Studies of the metal ion-catalysed oxidation of heterocyclic sulfur compounds.

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STUDIES OF THE METAL ION-CATALYSED OXIDATION OF HETEROCYCLIC SULFUR COMPOUNDS

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Abstract

Chemical oxidation by hydrogen peroxide is used for the treatment of hazardous organic materials present at low concentrations in contaminated soil and water. A knowledge of the oxidation of thiophene and its derivatives, with particular reference to oxidative destruction and the identification of intermediate oxidation products would be useful for a deeper understanding of reaction mechanisms in waste treatment and the optimization of conditions. In this thesis, the oxidation of thiophenes, namely thiophene and 2- and 3-methylthiophene, with hydrogen peroxide and catalyst systems, e.g. Fenton's reagent, Gif systems and titanium dioxide-assisted photocatalytic oxidations, all of which may involve the formation of free radicals, e.g. the hydroxyl radical ($HO^{\bullet}$), has been studied. Fenton-related catalyst systems, mixtures of iron salts (and sometimes also with copper salts) and hydrogen peroxide, have been suggested in the literature and their reactions with thiophenes have been investigated. Additionally, other catalytic systems that have also been suggested in the literature as having potential have been studied. The oxidation of thiophene derivatives with Fenton-like reagents involving a combinations of hydrogen peroxide with other metal salts including vanadium(IV), titanium(III), copper(I) and copper(II) have been explored, since all of these systems appear to form hydroxyl radicals. Further Fenton-related oxidations of reaction intermediates have been carried out in order to help understand whether the oxidation products described are derived directly from the original compound or from further oxidation of a reaction intermediate. The progress of the oxidation reactions was followed by chromatographic analysis, using Gas Chromatography-Mass Spectrometry and High Performance Liquid Chromatography, so as to establish the nature of the oxidation products and the possible reaction pathways. Components of the mixtures were identified by comparison with commercially available products or synthetic standards. Oxidation reactions were monitored over set time intervals and the amounts of residual thiophenes were determined. In all of the oxidation reactions investigated, Fenton-related and Fenton-like, heteroaromatic ring destruction was observed, together with the formation of small amounts of hydroxylated ring products and dimeric structures. The oxidative destruction of thiophenes was successfully achieved with the above catalyst systems in the presence of excess hydrogen peroxide.

Recent literature has questioned the formation of hydroxyl radicals in Fenton-related systems, and in order to contribute to the debate regarding the oxidizing species responsible for the destruction of each of the thiophenes, the oxidation reactions have been carried out in the presence of a complexing agent such as ethylenediaminetetraacetic acid (EDTA), and a radical trapping reagent 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), respectively. Evidence of radical trapping was observed. Gif chemistry may involve the formation of high oxidation state iron complexes rather than free radicals. The oxidation of thiophenes was carried out using Fenton's reagent under Gif conditions and the results were compared with those from conventional Fenton and related conditions, to determine whether free radical species are involved in the latter. Radical derived products were again observed.

Titanium-catalysed photooxidation has also formed part of this study to determine the nature of intermediate products which might be similar to those from Fenton-catalysed systems. For these reasons, the photocatalytic oxidation of 2-methylthiophene was studied in aqueous solution and the reaction was conducted in the presence and absence of titanium dioxide under an oxygen atmosphere. A similar range of radical derived products was found as in the conventional Fenton and related systems.

CONTENTS

Page No.

Chapter 1

Chapter 2

Chapter 3

Chapter 4

Acknowledgment

Presentations and Conferances Attended

Meetings Attended

Published Paper

Abbreviations:

$HO^{\cdot}$ = hydroxyl radical

M^{ny} = metal ions

bpy = 2,2'-bipyridine

WAO = wet air oxidation

COD = chemical oxygen demand

MY = metal complexes

X_2 = halogens

EPR = electron paramagnetic resonance

ESP = electron spin resonance

ST = spin trap

EDTA = ethylene diamine tetraaceti acid

DNA = deoxyribonucleic acid

DMPO = 5,5-dimethyl-1-pyrroline N-oxide

PA = picolinate

TBHP = t-buthylhydroperoxide

t-$BuO^{\cdot}$ = t-butylradical

e^{-}_{CB} = conductive band electrons

h^{+}_{VB} = positive charged holes on the surface of semiconductor

2,4-D = 2,4- dichlorophenoxyacetic acid

2,4,5-T = 2,4,5-trichlorophenoxyacetic acid

$h\gamma$ = radiation

RMM = relative molecular mass

RSD = relative standard deviation

CHAPTER 1

INTRODUCTION

This thesis is concerned with a study of the oxidation chemistry of thiophenes and related compounds in the context of the disposal of organic wastes. There follows a description of the various methods which are available for disposal of such wastes, focusing on those methods which use oxidation chemistry. This leads to a discussion of the background chemistry of a number of oxidation processes.

1.1. Hazardous Substances and Wastes

A hazardous substance is a material that may pose a danger to living organisms, materials, structures, or the environment by explosion or fire hazards, corrosion, toxicity to organisms, or other detrimental effects. In a simple sense, a hazardous waste is a material that has been left somewhere such that it may cause harm if encountered and such substances pose a great danger to living organisms.

Environmental pollution has increased steadily with the development of industry. During the 1700's, run off from mine spoils or tailing pipes began to create serious contamination problems in Europe. As the production of dyes and other organic chemicals developed from the coal tar industry in Germany during the 1800's, pollution and poisoning from coal tar by-products was observed. The quantity of chemical wastes produced each year has increased sharply with the development of new high technologies which require more sophisticated management techniques nowadays [1].

Hazardous substances and wastes can be classified as follows on the basis of their chemical reactivities, fire hazards, toxicities and other properties:

- Explosives, such as dynamite or ammunition
- Compressed gases, such as hydrogen and sulfur dioxide
- Flammable liquids and solids, such as gasoline, sodium hydride and calcium carbide
- Oxidizing materials, such as lithium peroxide, that supply oxygen for the combustion of normally nonflammable materials
- Corrosive materials, including oleum, sulfuric acid and caustic soda which may injure exposed flesh or cause disintegration of metal containers
- Poisonous materials, such as hydrocyanic acid or aniline
- Etiological agents including casuative agents of anthrax, botulism or tetanus
- Radioactive materials, including plutonium, cobalt-60, and uranium hexafloride.

Hazardous wastes may enter into the environment by various routes such as deliberate addition to soil, water or air by humans, evaporation or wind erosion from dumps, leakage from underground storage tanks or pipelines or release from improperly operated waste treatment, storage and disposal facilities. However, research is ongoing into waste treatment to make it possible to deal with waste either so that useful components may be retrieved from it and used again, or so that a threat is not posed to the environment when the waste is stored within it.

In 1996, world total production of hazardous and special wastes amounted to $338X10^6$ t, and of the hazardous waste produced in the USA, 79 % came from the chemical industries, petroleum refining produced 7 %, the metal industries 2 % and 12 % came from miscellaneous other sources [1]. So hazardous waste management has become a very important issue for the industrial world. Where possible, the industrial process producing the waste should be modified so that as far as possible, hazardous by-products are either avoided, re-used, or at least minimized.

The treatment of hazardous waste has gained increased attention over the past decades. The most common ways of disposing of waste have been excavation and landfilling as well as dumping to sea or stream. However, environmental impact and growing volumes have led to the development of on-site and in-situ treatment technologies, such as incineration and biological treatment [2].

The procedures used to treat the hazardous wastes that are produced include [3].

Physical methods

. phase separation (filtration / sedimentation)
. phase transition (distillation, evaporation, physical precipitation)
. phase transfer (extraction, adsorption)
. membrane separation (reverse osmosis, hyper and ultrafiltration)

Chemical methods

. acid / base neutralisation

. chemical extraction and leaching

. chemical precipitation

. oxidation / reduction

. ion exchange

. electrolysis

. hydrolysis

. photolysis

Thermal treatment

. incineration

. wet oxidation

. plasma arc

. molten salt

. super heated water

Biotechnological methods

. ocean dumping

. prolonged storage

. landfill

. underground injection

. salt formation

1.2. Chemical Deactivation

Chemical deactivation processes are especially applicable for the treatment of hazardous organics present at low concentration, as a pretreatment step before biological treatment for waste components that are biorefractory or toxic to microorganism and as a post treatment step to reduce aquatic toxicity [4]. Chemical deactivation technologies which involve degradation and/or transformation of hazardous material can be combined with other technologies to achieve a more effective treatment.

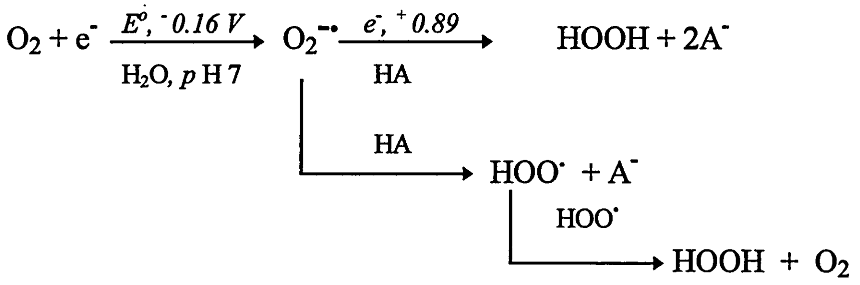
Chemical treatment methods have been reviewed by Manahan according to the nature of the waste[1]. The applicability of chemical treatment to wastes depends upon the chemical properties of waste constituents; particularly acid-base, oxidation-reduction, precipitation and complexation behaviour, reactivity, flammability, combustibility, corrosivity, and compatibility with other wastes. The chemical behaviour of wastes translates to various unit operations for waste treatment that are based upon chemical properties and reactions. Methods of deactivating hazardous chemical wastes can reduce the exposures of workers to such wastes, ease storage problems prior to disposal of waste products, and permit recovery of useful substances. Deactivation by chemical conversion is a process by which a waste or constituent of the waste is transformed to at least one substance that is less hazardous than and chemically different to the original material. Especially, organic wastes can be chemically converted to less hazardous products. Under ideal conditions organic molecules can break down to simple molecules, e.g. carbon dioxide, sulphur dioxide, and acetic acid. The aim of these conversions is to attain the complete mineralization of wastes. In reality chemical waste treatment methods must be multicomponent in several senses. First, multiple organic contaminants are routinely expected from materials such as gasoline (benzene, toluene, xylene) or from leaks from halogenated solvent tanks (perchloroethylene, trichloroethylene) into underground or surface waters. Second, deactivation process will produce a series of intermediates which have higher oxygen to carbon ratios on the way to carbon dioxide. Such intermediates make the conversion process multicomponent even if only a single contaminant exists in the feed. Hence, demonstration of the formation and elimination of intermediates also is important for showing complete removal of undesirable compounds.

1.3. Oxidation Chemistry and Catalytic Oxidations

Oxygen atoms react spontaneously with the atoms of all elements except the noble gases to form polyatomic molecules via formation of covalent bonds and are present in nature in varied forms like dioxygen, hydrogen peroxide, water and ozone. In the 18th century, it was established that dioxygen comprises about 21 % (by volume) of the Earth's atmosphere, being essential for aerobic life but toxic to plant life at higher concentrations, and it is the essential oxidant for the combustion of organic molecules.

Aerobic life makes use of dioxygen as an oxidant in all of its respirative and oxidative metabolic processes. Since the ground state of dioxygen is a triplet with two unpaired electrons with parallel spins, its reactivity with organic molecules in the singlet state is severely restricted particularly at room temperature.

Although dioxgen is a strong oxidant at *p*H 7.0 when utilized as a concerted four-electron transfer agent, it is an extremely weak one-electron oxidant. The addition of an electron to dioxygen yields $O_2^{-\bullet}$ (superoxide anion), which is a much stronger oxidizing reagent than O_2 and a species that can abstract protons from weak acids to give a neutral radical ($HOO^{\bullet}$) that spontaneously decomposes to hydrogen peroxide and oxygen.



