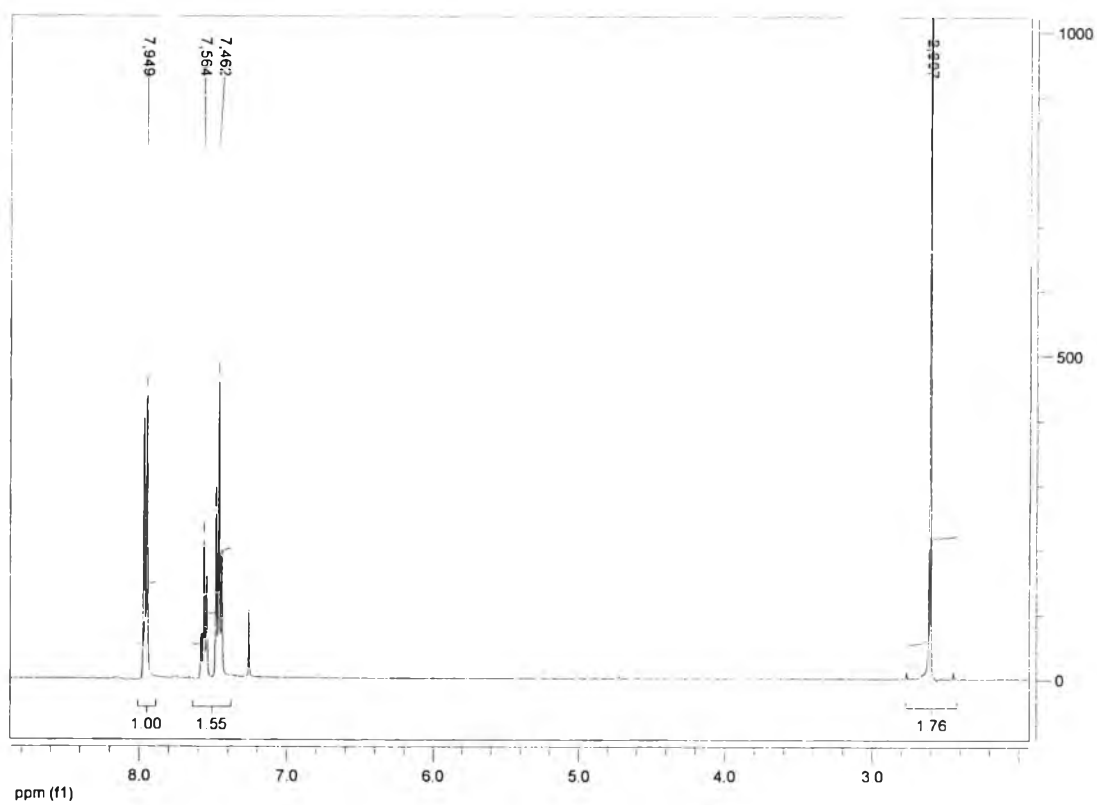


Figure 2.5 $^1\text{H-NMR}$ spectrum of isolated acetophenone

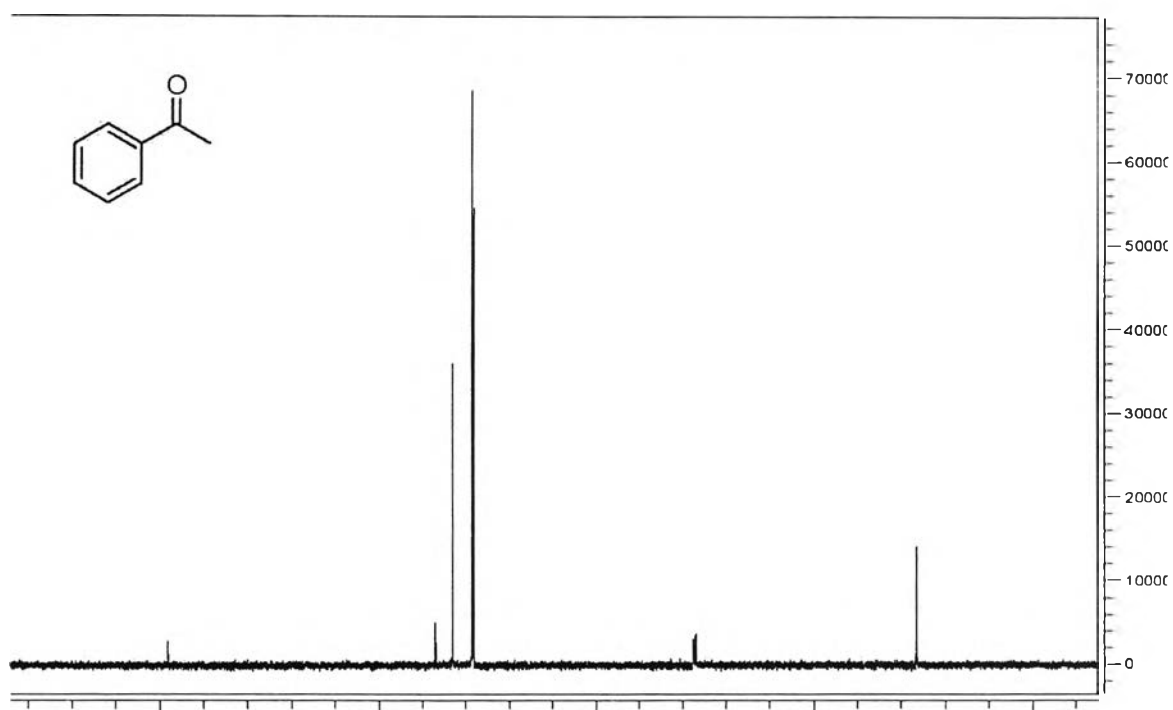

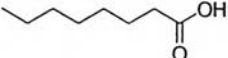
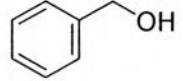
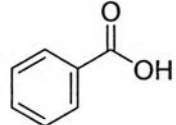
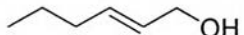
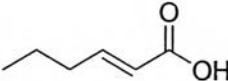
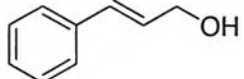
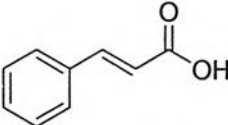
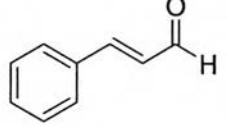
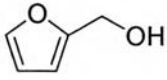
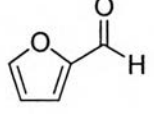
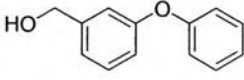
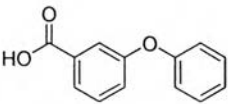


Figure 2.6 $^{13}\text{C-NMR}$ spectrum of isolated acetophenone

2.4.1.4 Oxidation of primary alcohols catalyzed by Cr(str)₃

In order to investigate the scope of this catalytic system, the oxidation of primary alcohols was considered. Having established the best reaction conditions, the method was applied to primary alcohols. A series of selected primary alcohols were then applied and the results are presented in Table 2.9.

Table 2.9 The catalytic oxidation of primary alcohols catalyzed by Cr(str)₃

entry	substrates	products	% recovery	% isolated yield	mass balance
1			42	50	92
2			0	82	82
3			33	53	86
4			44	19	90
				37	
5			0	93 ^a	93 ^a
6			76	24	100

Reaction conditions: alcohols (5 mmol), Cr(str)₃ (0.2 mmol), isoctane (5 mL), TBHP (9 mmol), at 70^oC for 5 h, ^a 3 h.

From Table 2.9, the oxidation of primary alcohols provided moderate yields of the corresponding carboxylic acids such as the oxidation of unactivated saturated

compound, 1-octanol (entry 1) to octanoic acid. Compared with previous report, the oxidation of *n*-decanol catalyzed by (salen)chromium complex with iodozobenzene afforded only 18% conversion to *n*-decanal even on prolonged (72 h) reaction time [34].

Benzyl alcohol was oxidized to benzoic acid in 82% yield. Similarly, the allylic alcohols, *trans*-2-hexenol and cinnamyl alcohol (entries 3, 4), smoothly underwent oxidation without affecting the C=C. The heterocyclic alcohol, 2-furfural, could be transformed to the corresponding aldehydes in excellent yield only in 3 h. However the oxidation of 2-furfural was a very rapid reaction giving an unknown product, possibly polymerized products. Furthermore, the significantly lower oxidative yield was observed when bulky groups were present such as in entry 6 compared with benzyl alcohol. This outcome still confirmed that the oxidation catalyzed by Cr(str)₃ was sensitive to steric effect.

The oxidation of primary alcohols catalyzed by Cr(str)₃ revealed the overoxidation of aldehydes to the corresponding carboxylic acids. To solve this problem, a study on the variation of reaction time was carried out. The results of the oxidation of benzyl alcohol with several time intervals between 0.5 to 24 h are displayed in Table 2.10 and Figure 2.7.