(1)

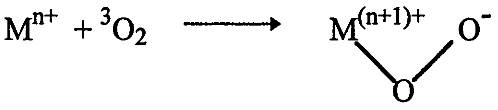
Hence, the consequence of the addition of an electron to dioxygen is the production of a range of reactive intermediates including the strongest oxidant of the oxygen family, hydroxyl radicals ($HO^{\bullet}$) [5].

$$O_2 + e^- \xrightarrow{H_2O,\ HA} \longrightarrow \longrightarrow (O_2^{-\bullet}, HOO^{\bullet}, HOOH, HOO^-, HO^{\bullet}, HO^-) \qquad (2)$$

The half-filled antibonding molecular orbitals (relocation and/or pairing of the unpaired electrons in the 2pπ* antibonding molecular orbitals) of ${}^3O_2$ can accommodate two additional electrons. The addition of a second electron gives the peroxide ion O_2^{2-}. The direct reaction of ${}^3O_2$ with singlet organic molecules to give singlet products is a spin forbidden process and occurs at very low rate. This energy barrier can be overcome in different ways, one of which proceeds via a free radical pathway:

$$RH + {}^3O_2 \longrightarrow R^{\cdot} + HO_2^{\cdot} \qquad (3)$$

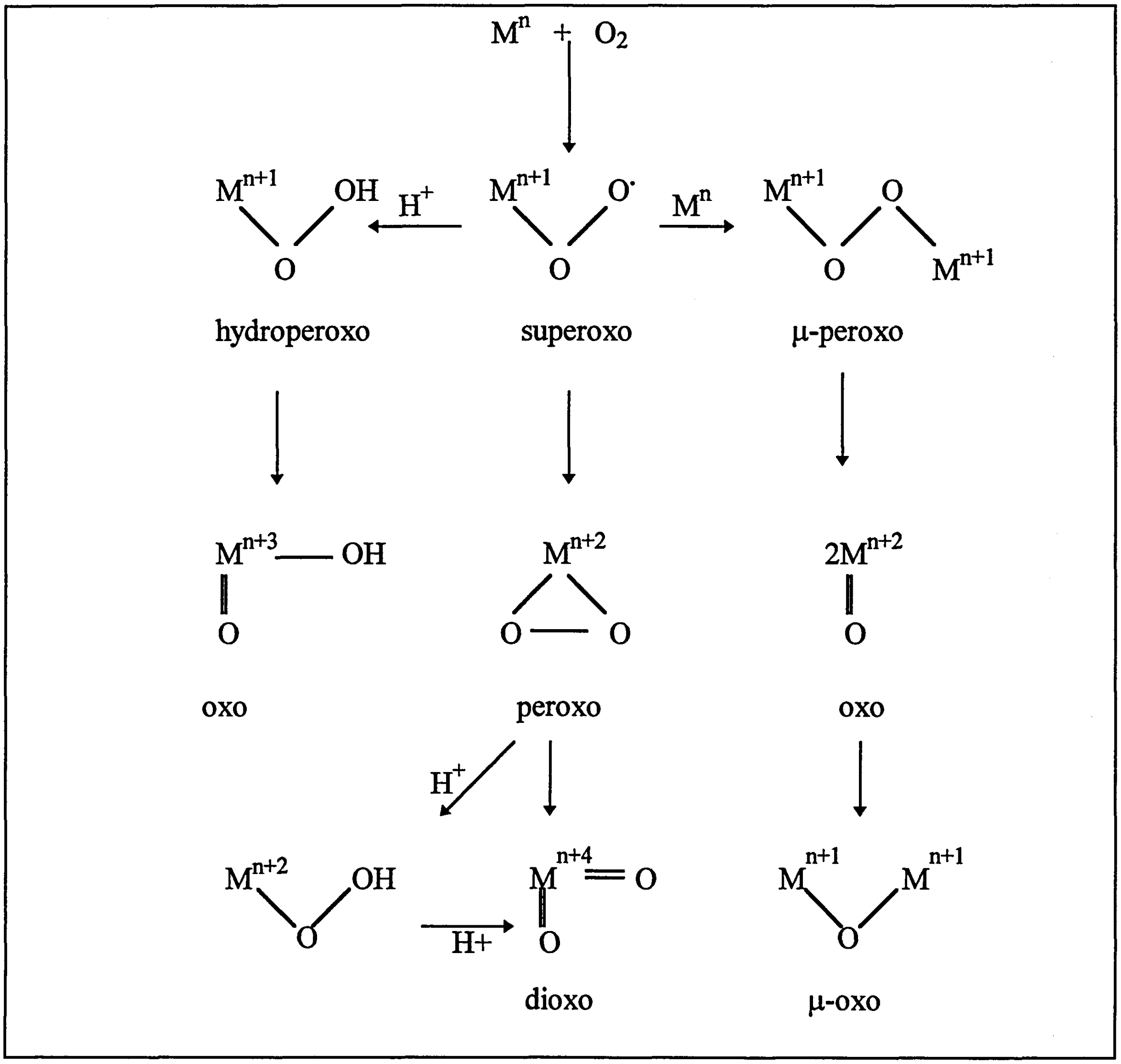
Despite the formation of free radicals which is a "*spin allowed*" process, this is very endothermic and requires the use of highly reactive substrates at moderate temperatures. A second way to overcome the spin conservation obstacle is for ${}^3O_2$ to combine with a paramagnetic transition metal ion:



(4)

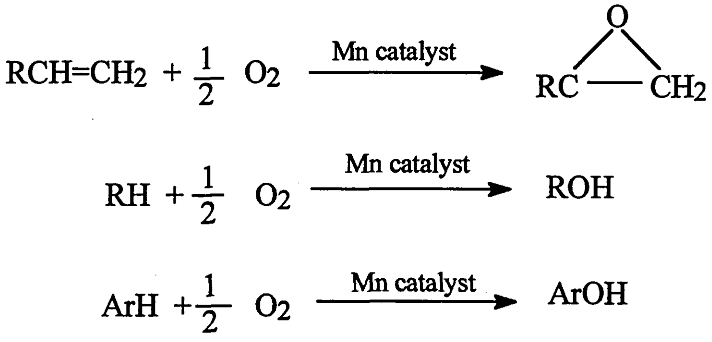
The resulting metal-dioxygen complex may react selectively with organic molecules at moderate temperatures to produce intermediates which then follow a free radical pathway. The various possible oxygenated metal species are depicted in Scheme 1.1 [6].

Scheme 1.1.



Catalytic oxidation is an area of particular significance for homogenous catalysis, and is the field where the largest contribution of homogenous catalysis to industrial organic chemistry is found. This approach can be used for deactivation of hazardous compounds as well as for the production of bulk chemicals. Metal catalyzed selective oxidation of organic compounds with molecular oxygen is extensively used in the chemical industry and has an enormous potential both in synthesis, and also in purification of waste streams.

Thus, e.g., the following are important oxidation processes using molecular oxygen as an oxidant.



The interaction of molecular oxygen with water at elevated temperature and pressure generates hydrogen peroxide and ozone via the formation of oxygen radicals as mentioned earlier in equations 1 and 2. The presence of transition metal ions dramatically increases the activation of molecular oxygen. This advantage associated with transition metal promoted reactions has led to extensive research activity, and as a result iron, cobalt, copper, titanium, vanadium, manganese, and their related complexes have been used for oxidations in organic synthesis. The reaction efficiencies and product selectivities for a group of ML/HOOH hydrocarbon-substrate systems (ML=seven iron complexes and one cobalt complex) that ketonize methylenic carbons via the initial formation of intermediate hydroperoxide-substrate $[Co^{II}(bpy)_2]^{2+}$ and $[Fe^{II}(bpy)_2]^{2+}$ complexes and provide unique selectivities and good conversion efficiencies have been summarized by Sobkowiak [7]. Other 2,2'-bipyridine complexes of transition metals (Cu, Mn, Cr, V, Mo, and Ru) have also been studied [8] and it has been shown that the bis (bipyridine) copper(I) complex

$[Cu^I(bpy)_2]^{2+}$ in acetonitrile/pyridine activates hydrogen peroxide for the selective ketonization of methylenic carbons [closely similar to the $[Co^{II}(bpy)_2]^{2+}$/HOOH system].

The use of metal catalysed oxidations within the area of waste treatment has received a great attention to obtain more effective and economic processes. There are examples in the literature of the use of a variety of different catalytic systems that have been shown to enhance the effectiveness of the oxidation process. Some catalytic oxidation methods which have been used for the treatment of organic wastes and recent developments in this area are summarized below.

1.3.1. Wet Air Oxidation

Wet air oxidation (WAO) is the process by which compounds suspended or dissolved in water are destroyed by oxidation at temperatures between 175 °C and 345 °C and high pressure usually between 20 and 200 atmospheres [9,10]. The aim of the WAO process is to chemically alter both organic and inorganic toxic compounds by a low temperature oxidation process in an aqueous phase. Air is dispersed by bubbling into the aqueous suspension to provide dissolved oxygen for the oxidation reactions [11]. Although it is not a novel technology, considerable advances have been made in the optimization of the process and to increase the effectiveness [12-18]. The oxidation is exothermic and the heat release helps to reduce the amount of energy needed to maintain the reaction temperature. Oxidation does not require an organic solvent; the process taking place in water (even dilute waste water) and the oxidation products include carbon dioxide, and biodegradable alcohols, ketones, aldehydes and carboxylic acids. Chloride ion is a product from chlorinated hydrocarbons and the sulfate ion from sulfur compounds such as mercaptans. This process is generally used as a pretreatment step, prior to final purification by a biological process. Many organic compounds can be destroyed efficiently by wet air oxidation without a catalyst. More than 99.8 % of each of the following compounds at initial concentrations of 5.0-12.4 g/L can be destroyed in 1h at 320 °C: phenol, 2-chlorophenol, pentachlorophenol, 2,4-dimethylphenol, 4-nitrophenol, acrolein, 2,4-dinitrotoluene, 1,2-diphenylhydrazine, acenaphthene and acrylonitrile. Toxicities of the final solutions after oxidation were reduced compared to the original waste. The toxicity of the resulting waste stream treated by WAO is measured by its chemical oxygen demand (C.O.D.)[2] or by using *Daphnia Magna* for toxicity tests[10]. The identification and characterization of the intermediate oxidation products gives some important evidence about the degradation mechanism.

Generally, the use of a catalyst in wet air oxidation will effect a greater degree of destruction at the same temperature and pressure in a given period. As mentioned before, interaction of molecular oxygen with water at elevated temperature and pressure generates hydrogen peroxide (H_2O_2), ozone (O_3), and when metal salts (ion, copper, cobalt) are present in the oxidation media, the most effective oxidant species, hydroxyl radicals ($HO^{\bullet}$), are formed. Wet air oxidation of oxygen-and nitrogen -containing organic compounds catalyzed by Co(III) oxide was studied by Masato *et al.*[19] and the reaction resulted initially in the form of simple aliphatic alcohols and amines via the formation of alkyl radicals ($R^{\cdot}$). These simple alcohols and amines then cleave to give formic acid and formaldehyde for the oxygen containing compounds, carbon dioxide and ammonia for the nitrogen containing compounds. Similar results were also observed by other authors [20-22] and all studies indicated the involvement of hydroxyl radicals. When iron and copper salts were used as a catalyst [22], a great effect on the wet air oxidation of various organic compounds was observed. It is known that iron salts, in the presence of hydrogen peroxide, produce free radicals according to the following equations:

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{-}OH + HO^{\cdot} \qquad (8)$$

$$Fe^{3+} + H_2O_2 \longrightarrow Fe^{2+} + HO_2^{\cdot} + H^{+} \qquad (9)$$

and copper salts behave in the following way:

$$Cu^{2+} + H_2O_2 \longrightarrow Cu^{3+} + {}^{-}OH + HO^{\cdot} \qquad (10)$$

$$Cu^{3+} + H_2O_2 \longrightarrow Cu^{2+} + HO_2^{\cdot} + H^{+} \qquad (11)$$

The mixture of Fe(II) and hydrogen peroxide is known as Fenton's reagent. When iron(II) salts are employed in the wet air oxidation process, Fe(II) and hydrogen peroxide provide a good source of hydroxyl radicals. Wet air oxidation of methylpyridines (2-, 3-, and 4-methylpyridine) in the presence and absence of metal ion catalysts was studied by Morris [23] by using simulated plant conditions in a laboratory autoclave operating at 250 °C and 250 atmospheres. Each of the autoclave oxidation reactions studied was discussed and the oxidation products observed were summarized and comparisons, where possible, were made. When the chemical oxygen demands of the oxidised systems were compared (COD % reduction values), it was shown that the oxidation of 2-, and 4-methylpyridine in the presence of the copper(II) containing catalyst achieved the best COD reductions, with 49.4 and 47.5 % for 2-methylpyridine and 4-methylpyridine respectively. These values were lower in the absence of catalyst, 25.6 and 37.5 % respectively. The presence of the Fenton catalyst also seems to improve the autoclave oxidation of 3- methylpyridine with a reduction in COD of 40.5 % compared to the uncatalysed system. The iron(II) catalyst was far more effective than related copper-based systems. This result compares well with that of Chowdbury *et al.* [22] who showed that, under WAO conditions, a mixture of iron(II) and copper(II) in the presence of hydrogen peroxide give rise to an efficient catalytic system for the oxidation of various organic substances.