Table 2.10 Catalytic oxidation of benzyl alcohol at selected time by Cr(str)₃

entry	time (h)	% recovery (GC) (benzyl alcohol)	%yield (GC) (benzaldehyde)	% isolated yield (benzoic acid)
1	0.5	89	9	-
2	1	76	21	-
3	3	69	30	-
4	5	50	35	14
5	7	30	40	20
6	16	5	30	52
7	24	-	-	82

Reaction conditions: benzyl alcohol (5 mmol), Cr(str)₃ (0.2 mmol), isooctane (5 mL), TBHP (9 mmol), at 70⁰C

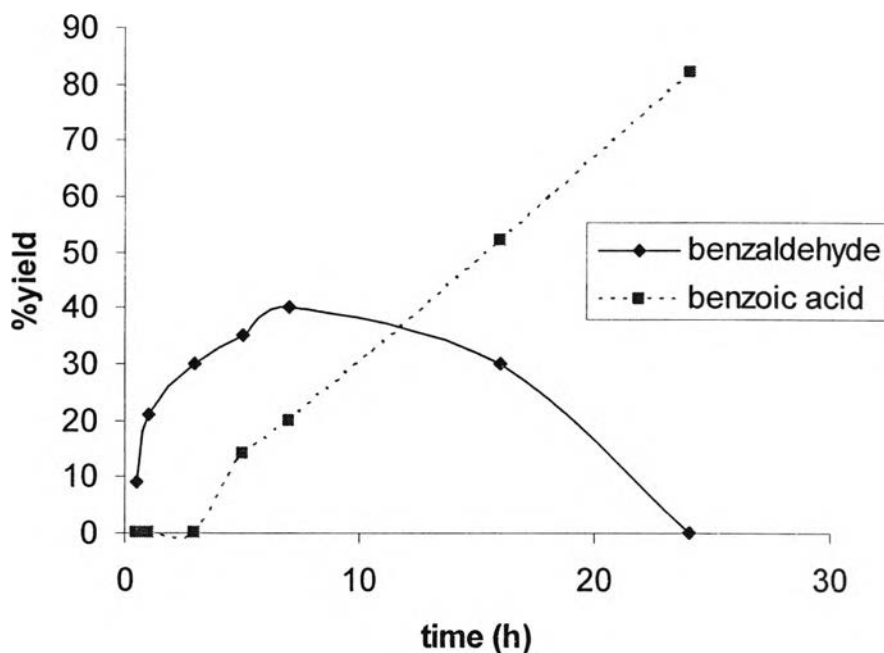


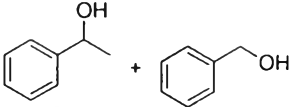
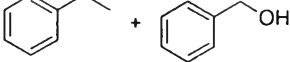
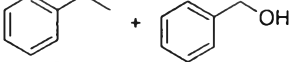
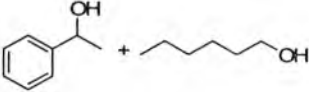
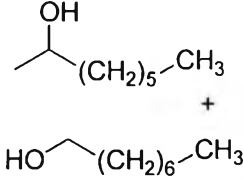
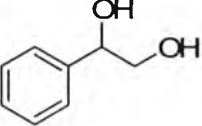
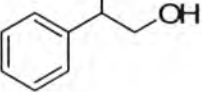
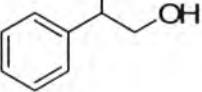
Figure 2.7 Time course for benzyl alcohol oxidation catalyzed $\text{Cr}(\text{str})_3$.

From Table 2.10 and Figure 2.7, it was observed that after 7 h the amounts of benzoic acid peaked to 82% yield while benzaldehyde gradually decreased after 3 h until 16 h, where benzaldehyde was completely consumed. The oxidation may afford benzaldehyde first then after 7 h, aldehyde was gradually oxidized to benzoic acid. It can thus be concluded that the oxidation mechanism of primary alcohol smoothly converted to carboxylic acid *via* aldehyde.

2.4.1.5 Reactivity and selectivity study on the oxidation of primary alcohols catalyzed by $\text{Cr}(\text{str})_3$

The reactivity and selectivity study would provide the significant characteristics of the reaction. For further study on chemo- and regioselectivity, the reaction of a 1:1 mixture of primary and secondary alcohols was carried out under this developed condition. The results are shown in Table 2.11.

Table 2.11 The competitive study on the oxidation of primary and secondary alcohols

entry	alcohols	TBHP (mmol)	time (h)	% product		
				ketone	aldehyde	acid
1		3	2	21	20	0
2		3	24	35	23	9
3		18	24	87	0	84
4		3	24	72	0	8
5		18	24	40	23	45
6		3	24	27	0	0
7 ^a		3	24	23	0	0
8		9	24	52	0	0

Reaction conditions: alcohol (2.5 mmol each), Cr(str)₃ (0.2 mmol), isooctane (5 mL), TBHP, at 70^oC, ^aCH₃CN (5 mL)

This observation convinced a plausible use of these conditions as a chemo- and regioselective protocol for oxidizing secondary alcohols in the presence of primary ones. The reaction of a 1:1 mixture of alcohol substrates was carried out under this developed conditions. The mixture of benzyl alcohol with 1-phenylethanol after 2 h preceded a smooth conversion of benzyl alcohol into benzaldehyde and 1-phenylethanol into acetophenone (entry 1). When prolonged the reaction time to 24 h, small amounts of acetophenone and benzaldehyde were slightly enhanced; however, benzoic acid was produced in low yield (entry 2). When 18 mmol of TBHP was used, the reaction furnished only acetophenone and benzoic acid in which should stem from further oxidation of benzaldehyde in excellent yields (entry 3). This result implied that the activation process of a hydroxyl group at benzylic position was occurred easier than that of primary alcohol. The competitive oxidation of 1-phenylethanol vs 1-hexanol (entry 4) displayed that even the oxidation of saturated primary alcohol to the corresponding carbonyl compound could not be competed with that at benzylic

position. Thus the activation process was mainly taken place at secondary benzylic alcohol. The competitive oxidation of saturated primary and secondary alcohols was performed (entry 5) and revealed that in fact the reactivity of the oxidation of primary alcohol was more significant. More informative results are obtained when primary and secondary alcohols in competition are in the same skeleton. The model compound used for this regard was 1-phenylethane-1,2-diol which could accomplishly prepare from the hydrolysis of styrene oxide [52]. The structure of obtained 1-phenylethane-1,2-diol was elucidated by $^1\text{H-NMR}$ (Figure 2.8) which exhibited a characteristic doublet peak with integration of 1H due to a benzylic hydrogen at δ 4.81 and doublet of doublet signals around δ 3.63 and 3.73 (1H each). Moreover, the hydroxyl protons were visualized at δ 3.28, while the aromatic proton signals were detected around δ 7.35.

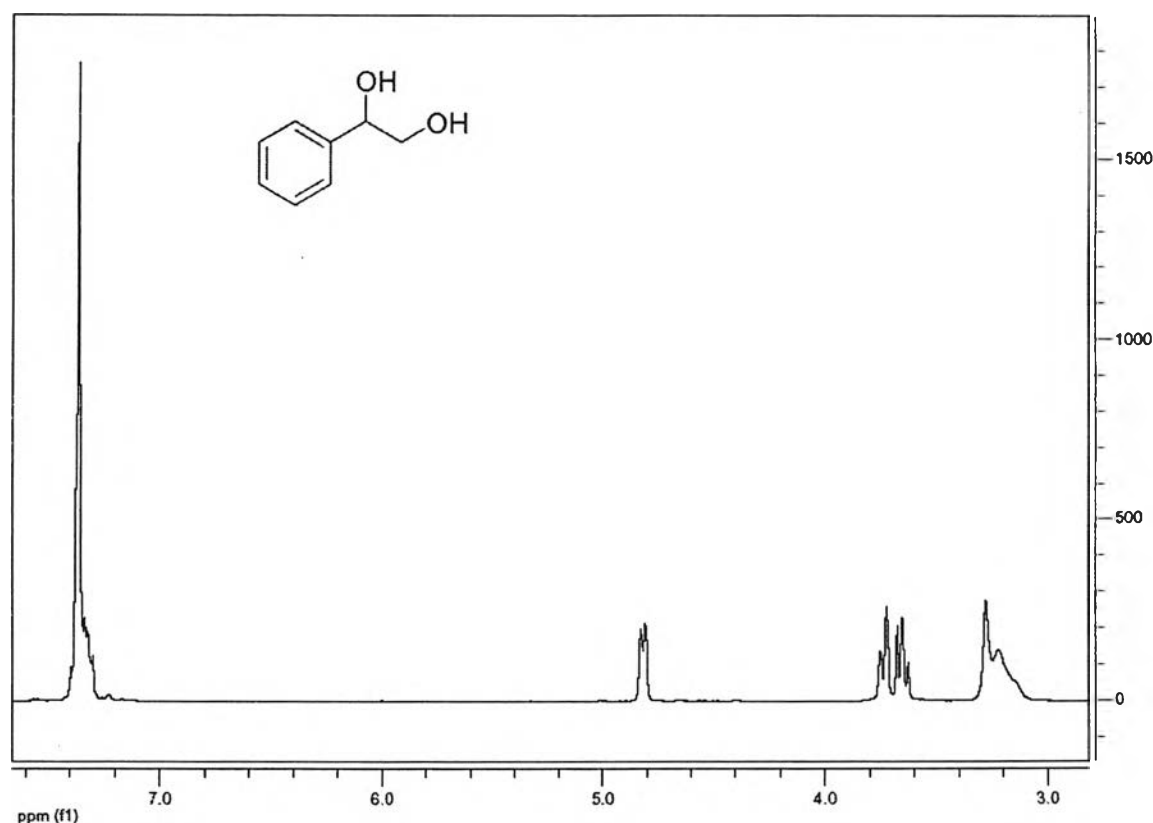


Figure 2.8 $^1\text{H-NMR}$ spectrum of 1-phenylethane-1,2-diol

The oxidation at secondary benzylic alcohol was found to be prevailed affording the corresponding ketone without the presence of aldehyde or carboxylic product. The depicted $^1\text{H-NMR}$ spectrum of 2-hydroxy-1-phenylethanone (Figure 2.9) revealed a characteristic singlet with integration of 2H due to the $-\text{CH}_2$ at δ 4.95 and

presented the important aromatic protons around δ 7.30 – 8.00. Moreover, the ^{13}C -NMR spectrum of 2-hydroxy-1-phenylethanone (Figure 2.10) showed a singlet peak of new C=O at δ 198.4 along with δ 65.4 due to the carbon atom of $-\text{CH}_2-$ and the six signals belonging to aromatic carbons were detected around δ 130-140 as shown in Figure 2.10.