1.3.2. The Use of Hydrogen Peroxide as an Oxidant

Hydrogen peroxide is a well known strong oxidant (standard potentials 1.80 and 0.87 V at *p*H 0 and 14 respectively), cost effective and environmentally friendly. When the oxidation is completed and the oxidizing power of the peroxide is spent, only water is left as a by-product so eliminating the need for expensive effluent disposal treatments [24]. Because of this potential, its application in the treatment of various inorganic and organic pollutants is well established. Wet air oxidation occurs under high temperature and pressure conditions, but hydrogen peroxide is commonly used for the oxidation of organic wastes in the chemical industry at room temperature and atmospheric pressure. Chemical oxidation by hydrogen peroxide is used for the treatment of hazardous organic materials present at low concentrations in contaminated soil and water. This deactivation method may offer such environmental and economic benefits. A few industrial applications of hydrogen peroxide (oxidation or reduction) are outlined below [2]:

1. Detoxification of waste water and concentrates containing cyanide by oxidation to cyanate;
2. Purification of iron- and manganese- containing groundwater by oxidation of the heavy metals to insoluble hydroxide/oxides which can be removed by precipitation/ clarification;
3. Treatment of photographic effluents containing sulfites and silver by conversion to sulphate and a precipitated silver complex, respectively;
4. Degradation of formaldehyde in air emissions by washing with hydrogen peroxide and ammonia;
5. Prevention of odors by conversion of sulfides, thioethers, disulfides, sulfites, and thiosulfites to elemental sulphur or sulfate in the washing solution;
6. Treatment of sulphur and nitrogen oxides present in air emissions from coking plants, sulphuric acid production, pickling, and other chemical plant processes, by conversion to the corresponding acids;
7. Removal of excess chlorite and hypochlorite in wastewater, or in bleached textiles and pulps, by reduction to chloride salts.

It is also used in the surface treatment industry concerned with the cleaning, decorating, protecting and etching of metals, and also used in biological treatment and in bioremediation of contaminated sites as well as being a disinfecting agent in the control of undesirable biofilm growth. Treatment with hydrogen peroxide can reduce the toxicity and improve biodegradability of organics. Examples of organics which can be oxidized by hydrogen peroxide include nitrobenzene, aniline, cresols, monochlorophenols, dichlorophenols and trichlorophenols. Organic contaminants such as formaldehyde, phenols, fat, oil, grease and suspended solids can also be removed from wastewater by hydrogen peroxide[2]. Hydrogen peroxide has a number of advantages compared to the other common oxidants.

The first one is that some of these oxidants, for example sodium perborate, potassium hydrogenperoxysulfate or many organic peroxy acids, e.g. peracetic acid, are prepared from hydrogen peroxide and this results in extra cost. Hydrogen peroxide is a relatively inexpensive reagent. A second advantage comes from the high active oxygen content. The active oxygen content of common oxidants is shown in Table 1.1 [25].

Table 1.1. Single Oxygen donors

Donor	% Active Oxygen	Product
H_2O_2	47.0[a]	H_2O
O_3	33.3	O_2
t-BuOOH	17.8	t-BuOH
NaClO	21.6	NaCl
NaBrO	13.4	NaBr
HNO_3	25.4	NO_x
$KHSO_5$	10.5	$KHSO_4$
$NaIO_4$	7.2[b]	$NaIO_3$
PhIO	7.3	PhI

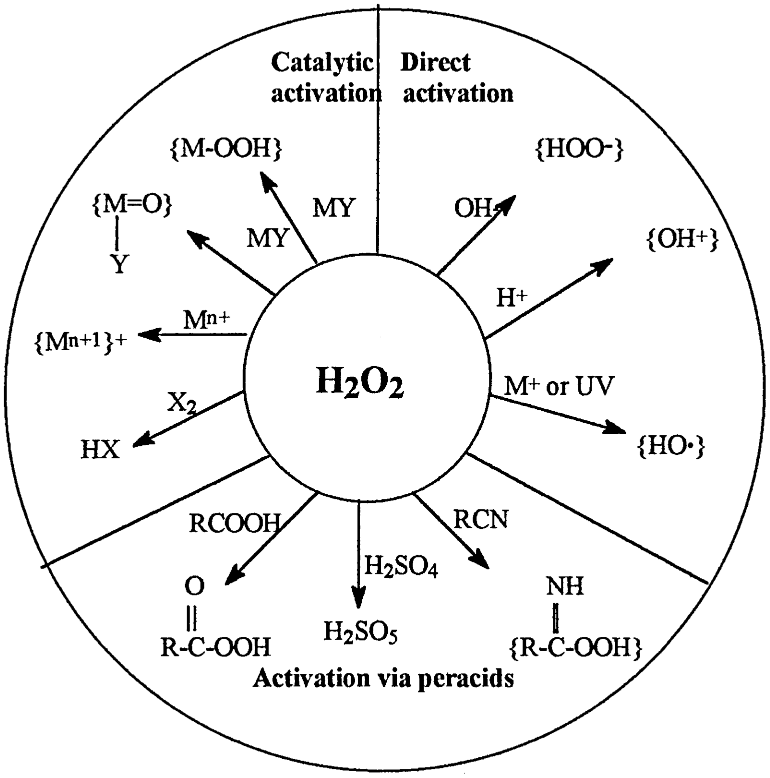
a Calculated on 100 % H_2O_2 *b* Assuming only the one oxygen atom is utilized

Despite the high active oxygen content, hydrogen peroxide needs to be activated in some way. Activation methods are shown in Figure 1.1 [24].

Because of the main interest of the work described in this thesis, activation of hydrogen peroxide in the presence of transition metals will be considered further in this chapter. Conversion of hydrogen peroxide to more active species can be classified into three general methods [25];

1. By using hydrogen peroxide with metals capable of generating metal peroxo (M-OOH) or hydroperoxy (HOO^-) species, where the peroxo bond remains intact. This occurs

Figure 1.1. Common hydrogen peroxide activation methods.



with, for instance, Ti(IV), V(V), Mo(VI), W(VI) (d^0 metal centres) and with Pd(II) and Pt(II) (d^8 metal centres) and the result is an increase in either the electrophilic or nucleophilic character of the peroxygens with respect to the original oxidant.

2. By using hydrogen peroxide as an oxygen donor to produce highly reactive metal-oxo ($M^{n+} = O$) species. This behaviour is typical of biomimetic systems based for example on Fe(II), Ru(II) and Mn(II).

3. Through radical decomposition of hydrogen peroxide with one electron redox couples like Fe(II)/Fe(III) or Ti(III)/Ti(IV). These are the basis of the well known Fenton and Udenfriend systems and a simple way of generating the highly reactive $HO^{\cdot}$ radical.

1.3.2.1. Fenton and Related Oxidations of Organic Compounds

Nearly a century ago Fenton reported that hydrogen peroxide acts as a strong oxidant in the presence of the ferrous ion, when he published his work entitled “Oxidation of tartaric acid in presence of iron”[26]. Forty years later, Haber and Weiss [27] proposed the formation of the hydroxyl radical ($HO^\cdot$) in the reaction of Fenton’s reagent.

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + HO^\cdot$$

The reactive product of Fenton reaction is the hydroxyl radical, and therefore the chemistry related to the use of Fenton reagent is above all the chemistry of this radical. The hydroxyl radical is also produced in the presence of other metal ions (M^{n+}) and these systems are often called “Fenton-like” oxidations. The Fenton reaction may be represented as follows;

$$M^{n+} + H_2O_2 \longrightarrow M^{(n+1)+} + HO^- + HO^\cdot \qquad (12)$$

The reactions of hydroxyl radicals may be classified as follows:

a) Reactions proceeding with the abstraction of hydrogen from a substrate,

$$R\text{-}H + HO^\cdot \longrightarrow H_2O + R^\cdot \qquad (13)$$

b) addition reactions,

$$ArH + HO^\cdot \longrightarrow HO\text{-}ArH^\cdot \longrightarrow \text{products} \qquad (14)$$

(15)

c) Oxidation reactions,

$$ArH + HO^\bullet \longrightarrow HO^- + ArH^+ \qquad (16)$$

$$M^{n+} + HO^\bullet \longrightarrow HO^- + M^{(n+1)+} \qquad (17)$$

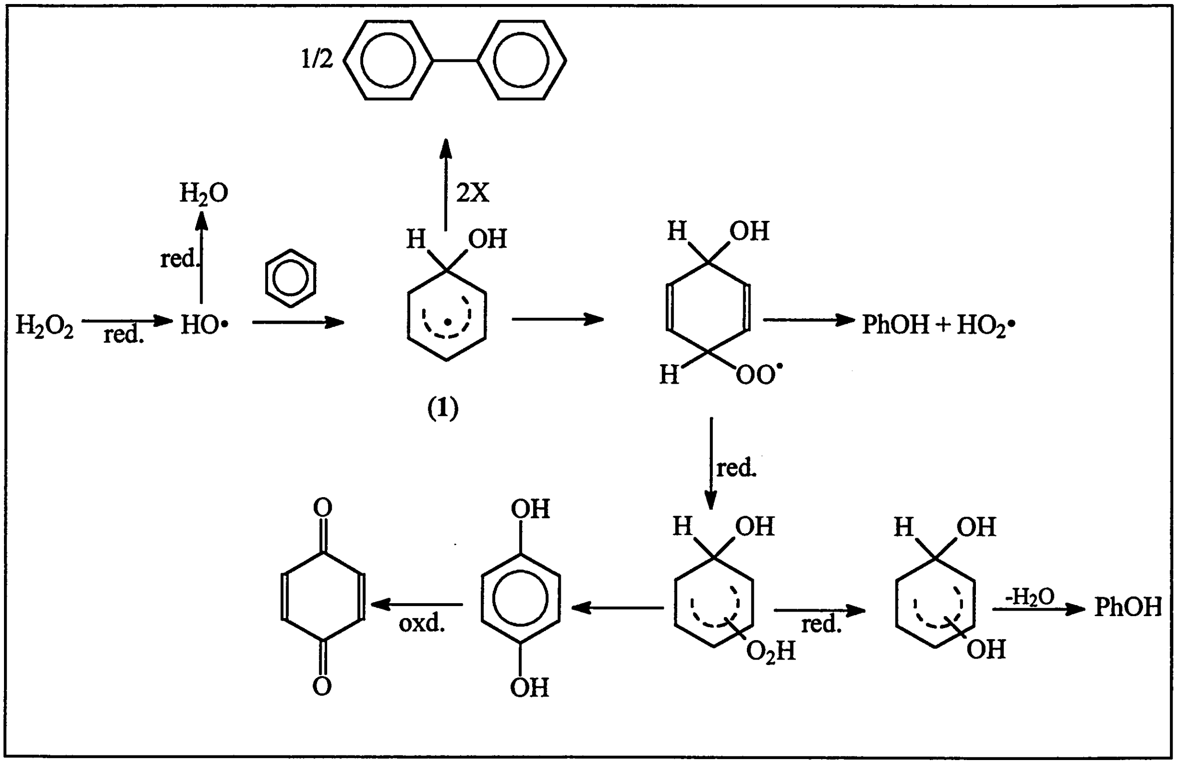
The above carbon centered radicals may then undergo further oxidation steps, as proposed by Walling *et al.* [28],

$$\mathbf{HO^\bullet} + \text{substrate}\left|\begin{array}{llr} \longrightarrow R_i^\bullet \xrightarrow{Fe^{3+}} & \text{Product} + Fe^{2+} & (18) \\ \longrightarrow R_j^\bullet \longrightarrow & \text{Dimerization} & (19) \\ \longrightarrow R_k^\bullet \xrightarrow{Fe^{2+}} & \text{Product} + Fe^{3+} & (20) \end{array}\right.$$

The radicals formed ($R_i^\bullet$, $R_j^\bullet$, and $R_k^\bullet$) either undergo oxidation (eq.18), dimerization (eq.19) or reduction (eq.20).The hydroxyl radicals can be generated by a small amount of ferrous iron, as low as 0.05 mM, and also by using other transition metals instead of iron. Several papers have been published about the oxidation of organics, especially in industrial wastes, by the Fenton reagent: chlorophenols [29], 2,4-dichlorophenol, chlorobenezene and dinitro o-cresol [30], hydroxymethanesulfonic acid, formaldehyde, phenol, nitrophenols, nitrobenzene, polyaromatic hydrocarbons [2], polychlorobenzene [30], polychlorinated biphenyls [31a,b], hydrazine and benzene [32]. A more detailed review has been published by

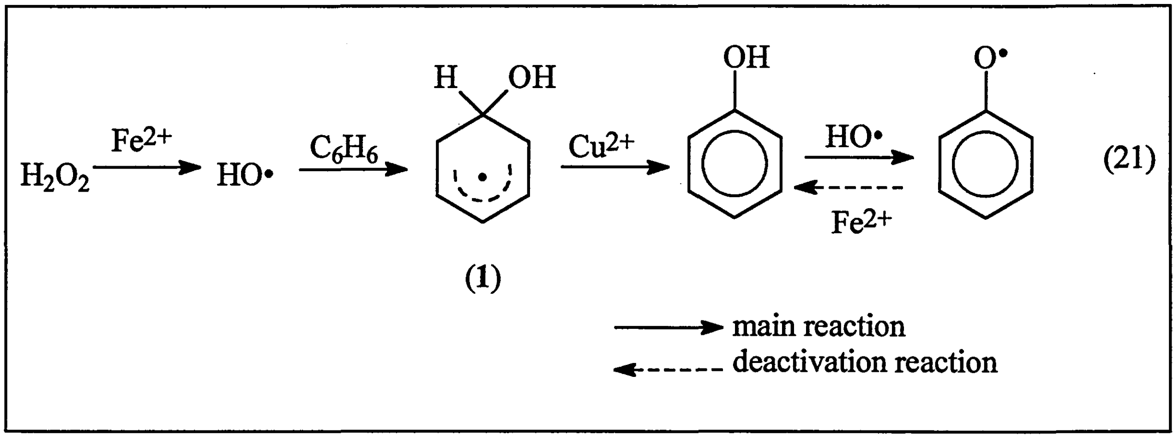
Venkatadri and Peters [2]. In 1969, Norman [32] found that the addition of Cu(II) ions to the Fenton oxidation of benzene significantly increases the yield of oxidation products, especially the formation of dimeric products. An earlier study [33a] proposed a mechanism for the oxidation of benzene in aqueous solution (Scheme 1.2). The main products of this reaction were phenol and hydroquinone, and the active species responsible for these products was concluded to be the hydroxyl radical. A tracer study using ($^{18}O_2$) indicated that the two hydroxyl groups of hydroquinone are introduced in two separate steps, and both phenol and hydroquinone are derived from the same intermediate, the hydroxycyclohexadienyl radical (**1**).

Scheme 1.2.



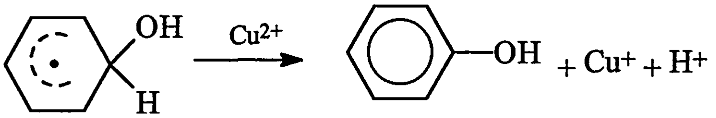
The hydroxylation of benzene has been studied most extensively and an adduct of the hydroxyl radical with the aromatic ring has been observed in several cases [28, 32, 33a, 33b, 34]. The final product is phenol and its yield depends on the amount of hydrogen peroxide used, varying considerably in range from 5 % [34] to 57 % [28]. The basic reaction scheme for the Fenton oxidation of benzene was outlined by Ito *et al.* [33b] as in Scheme 1.3.

Scheme 1.3.



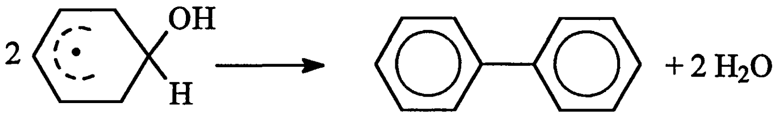
(21)

The rate-enhancing effect of copper(II) ions has been explained by the effective oxidation of the hydroxycyclohexadienyl radicals to give phenol according to equation 22.



(22)

or



(23)

Numerous metal ions and their complexes in their lower oxidation states, for example Cu(I), Cu(II), Ti(III), Cr(II), Co(II) and V(IV), were also found to have the oxidative features of the Fenton's reagent, and hence mixtures of these metal ions with hydrogen peroxide were named "Fenton-like" reagents[35]. Since the importance of the hydroxyl radical was recognized, many investigators have studied its formation by means of ever more sophisticated techniques and apparatus. Although there is much evidence, using an EPR spin trapping technique [32, 36-38], in favour of the formation of $HO^{\bullet}$ radicals from the Fenton-like reagents, it has also been reported by others [39-44] that the oxidizing intermediate is not the free hydroxyl radical $HO^{\bullet}$, but some type of high oxidation state iron species.

The formation of the hydroxyl radical was confirmed by Baxendale *et al.* [45] in his work in 1946 showing that the Fenton reagent initiates and catalyzes the polymerization of olefins via the addition of $HO^{\bullet}$ to the double bond. Later Merz and Waters [46-47] suggested that the involvement of $HO^{\bullet}$ was supported by the stoichiometry of the reactions taking place in the presence of the Fenton reagent. The predominant oxidising role of hydroxyl radicals was summarized by Walling in a review [48].

The main methods used for the identification of $HO^{\bullet}$ radicals are [35]:

1. Spin trapping

2. Reactions with known $HO^{\bullet}$ scavengers, and identification of the products which are formed.
3. Analysis of the relative yields of the products formed in the reaction of the oxidizing entity with two trapping agents.
4. The use of oxygen isotope effects.

The spin trapping methods are simply based on the reaction of short-lived radicals with a spin trapping reagent (ST) to yield relatively stable adducts ($^{\bullet}STR$) that can be observed easily by ESR spectroscopy.

$$ST + R^{\bullet} \longrightarrow {}^{\bullet}STR \qquad (24)$$

The trapping of hydroxyl radicals leading to the formation of $^{\bullet}STOH$ radicals is not completely understood. Several studies have shown that the formation of the spin adduct $^{\bullet}STOH$ can occur in several ways. It has been shown that the reaction of ST with O_2 yields a spin adduct $^{\bullet}STOOH$, which then decomposes easily to $^{\bullet}STOH$, resulting in uncertainty as to whether detection of $^{\bullet}STOH$ in an experimental system results from the presence of $O_2^{\bullet -}$ and/or $HO^{\bullet}$ [35]. Another possibility is that the spin trap itself may be oxidized by transition metal complexes in their higher oxidation states (eq. 25);

$$M^{(n+2)} + ST \longrightarrow M^{(n+1)} + ST^{\bullet +} \qquad (25)$$

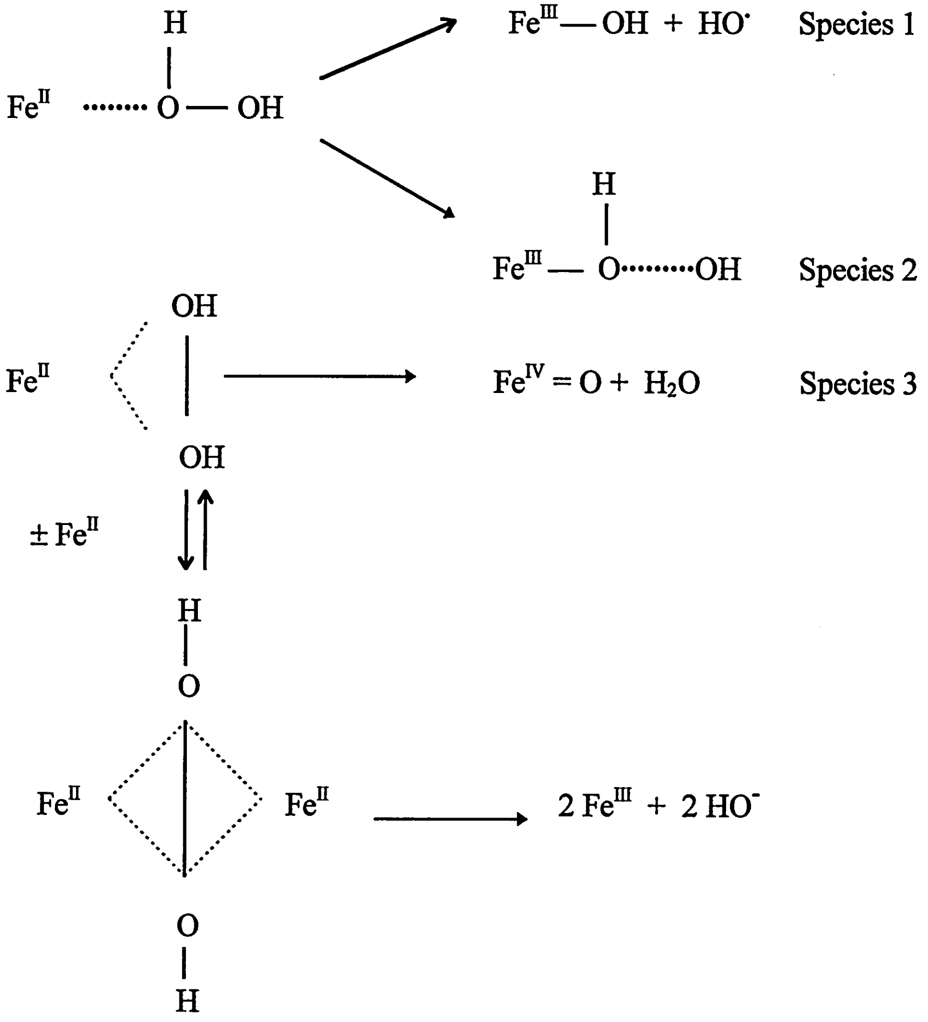
and this cationic radical then gives rise to $^{\bullet}STOH$ in aqueous solutions.

$$ST^{\bullet +} + OH^{-} \longrightarrow {}^{\bullet}STOH \qquad (26)$$

Direct evidence for the formation of the hydroxyl radicals has been given by several research groups [37] in studies using ESR spectroscopy for the determination of the hydroxyl radical in the reaction between Fe(II) and hydrogen peroxide in aqueous solution. From both the identification of hydroxyl radical adducts to alkenes and the observed site-selectivity of radical attack, it was shown that the hydroxyl radical is formed as the reactive intermediate in the presence of various chelators (e.g. EDTA, DTPA) [37b].

The involvement of Fenton's reagent in biological systems is another major research area which has been extensively studied. Pogozelski *et al.* showed that the hydroxyl radical was indeed responsible for DNA scission, when a modified Fenton's reagent , Fe(II)$^{\cdot}$-EDTA + hydrogen peroxide + ascorbic acid, was used for DNA cleavage [49]. Their results do not support the formation of high valent iron-oxo complexes and their involvement in DNA scissions, since DNA-cleavage patterns generated by a known source of hydroxyl radicals (the γ-radiolysis of water) are identical to those generated by the reaction of $[Fe(EDTA)]^{2+}$ with hydrogen peroxide in the presence of ascorbate.