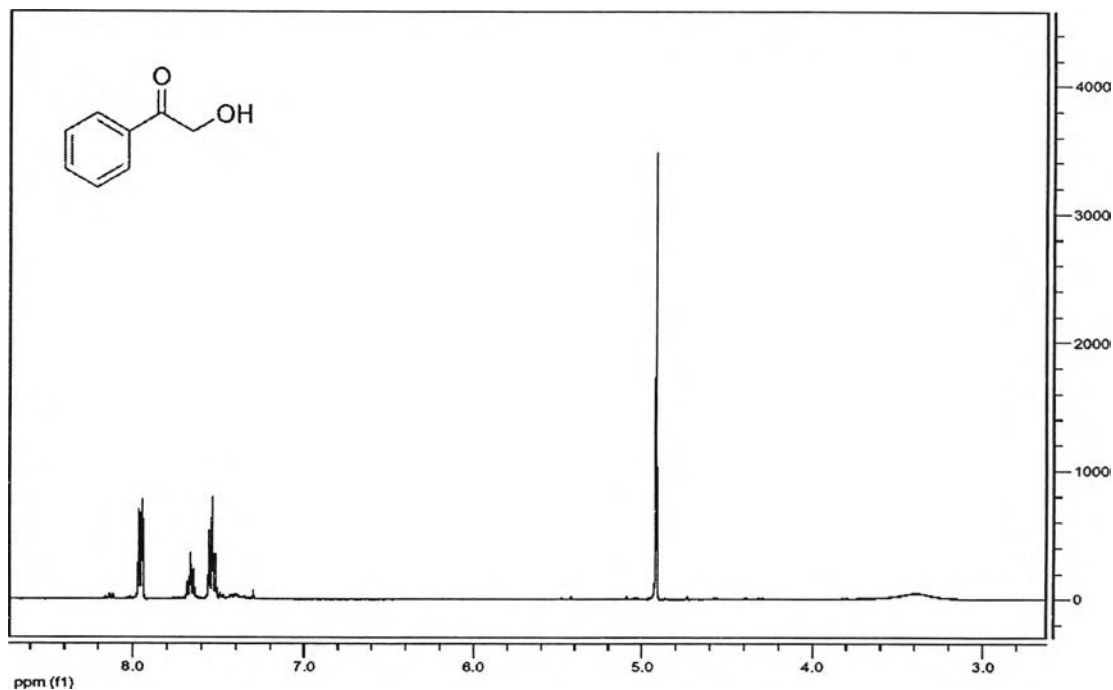


Figure 2.9 ^1H -NMR spectrum of isolated 2-hydroxy-1-phenylethanone

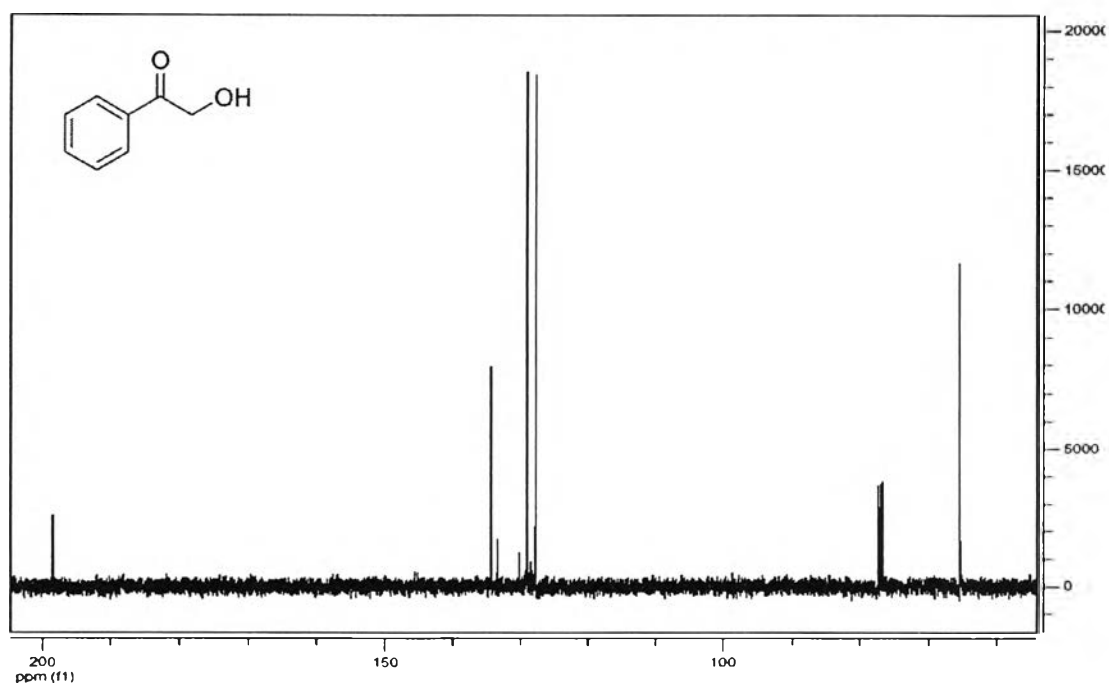


Figure 2.10 ^{13}C -NMR spectrum of 2-hydroxy-1-phenylethanone

It should be concluded that the functionization of both primary and secondary alcohols catalyzed by $\text{Cr}(\text{str})_3$ in the presence of TBHP afforded moderate to excellent yields. The oxidation gave high yields for unhindered secondary alcohols while primary alcohols produced the corresponding carboxylic acids *via* aldehydes.

However, the disadvantage of using $\text{Cr}(\text{str})_3$ catalyst is the inconvenience of separating the catalyst from the obtained product since both of them are well dissolved in organic solvent. The study of $\text{Cr}(\text{pic})_3$ catalyst for the oxidation of alcohols was subsequently developed to solve these problems.

2.4.2 The oxidation of alcohols catalyzed by $\text{Cr}(\text{pic})_3$

$\text{Cr}(\text{pic})_3$ (where pic = 2-carboxypyridine) is a well-known complex currently used as a very popular nutritional supplement [53a]. Its identification was fully characterized by various spectroscopic methods including (FTIR, ^1H and ^{13}C -NMR) [53b]. Nevertheless, there was no report concerning the use of $\text{Cr}(\text{pic})_3$ in the oxidation of alcohols.

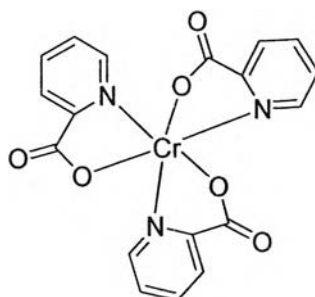


Figure 2.11 Structure of chromium(III) picolinate ($\text{Cr}(\text{pic})_3$)

2.4.2.1 Synthesis and characterization of $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ [54]

The catalyst was prepared from the reaction of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ and picolinic acid in aq solution to gain 5.96 g of pink crystal. The identity of synthesized $\text{Cr}(\text{pic})_3$ was confirmed by comparison of physical properties, EA, and IR spectroscopic data with those reported [55a]. $\text{Cr}(\text{pic})_3$ is moderately soluble in 2M aqueous HCl, DMF, and acetonitrile; slightly soluble in methanol; and insoluble in acetone, ethanol, DMSO and THF [55b]. From the oxidation of alcohol addressed previously, isooctane was used as solvent which $\text{Cr}(\text{pic})$ cannot be well dissolved in. Thus the advantage of using $\text{Cr}(\text{pic})_3$ catalyst is the ease of separation of the catalyst from the obtained

product. From the preliminary study, the oxidation of 2-octanol in isooctane catalyzed by $\text{Cr}(\text{pic})_3$ in the presence of TBHP afforded a good yield of 2-octanone (76% yield). Therefore, $\text{Cr}(\text{pic})_3$ was considered to further explore on its catalytic activity to the alcohol oxidations.