Some researchers have suggested that high-valent iron-oxo complexes are generated in the Fenton reaction instead of the free hydroxyl radicals, whereas others contend that both the hydroxyl radical and an oxidizing iron species are formed [42,50].A recent paper by Jiang *et al.* showed that $HO^{\cdot}$ is an oxidizing intermediate in the Fenton reaction [50], using a new technique which enabled them to measure the trapped hydroxyl radicals on a subsecond time scale by using 5,5-dimethyl-1-pyrroline N-oxide (DMPO) to give the spin adduct DMPO-$HO^\bullet$. On the other hand, Yamazaki has compared the ratio of rate constants for the reaction of $HO^\bullet$ with $HO^\bullet$ scavengers (e.g. benzoate, tert-butylalcohol) to those for the reaction with 5,5-dimethyl-1-pyrroline N-oxide (DMPO) and has concluded that the Fenton reaction involves some kind of complexed iron species depending upon the type of ligand rather than $HO^\bullet$ radicals. According to experimental data obtained by Yamazaki *et.al.* [42] the oxidizing species were classified as follows:



Using EPR spin trapping, they determined that three types of oxidizing species are produced in the Fenton reaction,

1) free $HO^{\cdot}$ (species 1)

2) bound $HO^{\cdot}$ (species 2)

3) a high-valence iron species (iron-oxo compound) (species 3)

Despite extensive work, the situation is still not clear. In recent research, Sawyer *et al.* suggested that [44a] the oxidation of benzene with Fenton reagents does not give rise to:

a) free hydroxyl radicals ($HO^{\cdot}$)

b) free carbon radicals ($R^{\cdot}$) or

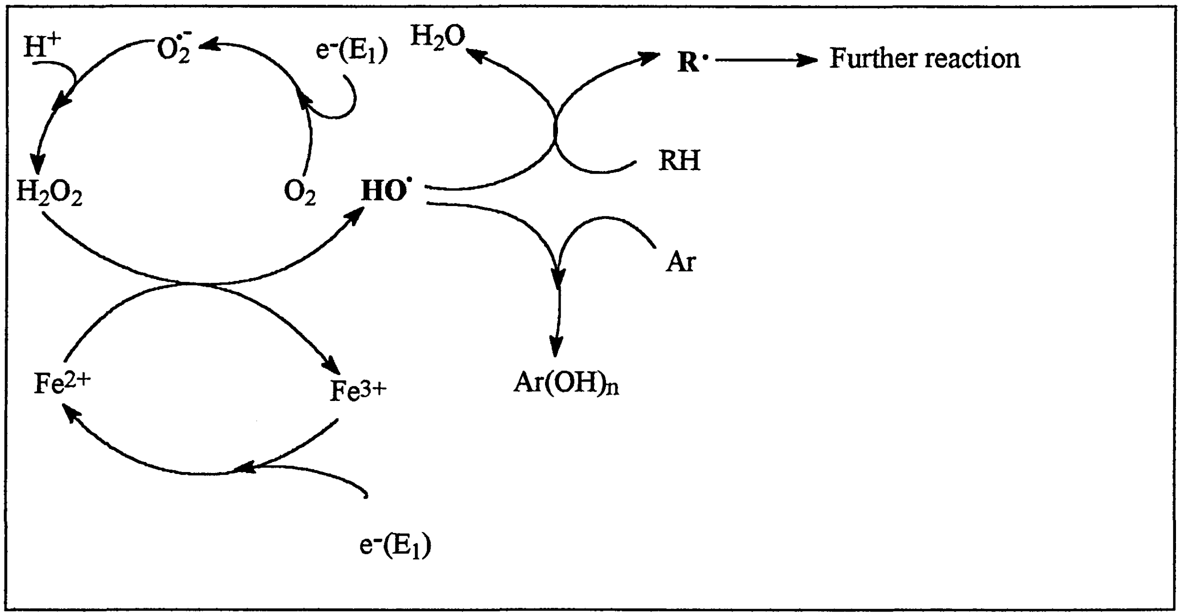
c)aryl adducts ($HO\text{-}Ar^{\cdot}$)

Electrophilic transition-metal complexes ($Fe(II)L_x$, $Cu(I)L_x$ and $Mn(II)L_x$) give the reactive intermediates by nucleophilic addition to the metal centers, e.g. $[(PA)_2\ {}^{\cdot}Fe(II)OOH]$ and $[(PA)_2\ {}^{\cdot}Fe(II)OOH]O_2$ rather than reacting directly with hydroxyl radicals[44a].

The formation of a metallo-oxo complex in the Fenton reaction has been suggested by several groups [51-53]. More recent work has given some evidence for the formation of Fe(IV)=O in the activation of trioxane from a dialkyl peroxide rather than, as usual, hydrogen peroxide [53b]. Two new oxidizing intermediates generated in the Fenton reaction were introduced by Wink *et al.* [54,55]. The first species was $[Fe(H_2O_2)]^{2+}$, as an iron complex which is formed by the direct reaction of hydrogen peroxide with Fe(II). The second species was $[FeO]^{2+}$. They concluded that $[Fe(H_2O_2)]^{2+}$ has a reactivity pattern similar to that of $HO^{\bullet}$ and this species might have been mistakenly identified as the hydroxyl radical.

Hydroxyl radicals can be generated radiolytically and/or electrochemically in aqueous solutions and this enables a comparison to be made as to whether Fenton oxidation of aromatic compounds follows a radical pathway or not. Recently, the hydroxylation of salicylic acid and benzoic acid was studied by Oturan and Pinson [56,57] by using electrochemically generated hydroxyl radicals. Mono and polyhydroxylated products were observed for both substrates, and the same hydroxylated products were formed in the presence of Fenton's reagent ($Fe(II)/H_2O_2$). The electrochemical Fenton reaction (simultaneous reduction of dioxygen and ferric ions) permits a controlled production of $HO^{\bullet}$ radicals. Electrochemical generation of hydroxyl radicals is shown in Scheme 1.4.

Scheme 1.4.



Another recent study has shown that the reaction of hydroxyl radicals, generated radiolytically in an N_2O-containing aqueous solution, with chlorobenzene [58] and chlorotoluene [59] in the presence of $Fe(CN)_6^{3-}$, resulted in the formation of chlorophenols and chlorohydroxytoluenes respectively.

1.3.2.2. Gif Chemistry

The Gif system is one of the most studied catalytic oxidation systems. Simply, this system is based on the reaction of ferrous iron with dioxygen in a pyridine/acetic acid solvent. Owing to its high activation capacity, some related systems use hydrogen peroxide as the oxygen donor instead of dioxygen. Although extensive studies have been carried out of intermediates which have been observed by indirect methods, the oxidation mechanism and precise nature of reaction intermediates are still in question. Since the 1980's, several model oxidation systems have been devised by Barton *et al.*, and called the "Gif" and "GoAgg" series. Some of the Gif oxidation systems are summarized in Table 1.2.

Table 1.2. Some "Gif" oxidation systems[a, 60]

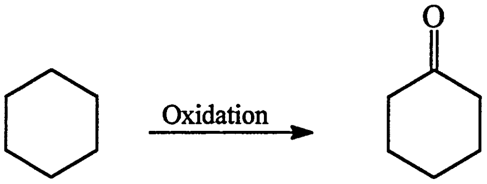
Gif III	Fe^{0}/O_2
Gif IV	Zn^{0} ; Fe^{II} (Cat.)/O_2
Gif-Orsay	e^- (Cathode) ; Fe^{II} (Cat.)/O_2
GoAgg I	Fe^{II} ; KO_2/argon
GoAgg II	Fe^{III} , H_2O_2
GoAgg III	Fe^{III} , added ligand[b]/H_2O_2
GoAgg IV	Fe^{III} ; Bu^tOOH
GoAgg V	Fe^{III} ; added ligand[b]/Bu^tOOH

a All of these systems utilize pyridine-acetic acid (10:1 v:v) as a solvent, and air is not normally excluded
b Usually picolinic acid

Until recently, as mentioned above, the solvent has invariably been a mixture of pyridine and acetic acid, in which pyridine is present in a large excess, being originally included as a simple iron coordinating species (eq. 27)

$$RH + O_2 + 2e^- + 2H^+ \xrightarrow{\text{Pyridine /HOAc/Fe(III)}} ROH + H_2O \qquad (27)$$

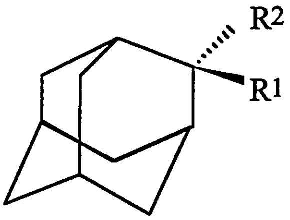
Briefly, Gif chemistry permits the conversion of saturated hydrocarbons into ketones at room temperature under nearly neutral conditions. Cyclohexane (2)was used as a model substrate and the oxidation reaction resulted predominantly in cyclohexanone (3)and not cyclohexanol (eq. 28).



(28)

(2) (3)

The catalytic oxidation of adamantane has been studied in extensively by Barton *et al.* Adamantane was selected as a suitable substrate due to its spherical and symmetric structure, possessing four tertiary and twelve secondary carbon hydrogen bonds [61].

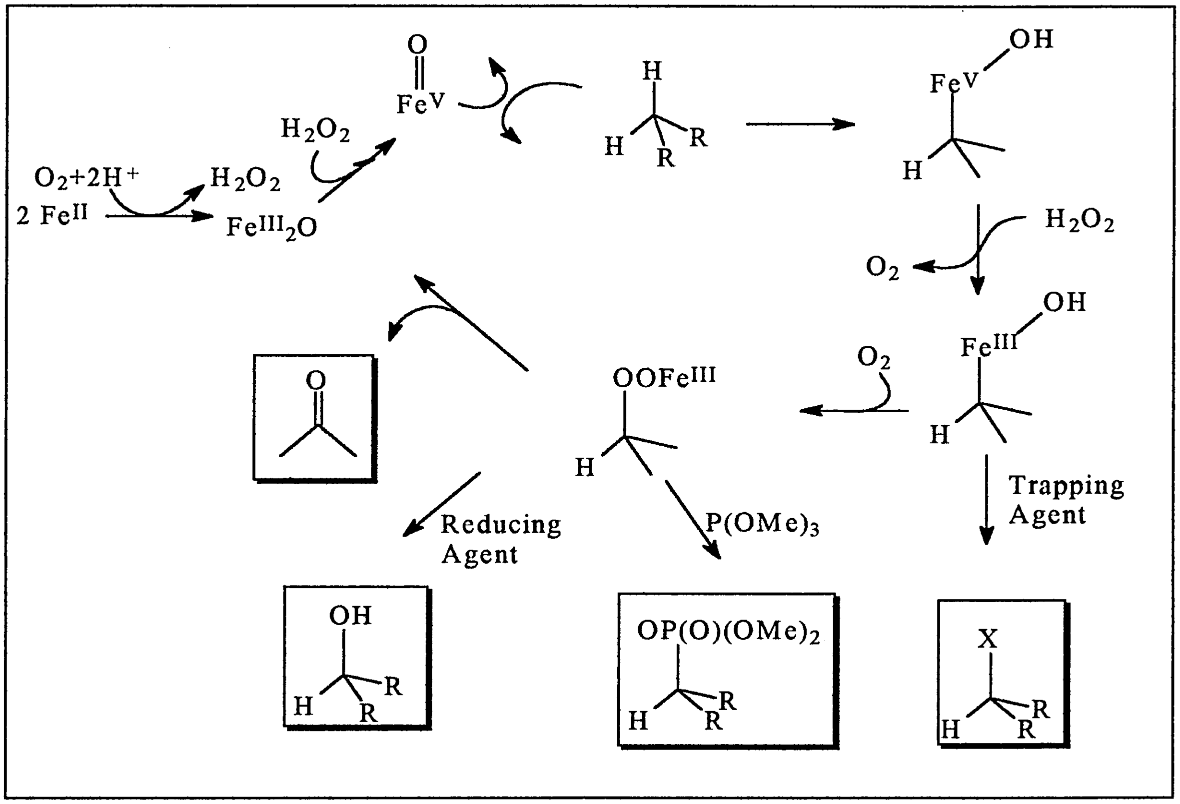


(4). R^1,R^2=H
(5). R^1,R^2=O

In early work on the Gif III systems, the iron powder was found to dissolve and the adamantane (4) was oxidized mainly to adamantanone (5). Further work, developing the Gif III system, led to an increase in the yield of ketone from 10 to 30 %.

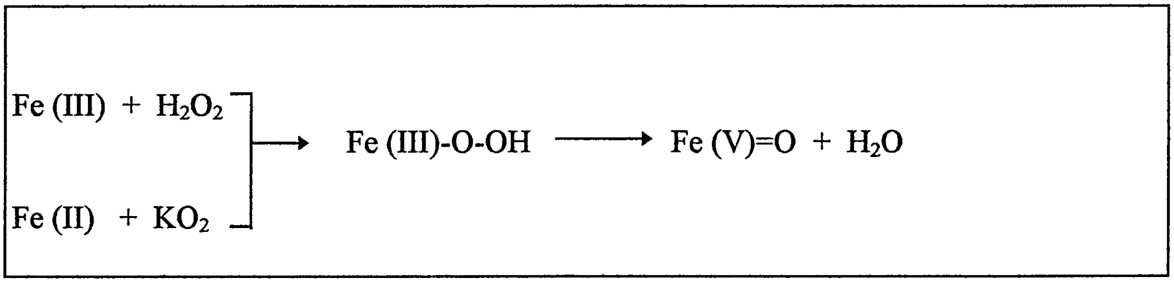
As suggested by Barton *et al.*, the formation of an alkylhydroperoxide (ROOH) occurs rather than the involvement of free radical processes and Gif type oxidation is selective for the secondary carbon functionalization. Several other new systems have been developed (Table 1.2) each of which differs from the others. The first of these developed by Barton *et al.* was GoAggI. In this, a combination of Fe(II) and superoxide (as KO_2) in pyridine/acetic acid under argon atmosphere result in the formation of Gif type intermediates. When hydrogen peroxide was used as the oxidant instead of oxygen, hydrocarbon activation was increased from 30 % (GoAgg I) to 91 % (GoAgg II). In addition, the reaction proceeded smoothly in a homogenous solution, this resulting in a more simple mechanism. It was found that catalytic amounts of picolinic acid, as a catalyst, also decreased the reaction half time, and this system is called GoAgg III (GoAgg II plus a ligand, generally picolinic acid). The mechanism of oxidation occurring under Gif and related conditions is thought to proceed by the formation of an alkylhydroperoxide and a catalytic cycle is thought to be involved. The reaction pathway shown in Scheme 1.5 was proposed for GoAgg II reactions and the ligands around the iron atom have been omitted for clarity [62].

Scheme 1.5.



The formation of a Fe^{V}=O species in the reaction between Fe (III) salts and hydrogen peroxide has been suggested as arising via the iron-containing hydroperoxide[63] and it is given in Scheme 1.6.

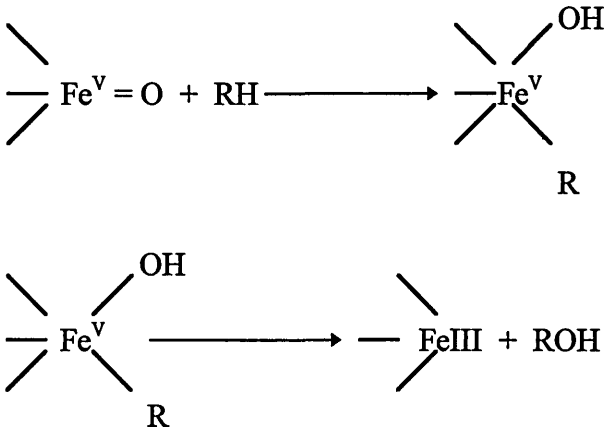
Scheme 1.6.



$$\left.\begin{array}{l}\text{Fe (III)} + H_2O_2 \\ \text{Fe (II)} + KO_2\end{array}\right] \longrightarrow \text{Fe (III)-O-OH} \longrightarrow \text{Fe (V)=O} + H_2O$$

This intermediate is similar to the high-oxidation-state iron species believed to be involved in the functioning of cytochrome P-450. The Gif mechanism, which is shown in Scheme 1.5, does not involve the reaction of oxygen with ferrous species in any of the important mechanistic steps. Molecular oxygen does oxidize the Fe(II) precatalyst to a (μ-oxo) diiron(III) compound and hydrogen peroxide. The global mechanism depends on the formation of an iron(V)-oxo species which inserts into the C-H bond of the substrate; subsequently, oxygen transfer to carbon leads to the products. These essential features are outlined in Scheme 1.7.

Scheme 1.7.



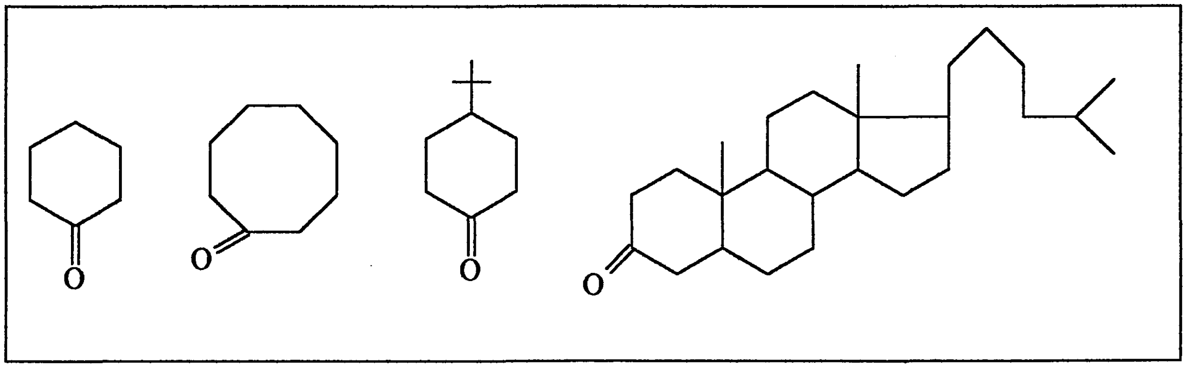
(29)

(30)

The possible involvement of the iron-oxo mechanism was extensively studied by Barton *et al.* and it was firmly supported by this group [64-71]. Barton *et al.* continued with the study of the oxidation of saturated hydrocarbons using different catalytic systems; e.g. copper-containing catalysts, rather than iron(III) systems [72, 73]. When the oxidation products were compared between iron and copper catalysed systems, under the same conditions, it was clear that the Gif type reaction products were different, depending on the iron and copper based systems used. This is also a good evidence for a non-radical reaction pathway, indicating that Gif type reactivity is metal-dependent, the nature of the metal determining the reactivity of the first reaction intermediate [73].

In their later work, Barton's group considered another strong oxidizing reagent, t-butyl hydroperoxide (TBHP) under Gif conditions. Usually the reaction of TBHP is more efficient for the oxidation of benzylic methylene groups under Fe(III)-TBHP and Fe(III)-TBHP-PA (picolinic acid as ligand) conditions [74]. The oxidation of allylic methylene groups under the same conditions resulted in the formation of α- and γ-ketonization products [75]. Studies of the oxidation of alcohols employing t-butyl hydroperoxide and an Fe(III) catalyst gave the corresponding ketones shown in Figure 1.2 in 91.7, 78.8, 85.1 and 78.5 % yields respectively .

Figure 1.2. Ketones obtained from corresponding alcohols in the Go Agg IV system.



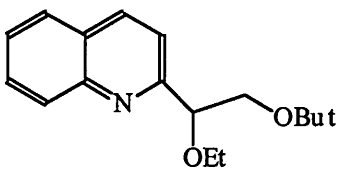
The oxidation of alcohols to the corresponding carbonyl compounds by employing high-valent metal complexes [77] is well known. The mechanistic pathway of alcohol oxidation under Fe(III)/TBHP conditions was therefore assumed to take place from a high-valent iron species (formally Fe^V=O). This high-valent Fe(V) oxenoid species subsequently reacts with the alcohol before collapsing to the final carbonyl compounds with the reduction of the iron, regenerating Fe(III).

Minisci *et al.* have suggested a new free radical synthesis, developed by using Gif-Barton conditions, involving the trapping of t-BuO$^\bullet$ radicals with electron-rich alkenes (vinylether, styrene, α-methyl styrene) and acetaldehyde [78]. Their early results indicated that not only alkyl radicals, but also t- BuO$^\bullet$ radicals were formed from t-BuOOH. This radical formation was proved by trapping the methyl radical derived from β-scission. This has been interpreted by this group in terms of a well-established mechanism involving ligand-transfer oxidation of cyclohexyl radicals [79]. Cyclohexyl radicals from cyclohexane oxidation, as well as methyl radicals from butoxyl fragmentation were trapped as alkyl quinolines when quinoline was added as a radical trap, but this conclusion was not adequate for a full explanation of the formation of the t-BuO$^\bullet$ radical because of the small quantity of the trapped radical detected, and the involvement of the solvent. New strong evidence of the involvement of t-BuO$^\bullet$ radicals was provided by trapping the t-BuO$^\bullet$ radicals with the electron rich alkenes as the trapping agent as mentioned above.

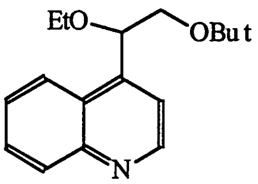
$$C_6H_{12} + t\text{-}BuO^{\bullet} \longrightarrow C_6H_{11}^{\bullet} + t\text{-}BuOH \quad (31)$$

$$C_6H_{11}^{\bullet} + Fe(III){-}Cl \longrightarrow C_6H_{11}Cl + Fe(II) \quad (32)$$

There is a strong evidence that the cyclohexyl radical is formed by hydrogen abstraction from cyclohexane by t-BuO$^{\bullet}$ (eq. 31) in the presence of halide ions (as an iron(III) complex) and chlorine is transferred from the complex to the cyclohexyl radical (eq. 32). When ethylvinyl ether was made to react under Gif conditions in the presence of quinoline and in the absence of halide ions, the two isomeric compounds **(6A)** and **(6B)** were formed.



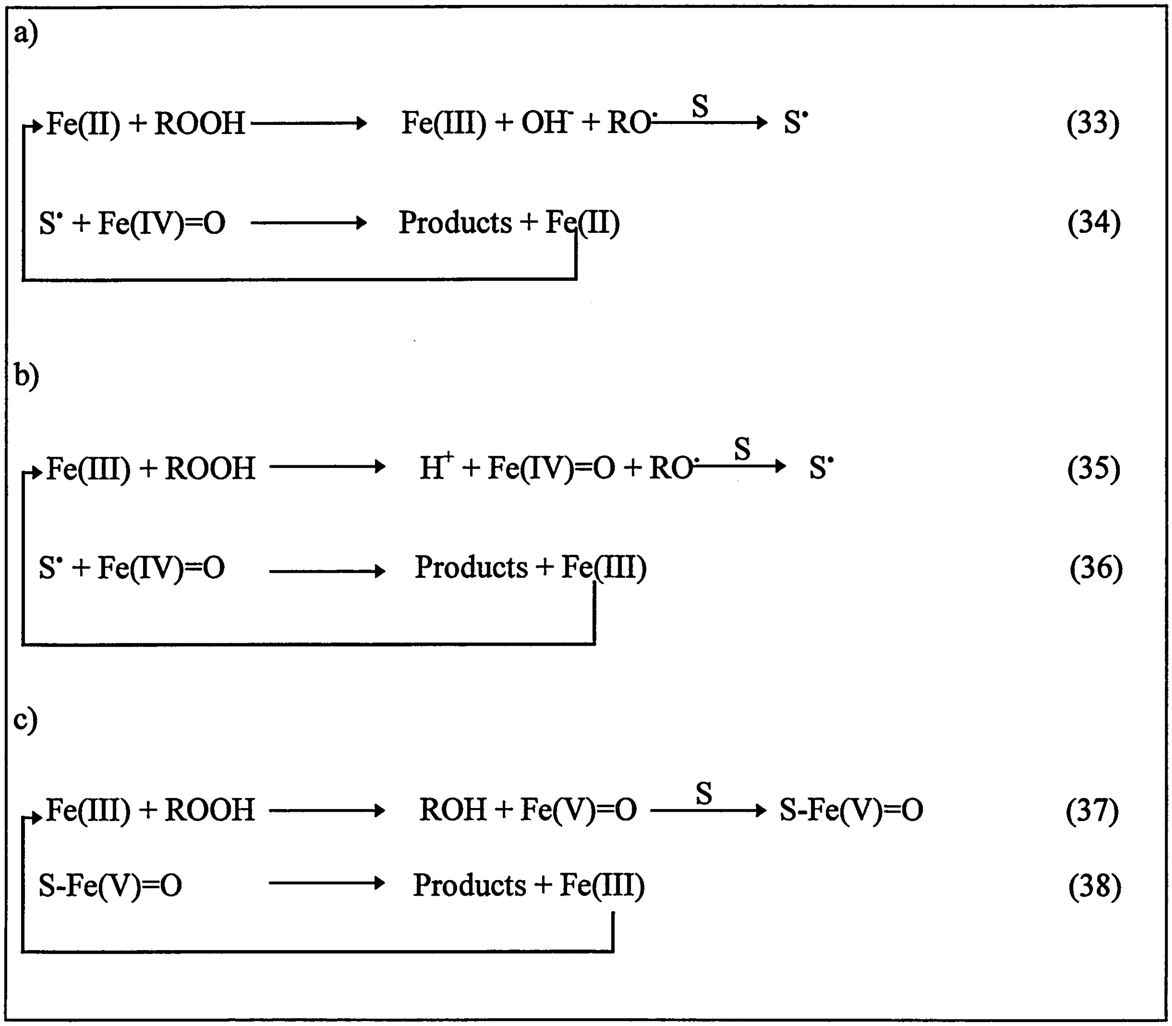
(6A)



(6B)

As a result of all these studies it was suggested that three different redox chains can be envisaged (Scheme 1.8., S=Substrate). Although there is strong evidence that free radicals, initiating the chain of 1.8a, are formed under Gif conditions, investigations of the reactions depicted in 1.8b and 1.8c are still in progress.