Elemental analysis (EA)

Percent composition of carbon, hydrogen and nitrogen in $\text{Cr}(\text{pic})_3$ was analyzed by EA. The result is presented in Table 2.12

Table 2.12 Elemental analysis of prepared $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$

Value	%C	%H	%N
Theoretical	48.54	3.37	9.44
Experimental	48.35	3.27	9.44

Table 2.12 presents the composition of prepared $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ and the theoretical values. The result expressed that the complex contained 48.35%, 3.27% and 9.44% of carbon, hydrogen and nitrogen respectively vs the theoretical value of 48.54% carbon, 3.27% hydrogen and 9.44% nitrogen. The theoretical and experimental values for both carbon and hydrogen were well matched. From the data above, it was confirmed that the synthesis of $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ was achieved.

Infrared spectroscopy (IR)

The identification of $\text{Cr}(\text{pic})_3$ was carried out by FT-IR compared with that reported in literature. The FT-IR spectrum of $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ is presented in Figure 2.12.

In IR spectrum, a strong series of absorption bands centered around 1500 and 700 cm^{-1} were due to the pyridine ring. Broad absorption bands centered at 2500 cm^{-1} were assigned for carbonyl C-C=O bonds. The sharp peak at 3100 cm^{-1} of the single OH of the carboxylic group was absent. The 2900-3600 cm^{-1} absorption feature was the characteristics of the $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ complex, and may reflect vibrations of OH-Cr-N bonds [55].

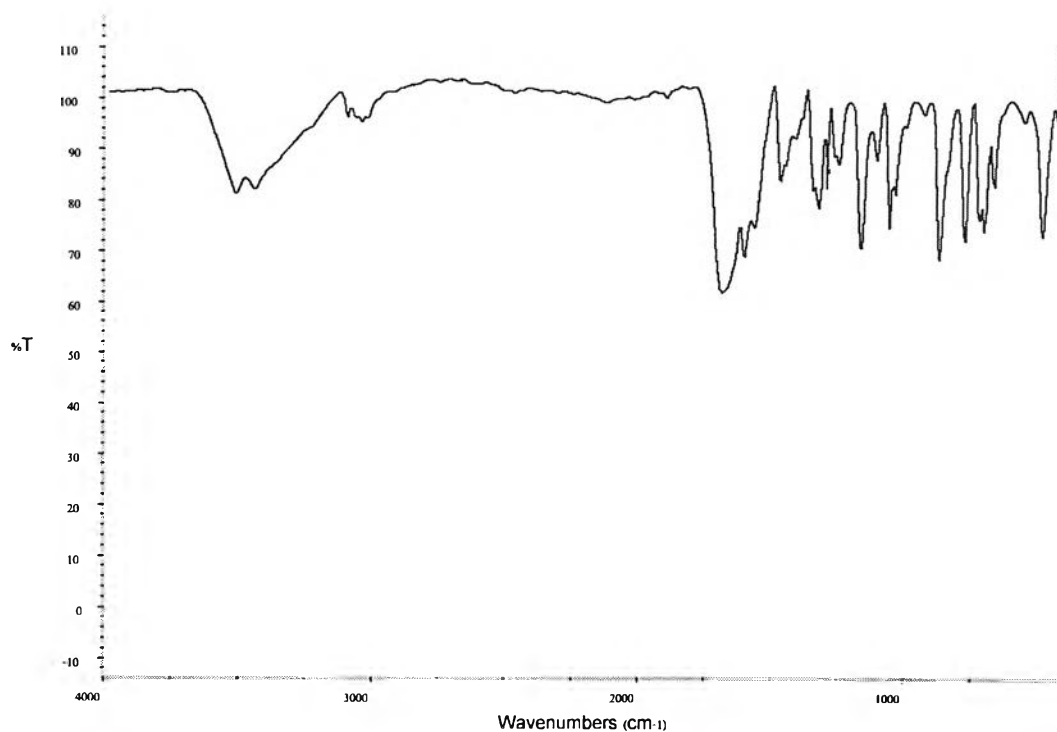


Figure 2.12 IR spectrum of $\text{Cr}(\text{Pic})_3 \cdot 1.5\text{H}_2\text{O}$

2.4.2.2 Optimum conditions for the oxidation of alcohols by $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$

Effect of the amount of catalyst

The oxidation of 2-octanol was selected to optimize oxidation conditions. The amount of catalyst was the first factor to consider and the results are shown in Table 2.13.

Table 2.13 Effect of amount of $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ on the oxidation of 2-octanol

entry	$\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$ (mmol)	% recovery of 2-octanol	% yield of 2-octanone	mass balance
1	0.1	71	24	95
2	0.2	25	75	100
3	0.3	24	72	96
4	0.4	25	66	91

Reaction conditions: 2-octanol (5 mmol), $\text{Cr}(\text{pic})_3$ (0.1-0.4 mmol), isooctane (5 mL), TBHP (18 mmol), at 70°C for 24 h.

The use of 0.2 mmol of catalyst gave the best yield of the desired product, 2-octanone. When the amount of catalyst was more than 0.2 mmol, the yield of product was slightly decreased because of an excess of catalyst may obstruct the reaction between substrates and oxidants [50].

Effect of solvents

The effect of solvents on the oxidation of 2-octanol was the second factor to explore. Chloroform, isooctane, THF, acetonitrile and acetic acid in pyridine (1:3) were used as solvents to screen for suitable reaction medium.

Table 2.14 Effect of solvent on the oxidation of 2-octanol

entry	solvent	% recovery of 2-octanol	% yield of 2-octanone	mass balance
1	chloroform	82	18	100
2	isooctane	21	76	97
3	THF	83	14	97
4	acetonitrile	31	62	93
5	pyridine-AcOH (3:1)	41	52	93

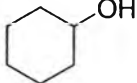
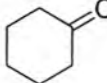


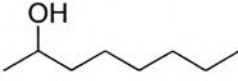
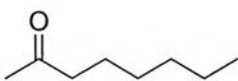
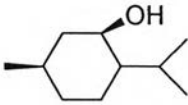
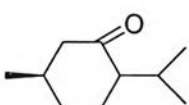
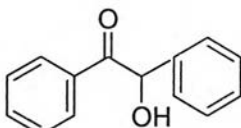
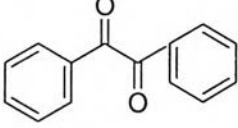


Reaction conditions: 2-octanol (5 mmol), Cr(pic)₃ (0.2 mmol), solvent (5 mL), TBHP (18 mmol), at 70⁰C for 24 h

The use of isooctane as solvent provided the highest yield of product. Comparing the activity of catalyst with Cr(str)₃, it was found that there was no difference of the obtained product between using Cr(str)₃ (80% yield) and Cr(pic)₃ (75% yield) for 2-octanol oxidation.

2.4.2.3 Oxidation of secondary alcohols catalyzed by Cr(pic)₃

The oxidation was extended to a variety of alcohols included primary and secondary alcohols. The results of the oxidation of secondary alcohols are presented in Table 2.15.

Table 2.15 The catalytic oxidation of secondary alcohols catalyzed by Cr(pic)₃

entry	substrates	products	% recovery of alcohol	% yield of product	mass balance
1 ^a			55	45	100
2			15	70	85
3			18	82	100
4			74	26	100
5			75	23	98
6			52	48	100

Reaction conditions: alcohol (5 mmol), Cr(pic)₃ (0.2 mmol), iso-octane (5 mL), TBHP (18 mmol), at 70°C for 24 h, ^a 9 mmol

It should be noted at this point that the use of Cr(pic)₃ as the oxidation catalyst for saturated and cyclic secondary alcohols afforded high yields of the corresponding ketones (entries 2,3). The reaction without either catalyst or oxidant gave very poor yield of product (5-10% yield). Besides the high yield of product, another advantage of this catalytic system as mentioned earlier is the ease of separation of the catalyst from the reaction medium since it acted as a heterogeneous catalyst. The significantly lower yields in entries 4 and 5 are due to the sterically hindering isopropyl-substituent in menthol and bulky phenyl group in benzoin as used to be observed in previous section. When compare the catalytic activity between Cr(str)₃ and Cr(pic)₃, it was found that Cr(str)₃ is better because it didn't affect by isopropyl-substituent in


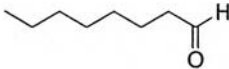
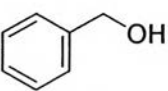
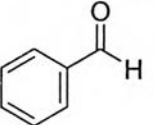
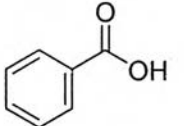
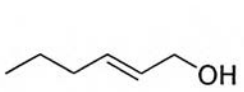
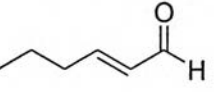
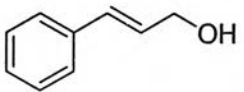
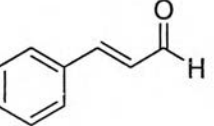
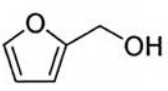
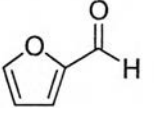
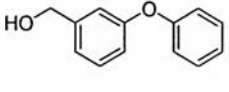
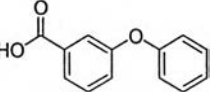
menthol. The oxidation of 1,4-cyclohexanediol gave a moderate yield of 1,4-cyclohexanedione.

Moreover, if the amount of oxidant was increased from 9 to 18 mmol, overoxidation may occur as indicated by the observed decrease in mass balance. The intention to explore the overoxidation was achieved by the oxidation of cyclohexanone. The result suggested that the overoxidation could take place by increasing amount of oxidant, amount of catalyst and time. However, the overoxidation products could not be detected by GC analysis after work up using the standard procedure performed.

2.4.2.4 Oxidation of primary alcohols catalyzed by Cr(pic)₃

In order to investigate the scope of this catalytic system, the oxidation of primary alcohols was conducted. The results are presented in Table 2.16.

Table 2.16 The catalytic oxidation of primary alcohols catalyzed by $\text{Cr}(\text{pic})_3 \cdot 1.5\text{H}_2\text{O}$

entry	substrates	products	% recovery of alcohol	% yield of product	mass balance
1			50	35	85
2 ^b			54	39	93
3			0	100 ^a	100
4			46	54	100
5			0	100	100
6 ^b			30	60	90
7			72	28 ^a	100

Reaction conditions: alcohol (5 mmol), $\text{Cr}(\text{pic})_3$ (0.2 mmol), isoctane (5 mL),

TBHP (18 mmol), at 70°C for 24 h, ^a isolated yield, ^b for 5 h

In the case of saturated alcohols, the desired product was afforded in moderate yield (entry 1). Conveniently, the reactants in entries 4 and 5 were smoothly oxidized to the corresponding aldehydes without the competition with epoxidation or appreciable oxidation of C=C. Nevertheless, both cinnamyl alcohol and 3-phenoxybenzyl alcohol gave poor yield because of steric effects. The oxidation at benzylic hydroxyl group gave very good yields. Both benzaldehyde and in particular, benzoic acid have been isolated from the oxidation of benzyl alcohol. Thus, benzaldehyde may be oxidized to benzoic acid under these conditions. To prove this

assumption the amount of benzaldehyde and benzoic acid was determined at several time intervals during the reaction as reported in Figure 2.13.

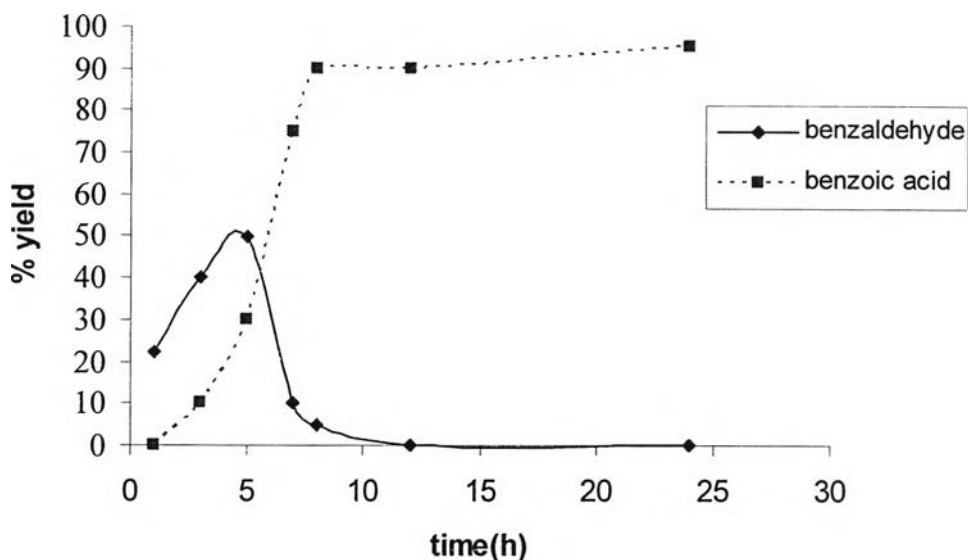


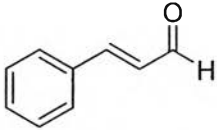
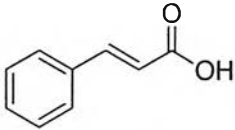
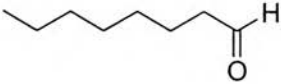
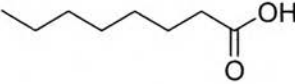
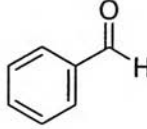
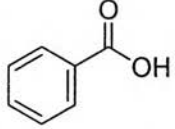
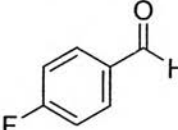
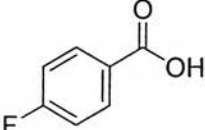
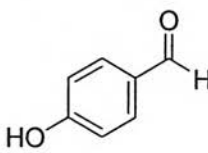
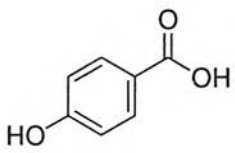
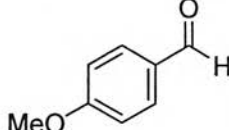
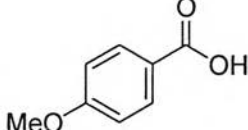
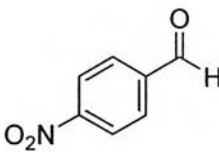
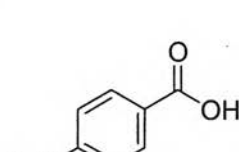
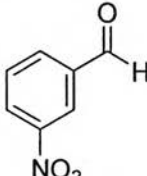
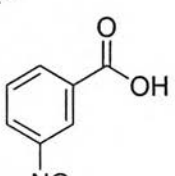
Figure 2.13 Time course for benzyl alcohol oxidation catalyzed by $\text{Cr}(\text{pic})_3$.

In Figure 2.13, after 5 h the amounts of benzoic acid reached to 95 % yield while benzaldehyde gradually decreased after 5 h until 12 h where benzaldehyde was completely consumed. It can be concluded that the oxidation mechanism of primary alcohols to the corresponding carboxylic acid involve *via* an aldehyde intermediate.

2.4.2.5 Oxidation of selected aldehydes catalyzed by $\text{Cr}(\text{pic})_3$

The previous result manifestly revealed that the oxidation of an aldehyde to a carboxylic acid could be successful under studied conditions. A variety of aldehydes were then selected and subjected to the oxidation reaction and the results are presented in Table 2.17.

Table 2.17 The oxidation of aldehydes by Cr (pic)₃

entry	substrate	Product	% isolated yield
1			22
2			86
3			85
4			97
5			0
6			30
7			85
8			81

Reaction conditions: aldehyde (5 mmol), Cr (pic)₃ (0.2 mmol), isooctane (5 mL), TBHP (18 mmol), at 70^oC for 6 h

The reaction provided the product in high yield within 6 hours, except for sterically hindered substrates such as cinnamaldehyde or the electron donating substituent such as 4-hydroxy benzaldehyde and anisaldehyde. The extensive mechanistic studied on the catalytic oxidation of aldehyde by metal catalyst

complexes with the various source of oxygen presented acylperoxy radicals as an intermediate [56]. It might be that these electron donating groups could not stabilize the formation of these radical [1]. On the other hand, the electron withdrawing substituted group in entries 4, 7 and 8 afforded very high yields where the position of substituent did not affect to the reaction (entries 7, 8). All the corresponding carboxylic acids products were verified their identities by $^1\text{H-NMR}$ spectra. The $^1\text{H-NMR}$ spectrum of benzoic acid (entry 3) (Figure 2.14) visualized aromatic protons could be assigned at δ 7.48-8.12 (5H). 2 H near carboxylic group expressed doublet signal low field at δ 8.12 while 2 H at *para* position with carboxylic group showed triplet signal at δ 7.48 and residue 1 H could be assigned at δ 7.62.