Scheme 1.8.



a)

$$\mathrm{Fe(II) + ROOH \longrightarrow Fe(III) + OH^{-} + RO^{\bullet} \xrightarrow{S} S^{\bullet}} \tag{33}$$

$$\mathrm{S^{\bullet} + Fe(IV){=}O \longrightarrow Products + Fe(II)} \tag{34}$$

b)

$$\mathrm{Fe(III) + ROOH \longrightarrow H^{+} + Fe(IV){=}O + RO^{\bullet} \xrightarrow{S} S^{\bullet}} \tag{35}$$

$$\mathrm{S^{\bullet} + Fe(IV){=}O \longrightarrow Products + Fe(III)} \tag{36}$$

c)

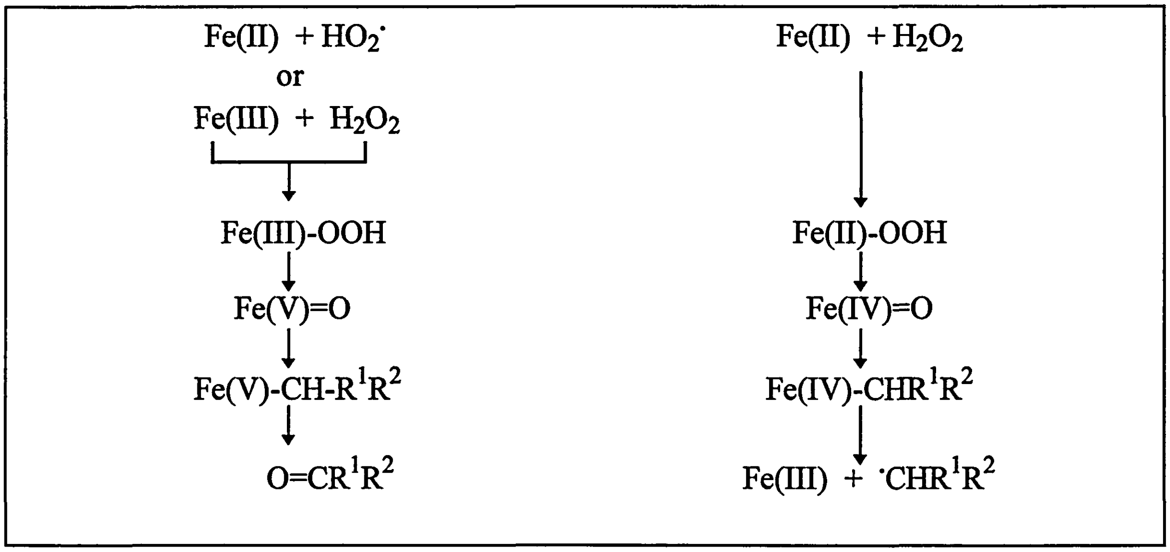
$$\mathrm{Fe(III) + ROOH \longrightarrow ROH + Fe(V){=}O \xrightarrow{S} S\text{-}Fe(V){=}O} \tag{37}$$

$$\mathrm{S\text{-}Fe(V){=}O \longrightarrow Products + Fe(III)} \tag{38}$$

Minisci's mechanistic proposals, which depend essentially upon iron(II)-promoted decomposition of hydroperoxide, led Barton *et al.* to investigate involvement of the *t*-butoxyl radicals in the Gif and related systems and it has now been accepted that hydrocarbon activation in the Fe(II) or Fe(III)/t-BuOOH systems does involve *t*-butoxyl radicals.

In Gif chemistry, Barton *et al.* postulated two different reaction pathways which are shown in Scheme 1.9 to explain the reaction intermediates

Scheme 1.9.



Both routes afford smilar Fe(III)-OOH and Fe(II)-OOH species following intermediate Fe(IV and V) oxenoid species which then react with a saturated hydrocarbon ($CH_2R^1R^2$). Although the Fe(III)-hydrogen peroxide system results in the formation of ketones selectively, showing preferred insertion into secondary C-H bonds, the Fe(II)-hydrogen peroxide system forms Fe(IV)-CHR^1R^2 species which rapidly break down to Fe(III) and a carbon radical. Scheme 1.9, distinguishes two manifolds: Fe(III)-Fe(V), the non-radical producing manifold and Fe(II)-Fe(IV), the radical manifold [80-87]. All recent papers deal with the involvement of these two manifolds. The formation of alkyl chlorides was shown to be derived from an Fe(II)-Fe(IV) manifold and is distinct from the usual ketonization process (Gif chemistry) produced by an Fe(III)-Fe(V) manifold and the importance of a carboxylic acid (such as picolinic acid) for alkane activation was highlighted [84]. A comparison was made of electrochemical oxidation of cyclohexane in the Fe(II)-Fe(IV) and Fe(III)-Fe(V) manifolds [87a]. In the first manifold, the presence of chloride ion diverts, by radical chemistry, ketone formation to cyclohexyl chloride formation. In contrast, the second manifold occurs with the formation of only cyclohexanone by a non-radical pathway.

A major reappraisal of Gif chemistry was recently proposed by Perkins[87b] who has argued that, contrary to the views of Barton *et al.*, many of the Gif and related systems can be interpreted on the basis of a significant involvement of free radicals. Barton [80] has replied to these arguments, and defended his point of view. However, in their most recent papers, Barton and his group seem to be changing their views in favour of the significant involvement of free radicals.

1.3.3. Photocatalytic Oxidations

Solar energy is a renewable energy form; cost effective, completely free, and which can be used directly to oxidise hazardous organic chemicals to carbon dioxide, water and simple mineral acids. Although a few compounds can undergo direct reactions when they are exposed to light, a wide range of other organic compounds can be destroyed in the photochemical processes mediated by certain organic dyes, photo-Fenton's reagents or photoactive semiconductors [88]. Light can have a dramatic effect on a molecule. During a photocatalytic process, light activates a photocatalyst and establishes a redox environment in the water. When a molecule absorbs light, its ground state electrons achieve an electronically excited state which is both a better oxidizing and a better reducing agent than the ground state counterpart. Electron transfer processes can generate very reactive radicals ($O_2^{\cdot -}$) in the aqueous medium. These active species break down any organic pollutants to harmless by-products. A semiconductor photocatalyst absorbs impinging photons and generates oxidation sites on its surface leading to electron transfer and production of active species like radicals.

Photocatalytic processes can take place either in a homogenous medium containing a suitable additive, (e.g. hydrogen peroxide or ozone) or in a colloidal (heterogeneous) suspension of semiconductor particles, e.g. titanium dioxide [89]. The individual redox power of active species responsible for the oxidation of organic pollutants is given in Table 1.3.

Table1.3. Redox power of agents involved as potential intermediates in photooxidation.

Species	**Standard reduction potential vs normal hydrogen electrode***
Hydrated electrons	-2.9
Hydroxide radical, $HO^{\cdot}$	2.80
Superoxide radical, $O_2^{\cdot -}$	-0.33
Ozone, O_3	2.07
Hydrogen peroxide, H_2O_2	1.78
e^-_{CB} (TiO_2)	-0.50
h^+_{VB} (TiO_2)	2.70

* The more negative the potential, the better the species is as a reducing agent

e^-_{CB} =conductive band electrons

h^+_{VB} =positive charged holes on the surface of semiconductor

As seen from the Table 1.3, combination of light (usually UV) with a strong oxidant can achieve complete destruction of waste chemicals. Although light or chemical oxidant alone (hydrogen peroxide, ozone) produces partial destruction of contaminant, the simultaneous use of light and an oxidant (ozone, hydrogen peroxide or molecular oxygen with photocatalyst) has often been shown to yield complete oxidation of organic carbon to carbon dioxide. These techniques can be classified as UV/hydrogen peroxide; UV/ozone and UV/titanium dioxide. UV/hydrogen peroxide oxidation involves the single step dissociation of hydrogen peroxide to form two hydroxyl radicals ($OH^{\cdot}$). The reactive species behaves in the same manner as Fenton's reagent does. The various reactions which occur during UV/hydrogen peroxide oxidation are as follows [2];

$$H_2O_2 \xrightarrow{UV} 2HO^{\cdot} \quad (39)$$

$$H_2O_2 \longrightarrow HOO^{-} + H^{+} \quad (40)$$

$$HO^{\cdot} + H_2O_2 \longrightarrow HOO^{\cdot} + H_2O \quad (41)$$

$$HO^{\cdot} + HOO^{-} \longrightarrow HOO^{\cdot} + OH^{-} \quad (42)$$

$$2HOO^{\cdot} \longrightarrow H_2O_2 + O_2 \quad (43)$$

$$2HO^{\cdot} \longrightarrow H_2O_2 \quad (44)$$

$$HOO^{\cdot} + HO^{\cdot} \longrightarrow H_2O + O_2 \quad (45)$$

$$RH + HO^{\cdot} \longrightarrow H_2O + R^{\cdot} \dashrightarrow \text{Further oxidation} \quad (46)$$

As shown in Table 1.4, various organic compounds were catalytically destroyed in laboratory and field studies [88].

Table 1.4. Examples of photocatalytically degradable organic compounds.