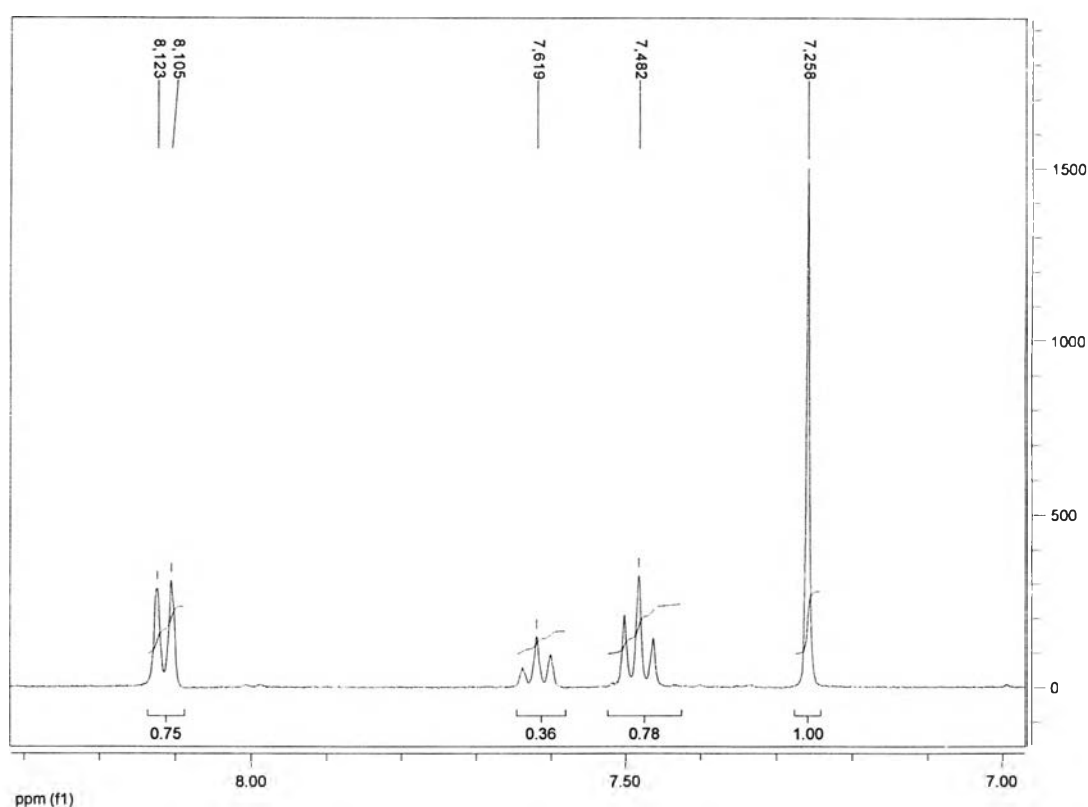


Figure 2.14 $^1\text{H-NMR}$ spectrum of isolated benzoic acid

The $^1\text{H-NMR}$ spectrum of *p*-anisic acid (entry 6) (Figure 2.15) visualized methoxy protons adjacent to aromatic moiety at δ 3.92 (3H,s). The proton adjacent to aromatic ring was detected around δ 6.90-8.00 (4H). 2 H near carboxylic group expressed doublet signal low field at δ 8.04 while 2 H near methoxy group showed doublet signal at δ 6.98.

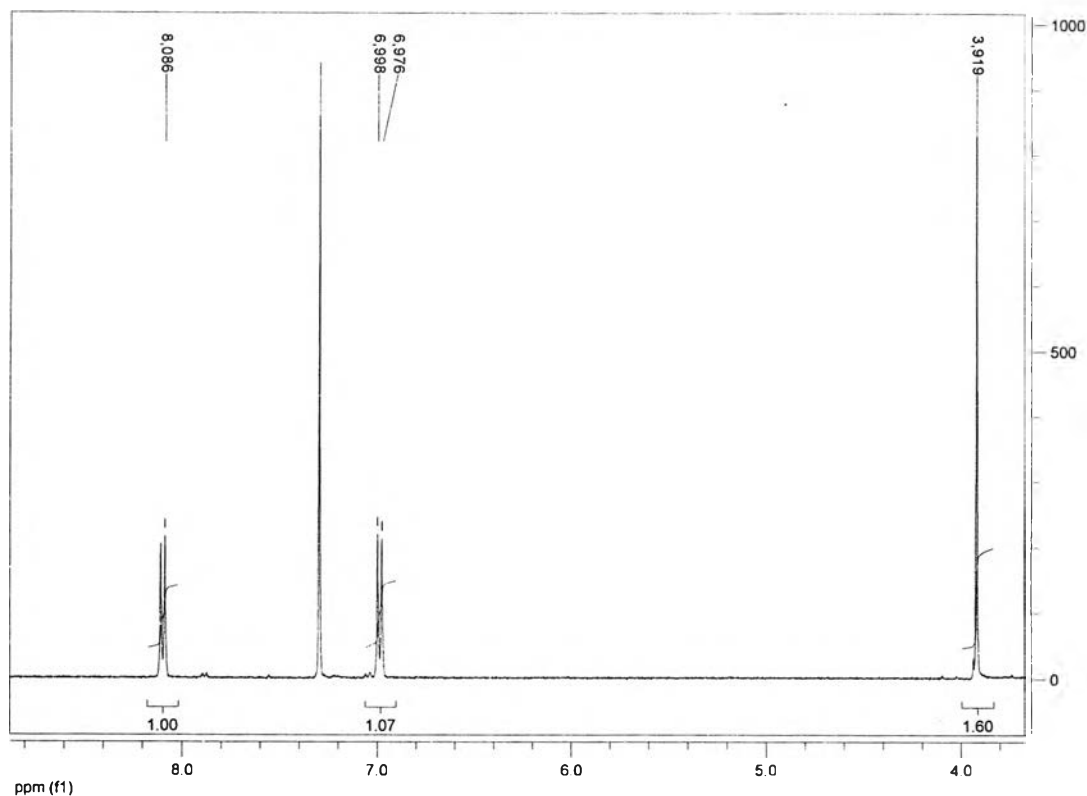


Figure 2.15 ^1H -NMR spectrum of isolated *p*-anisic acid

The ^1H -NMR spectrum of *p*-nitro benzoic acid (entry 7) (Figure 2.16) revealed 4 protons adjacent to aromatic ring around δ 8.18-8.36. There are two types of aromatic protons, 2 protons adjacent to carboxylic acid show doublet signal at δ 8.34 another group displayed 2H doublet proton adjacent to nitro group at δ 8.20.

The ^1H -NMR spectrum of *m*-nitrobenzoic acid (entry 8) (Figure 2.17) showed 4 protons in aromatic ring revealed around δ 7.65-8.90. The singlet lowest field proton at δ 8.89 adjacent to carboxylic and nitro group. 1 H near carboxylic group expressed doublet signal low field at δ 8.45 while 1 H near nitro group showed doublet signal at δ 8.36 and residue 1 H could be assigned at δ 7.65.

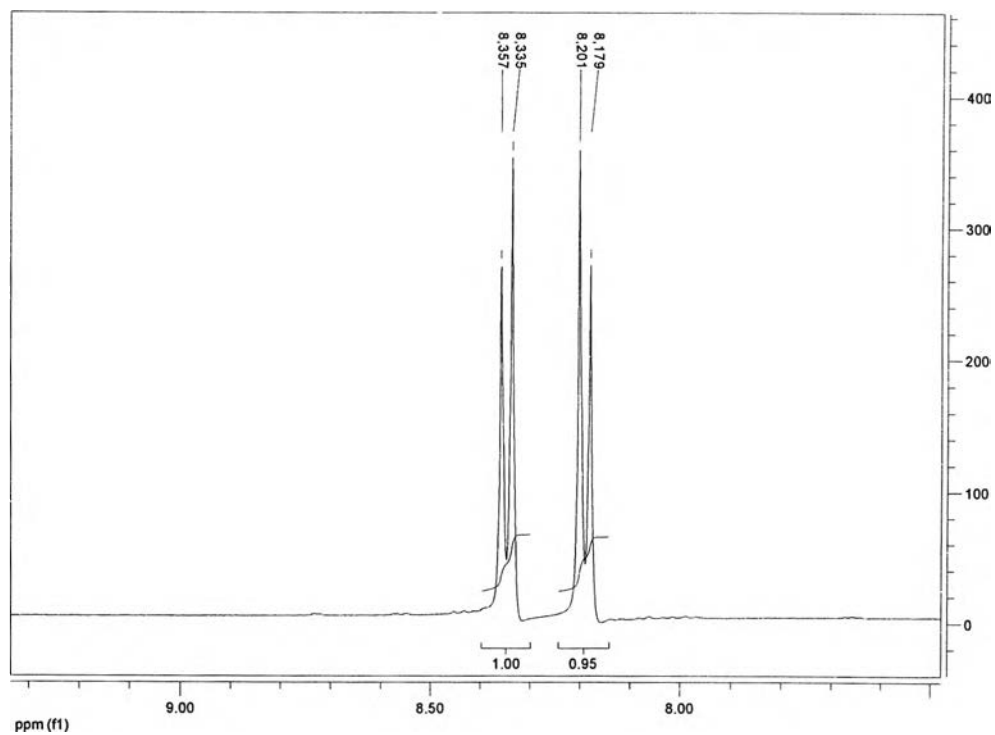


Figure 2.16 $^1\text{H-NMR}$ spectrum of isolated *p*-nitro benzoic acid

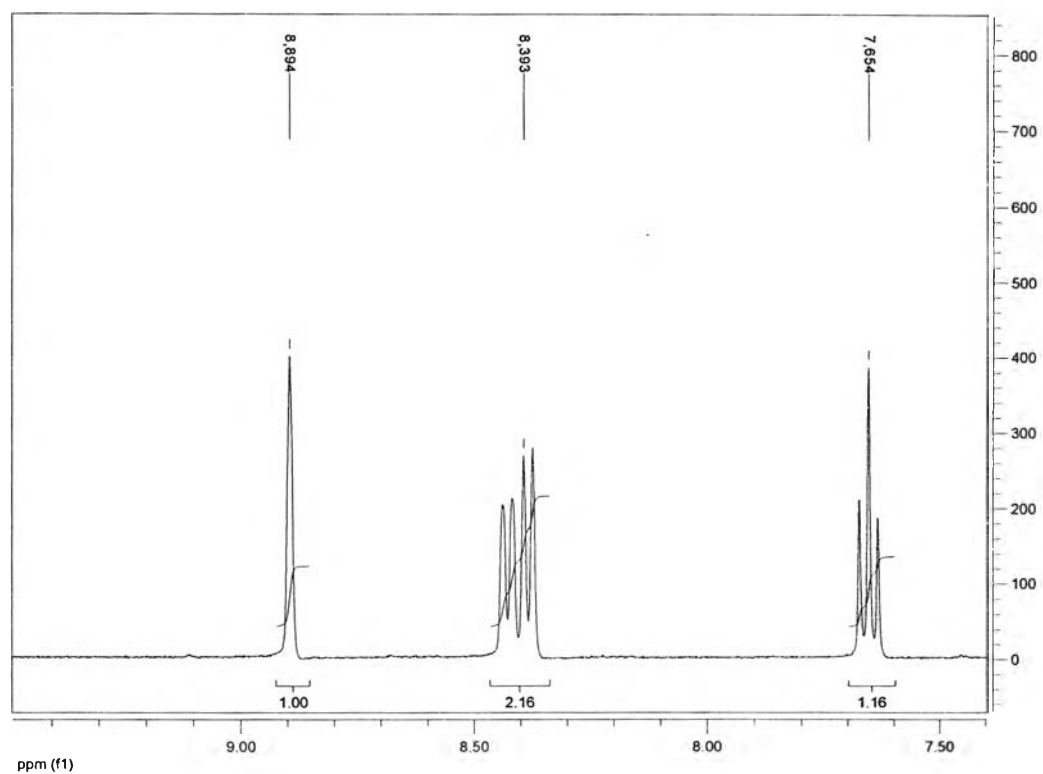
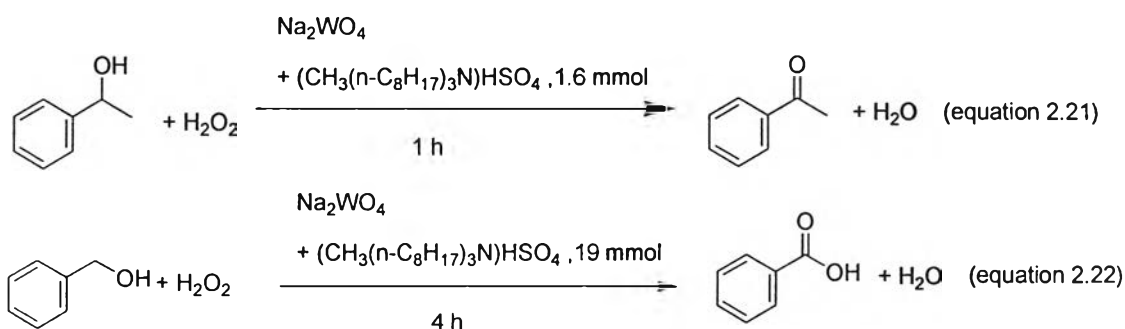


Figure 2.17 $^1\text{H-NMR}$ spectrum of isolated *m*-nitro benzoic acid

2.4.3 Oxidation of alcohols catalyzed by Cr(str)₃ and Cr(pic)₃ with various oxidants

2.4.3.1 Oxidation of alcohols by Cr(str)₃ and Cr(pic)₃ with H₂O₂

One favorite oxidant used to oxidize alcohols to the corresponding carbonyl compounds, H₂O₂ due to its environmental impact, since water is the only by-product. Simple secondary alcohols can be cleanly converted to ketones under organic/aq biphasic conditions using 3-30% H₂O₂ in the presence of a tungsten catalyst and a phase-transfer catalyst (PTC) (equation 2.21) [57]. The use of a lipophilic quaternary ammonium hydrogen sulfate as PTC is crucial for high reactivity, probably due to its sufficient acidity. Primary alcohols are 4-5 times less reactive than secondary ones. Significantly, however, they can be oxidized directly to carboxylic acids (equation 2.22).

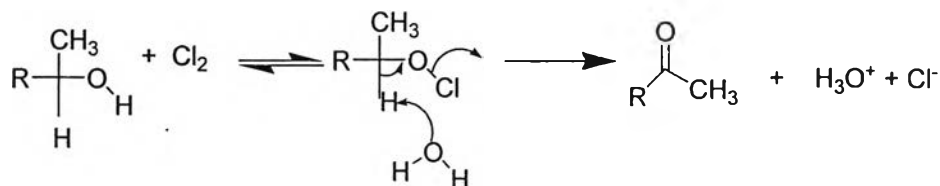


In this research, the use of H₂O₂ as oxidant chromium(III) complex as catalyst was studied and compared with previous data. Cyclohexanol and benzyl alcohol were selected as model substrates for secondary and primary alcohols, respectively under the oxidation conditions studied with H₂O₂ as oxidant.

It was observed that the oxidation of both cyclohexanol and benzyl alcohol catalyzed by Cr(str)₃ failed to afford the desired transformation and also gave poor yield (6% of cyclohexanone for 5 h, 9 mmol H₂O₂) even the amounts of oxidant and time were increased. (20% of cyclohexanone for 24 h, 18 mmol H₂O₂). A similar behavior was also observed with a related catalyst, Cr(pic)₃. Although the solvent was changed from isooctane to acetonitrile, with the aim of increasing the solubility of catalyst, the yield of product remained low (7% of cyclohexanone in CH₃CN for 24 h, 9 mmol H₂O₂).

2.4.3.2 Oxidation of alcohols by Cr(str)₃ and Cr(pic)₃ with sodium hypochlorite (NaOCl)

Sodium hypochlorite (bleach) in acetic acid provides an inexpensive and relatively non-toxic method for alcohol oxidation. The mechanism was proposed by the rapid formation of an alkyl hypochlorite intermediate, which is converted to a ketone in an E2 type reaction [58].



In this report, we show the oxidation of alcohol catalyzed by chromium complex with the presence of NaOCl. Cyclohexanol was chosen as a model to explore the reaction conditions. Both Cr(str)₃ and Cr(pic)₃ were used to catalyze the oxidation and the result are shown in table 2.18.

Table 2.18 The oxidation of cyclohexanol by Cr(str)₃ and Cr(pic)₃ with NaOCl

entry	catalyst	% recovery (substrates)	%yield (products)	mass balance
1	Cr(str) ₃	74	18	92
2	Cr(pic) ₃	50	40	90

Reaction conditions: alcohols (5 mmol), Catalyst (0.2 mmol), methanol (5 mL), NaOCl (9 mmol), at 70°C for 24 h

From Table 2.18, it was found that the oxidation of alcohols with these condition is not effective when compare with the use of TBHP as oxidant (80% yield). It may be because NaOCl decompose when using high temperature. From the literature, the selective oxidation of benzylic hydrocarbons to carbonyl compounds was achieved using a racemic Mn(III)salen complex as the catalyst in the presence of NaOCl. The reaction proceeded in good yields as shown by the conversion of ethyl benzene to acetophenone at 0°C which equated to a yield of 77 % [59]. In this study, the alcohol oxidation catalyzed by chromium complex with NaOCl was applied at 0°C. The results are shown in Table 2.19.

Table 2.19 Effect of solvent to the oxidation of cyclohexanol with NaOCl

Entry	solvent	catalyst	% recovery (substrates)	%yield (products)	Mass balance
1	acetonitrile	Cr(str) ₃	94	6	100
2	methanol	Cr(str) ₃	38	58	96
3	acetonitrile	Cr(pic)	88(83 ^a)	12(15 ^a)	100(98 ^a)
4	methanol	Cr(pic) ₃	85	2	87

Reaction conditions: alcohols (5 mmol), Catalyst (0.2 mmol), solvent (5 mL), NaOCl (9 mmol), 0^oC, 4 h, ^a NaOCl (18mmol)

Even though, acetonitrile was used as solvent at 0^oC the oxidation of cyclohexanol still afforded low yield of cyclohexanone when catalyzed by Cr(str)₃ and Cr(pic)₃ respectively (entries 1,3). It might be that acetonitrile generate radical species and obstruct substrate radical to react with oxidant. In the case of methanol as solvent (entries 2,4), the catalytic oxidation showed better yield (entry 2) when using Cr(str)₃ as catalyst. However, the use of Cr(pic)₃ still gave low yield of cyclohexanone, this may be because catalyst can not be dissolved in reaction.

It should be concluded that, the use of TBHP as the oxidant expressed the best result for alcohol oxidation catalyzed by chromium complex.

2.4.4 Oxidation of sulfur containing compounds by Cr (str)₃

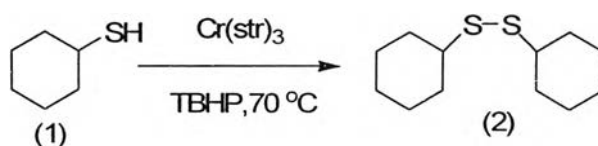
Among several methods addressed for the preparation of disulfides, most methods involve the oxidation of thiols. Oxidation of thiols is the most exploited method for disulfide synthesis mainly because a large number of thiols are commercially available and are easily synthesized. Disulfides are important functional groups in organic chemistry and biochemistry and have been extensively investigated over the years. Disulfide bond formation is important in peptides and bioactive molecules. This conversion has been accomplished using reagents such as molecular oxygen [60], sodium perborate [61], H₂O₂ [62], 2,6-dicarboxypyridinium chlorochromate (2,6-DCPCC) [63]. Of the various oxidants, oxygen is apparently the most convenient because it is inexpensive, easy to remove, and produce water as the only byproduct. Nonetheless, oxygen itself is inert to sulfur compounds, metal catalysts are thus needed [64].

Typically, copper phthalocyanine under alkaline conditions, is well known as a metal catalyst for the autoxidation of thiols to disulfides [65]. Although the mechanism is not fully clear, the reaction is considered to involve a coupling reaction of sulfur radicals, which are formed from thiolate anions by one-electron oxidation with the metal complex. Several thiol oxidation reactions with oxygen under neutral conditions were reported [66]. However, they often required long reaction time even at relatively high temperatures. RhH(PPh₃)₄/1,4-*bis* (diphenylphosphino)butane (dppb) was developed as a catalyst for the oxidation of thiols to disulfides in the presence of oxygen [67]. Primary and secondary thiols gave the products in quantitative yields using 0.1 mol % of catalyst in MeOH. Reactions of tertiary thiols required a higher catalyst loading while aromatic substituents did not affect the reaction. Functional groups such as carbamates, alcohols, and esters were not affected during the oxidation of thiols.

From the previous results, the oxidation of alcohols provided a high yield with good selectivity. It was thus trying to expand the scope of utilization of the developed system to apply for the oxidation of thiols. Cyclohexylthiol, butylthiol and 2-butylthiol were chosen to examine the capability of the catalytic system and to explore the scope of this developed oxidation system.

2.4.4.1 Optimum conditions for the oxidation of Thiols.

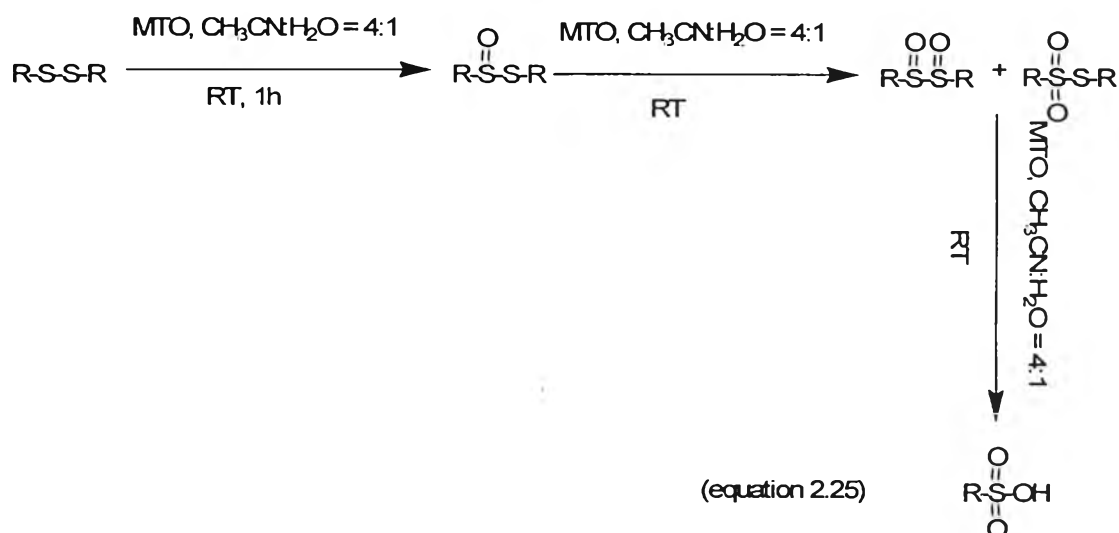
The parameters studied for this reaction included solvent and time to reach the optimal conditions. Cyclohexylthiol was chosen as substrate to study suitable condition. The results are tabulated in Table 2.20.

Table 2.20 The oxidation of cyclohexylthiol by $\text{Cr}(\text{str})_3$ 

entry	time (h)	isooctane		acetonitrile	
		% conversion	% yield	% conversion (1)	% yield (2)
1	1	96	36	100	24
2	2	96	36	100	24
3	3	100	24	100	20
4	5	100	20	100	20

Reaction conditions: thiol (5 mmol), Catalyst (0.2 mmol), solvent (5 mL),
TBHP (9 mmol), at 70°C

It should be worth to note at this point that the oxidation of thiol could be accomplished using this developed system. The conversion of thiol was 100% both in isooctane and acetonitrile. The products observed were, nevertheless, rather complicated (observed in TLC) cyclohexyldisulfide was obtained in $R_f = 0.68$ (EtOAc:hexane = 3:7). From table 2.20, The use of both acetonitrile and isooctane afford the comparable result (100% conversion) however the expect product (cyclohexyldisulfide) detected in low yield that maybe it is rapidly overoxidation to sulfonic acid. When compare with the using of CH_3ReO_3 (MTO) catalyzed both alkyl and aryl substituted disulfides oxidation [68]. The first step of the reaction is complete usually in an hour. The thiosulfinate, $\text{RS}(\text{O})\text{SR}$, can be detected in nearly quantitative yield. The thiosulfinate is then converted, also by MTO-catalyzed oxidation under these conditions, to the thiosulfonate, and over long periods, to the sulfonic acid, RSO_3H (equation 2.25). Thus in the same reason, the oxidation of cyclohexyl thiol catalyzed by $\text{Cr}(\text{str})_3$ in the presence of TBHP may result in overoxidation to the sulfonic acid which was lost during work up.



2.4.4.2 Oxidation of saturated thiols

n-Butylthiol and 2-butylthiol were selected as a model substrate for saturated thiols under the oxidation conditions studied. The results of the thiols oxidation catalyzed by Cr(str)₃ are presented in Table 2.21.

Table 2.21 The oxidation of n-butylthiol and 2-butylthiol by Cr(str)₃

entry	thiol	disulfide	% conversion of thiol	% yield of disulfide
1			40	60
2			40	44

Reaction conditions: thiols (5 mmol), Cr(str)₃ (0.2 mmol), acetonitrile (5 mL), TBHP (18 mmol), at 70^oC for 1 h.

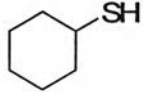
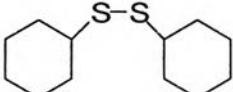
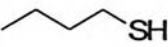
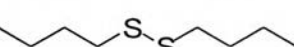
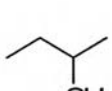
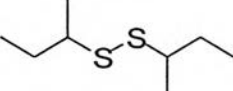
From table 2.21, n-butylthiol and 2-butylthiol were oxidized by this potential catalytic oxidation. It was observed that both substances could be converted to their respective disulfides in an hour. The amounts of saturated secondary disulfide was more than cyclic disulfide under the same condition however the mass balance was still less than 100 % due to overoxidation. From the above mentioned results, the catalytic oxidation gave good reactivity for cyclic secondary thiol and to a lesser extent secondary and primary saturated thiols, respectively. The oxidation of n-butyl thiol with NaBH₄ in methanol at ambient temperature also gave a low yield (39%

yield) of n-butyl disulfide, while cyclohexyl oxidation afforded the corresponding sulfinyl sulfur in moderate yield. [69]

2.4.4.3 Effect of amounts of oxidant

In order to discover the most appropriate selective oxidation system for the formation of disulfides, the amounts of oxidant required as 4.5 and 9 mmol respectively was explored. The results are summarized in Table 2.22.

Table 2.22 The oxidation of thiols by $\text{Cr}(\text{str})_3$

entry	substrates	products	%conversion of thiol		%yield of product	
			a	b	a	b
1.			93	79	14	19
2.			65	58	38	42
3.			86	55	40	25

Reaction conditions: thiols (5 mmol), $\text{Cr}(\text{str})_3$ (0.2 mmol), acetonitrile (5 mL), at 70°C for 1h, ^a TBHP 9 mmol, ^b TBHP 4.5 mmol

When the amounts of oxidant decreased, the yield of the corresponding disulfide increased. Nevertheless, the percent recovery was still low and mass balance was not close to 100 %.

Moreover, when using an excess of cyclohexylthiol (40 mmol) and 18 mmol of oxidant, the reaction was selective for the production of disulfide in quantitative yield (based on oxidant) and mass balance was 100%. It was concluded that the use of 0.45 mol percent of oxidant resulted in the selective conversion to disulfide in excellent yield.

2.4.4.4 Effect of time

This study was undertaken in order to assess the propagation of cyclohexylthiol to prove the overoxidation. The results are reported in Table 2.23.

Table 2.23 The oxidation of cyclohexyl thiols by Cr(str)₃

entry	time (h)	% yield of cyclohexyl disulfide
1	1	50
2	3	40
3	4	39
4	6	38
5	18	33

Reaction conditions: thiols (5 mmol), Cr(str)₃ (0.2 mmol), acetonitrile (5 mL), TBHP (2 mmol), at 70°C

The results showed that the cyclohexyl disulfide can be further oxidized to corresponding sulfonic acid product, with a percent yield of only 50% when 2 mmol of TBHP was used in 1 h. When the time was increased, the low percent yield would be due to overoxidation of the disulfide.

It can be concluded that the catalytic oxidation of thiols by Cr(str)₃ smoothly converted to their corresponding disulfides with small amount of oxidant. Cyclic saturated thiols were more easily converted to the corresponding disulfides than secondary and primary saturated thiols. Although, the oxidation was not specific to disulfide, the % conversion afforded in excellent value. These reaction should be able to apply as remedial method for sulfur waste treatment. Moreover, the synthesis of disulfide can be utilize by using excess of substrate with diminutive oxidant.