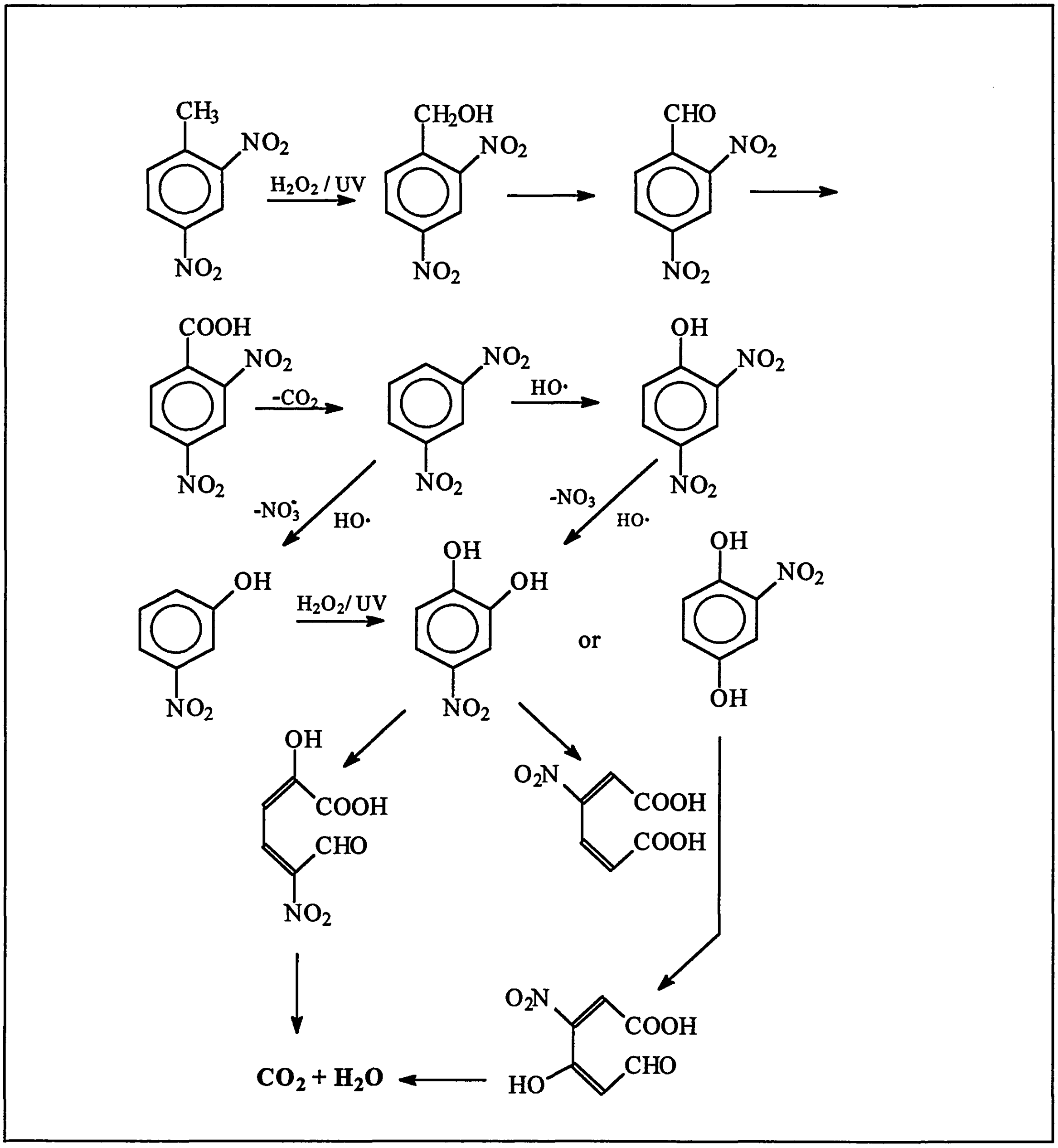
Alcohols	Aldehydes
Carboxylic acids	Ketones
Amines	Thioethers
Mercaptans	Dioxins
Herbicides	Surfactants
Polychlorinated biphenyls	Pesticides (DDT, Lindane)
Chlorinated hydrocarbons	Solvents
Fuel constituents	

Solar photocatalytic oxidation has been used in several industrial cleaning process, as well as for detoxification of toxic organic compounds, and also of offensive compounds, which provide bad color, taste and odour problems. Detailed applications of this photocatalytic process have been extensively rewieved by Ventakandri [2]. Chlorinated hydrocarbons were the most studied example of oxidation by means of UV/hydrogen peroxide catalysis, and the complete dechlorination of several chlorinated aromatic compounds was demonstrated, again with removal efficiencies of 85-100 % in the case of mono-, di-, and trichlorophenols in a three hour reaction period.

The photocatalytic oxidation of nitro-containing aromatic compounds was also studied and the mechanism for the oxidation of 2,4 dinitrotoluene by using UV/hydrogen peroxide oxidation is outlined in Figure 1.3 [2].

Early studies involved the use of a low pressure mercury lamp but recent modifications involve high intensity UV lamps which possess higher energy outputs and higher electrical efficiencies with a lower cost, broad band spectrum output and increased efficiency. Advances in UV lamp technology, like the addition of dopants, makes this environmentally friendly process compatible for all kinds of organics present. UV/hydrogen peroxide systems have been used primarily for treating low levels of pollutants in the ppm range and this method may not be applicable for the treatment of high-strength wastes.

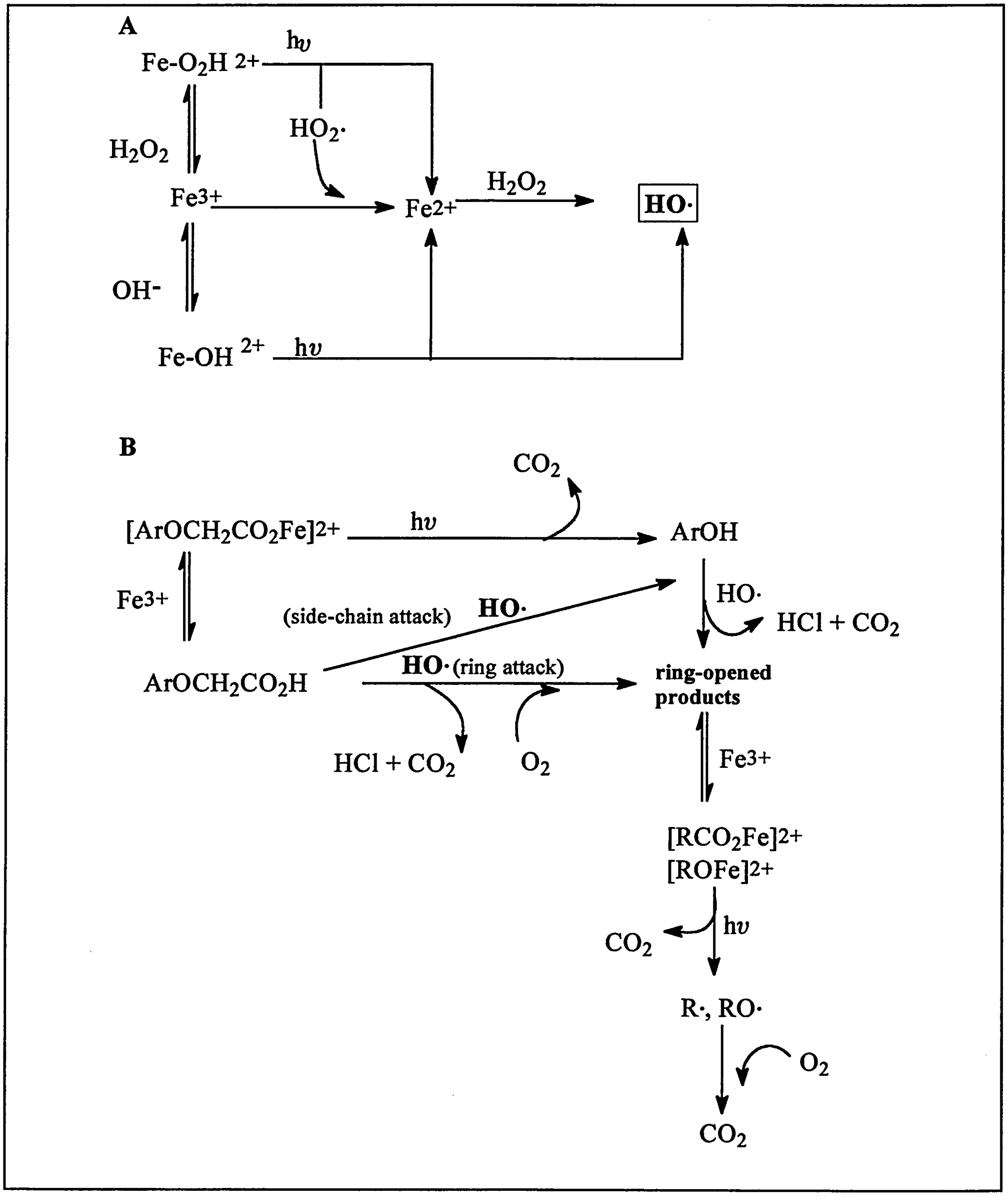
Figure 1.3. Pathways in the UV/ H_2O_2 oxidation of 2,4-dinitrotoluene.



The degradation capacity of the UV/hydrogen peroxide system can be increased by combining it with another hydroxyl radical generating system like Fenton's reagent or ozone and some of its applications are summarised below.

As mentioned before, Fenton's reagent produces the hydroxyl radical (eq. 8). It is now known that the oxidizing power of the Fenton-type systems can be greatly enhanced by irradiation with UV or UV/visible light [90-98]. The effect of metal ions on the hydroxylation of toluene, nitrobenzene, benzonitrile, anisole and fluorobenzene was extensively studied by Eberhardt [90-92] in the presence of Fe(II), Fe(III), Cu(II) and Cr(II) containing salts. Although in the radiation-induced hydroxylation of toluene, usually only a small fraction of the hydroxyl radicals are converted to cresol, the formation of cresol is increased significantly in the presence of metal ions [91]. Photocatalytic degradation of 2,4-D (2,4-dichlorophenoxyacetic acid) and 2, 4, 5-T(2,4,5-trichlorophenoxyacetic) acid was studied by Pignatello [94] by using Fe(II)/hydrogen peroxide and Fe(III)/hydrogen peroxide systems and dechlorination was almost complete in less than one hour's illumination and with 70 % conversion to carbon dioxide. The corresponding polychlorophenol was a transient intermediate. The mechanism of hydroxyl radical formation and the chlorophenoxy herbicide oxidation pathway was suggested by Sun *et al.* and shown in Scheme 1.10 [95].

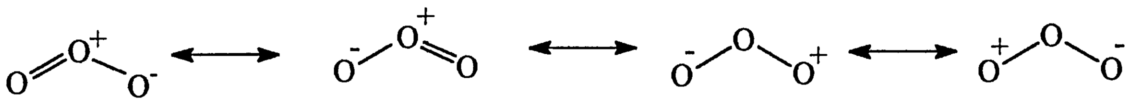
Scheme 1.10.



Photochemical degradation of cyclic organic contaminants in water from the photo-Fenton reaction has been studied and the oxidation of phenol, hydroquinone, 4-chlorophenol and

4-chloroaniline was achieved in yields of 92% to 98% after 5 hours of illumination with a 250 W tungsten lamp [96]. A total organic carbon reduction of 76% and 74% respectively has been achieved in the oxidation of 3- and 4-nitroaniline in this way. Another study showed that irradiation of an aqueous solution of 4-chlorophenols with light (λ>320 nm) in the presence of hydrogen peroxide and Fe(II) accelerated the degradation rate significantly [98]. Long hydrocarbon chain compounds e.g. detergents, together with herbicides and pesticides, have also been examined in photocatalysis. The complete decomposition of 2,4,5-T and 2,4,5-trichlorophenol (TCP) to free chloride ions in the final state (reaction time of 30-90 min. and ~100% recovery of initial chlorine) was demonstrated [99].

Ozone-containing photocatalytic processes have been established over recent years. Commercial applications of UV, hydrogen peroxide and ozone processes are increasingly being used in the treatment of a variety of industrial waste water and contaminated waters [100]. Ozone is particularly effective for disinfection, odour and colour removal, and the destruction of cyanides and toxic organic compounds in water. Ozone is an allotropic form of oxygen, whose structure has been explained as a resonance hybrid of the following four canonical forms (**7-10**) [101].



(7) **(8)** **(9)** **(10)**

The reaction of ozone depends strongly on *p*H, temperature and the rate of ozone decomposition. At lower *p*H values, the ozone molecule reacts directly with organic molecules. At higher *p*H values, ozone decomposes to form hydroxyl radical intermediates. Hydroxyl radicals play an important role in the ozonation oxidation process, under certain conditions. Although ozone is more expensive to generate and more difficult to handle than hydrogen peroxide, it has some advantages. Thus, for example, reactions involving ozone are self-propagating, so a stoichiometric amount of ozone is not needed. The primary steps in the UV/ozone process include formation of singlet oxygen atoms which generate additional hydrogen peroxide in contact with water (eq. 47 and 48) [89].

$$O_3 \xrightarrow{h\gamma} O(^1D) + O_2 \qquad (47)$$

$$O(^1D) + H_2O \longrightarrow H_2O_2 \qquad (48)$$

This additional hydrogen peroxide may prove to be a bonus in the UV/ozone process. Several pesticides (pentachlorophenol, malathion, Baygon, DDT and Vapam), and other systems , e.g. TNT, halogenated aliphatic compounds and aromatics have been oxidized by UV/ozone systems [2]. This system can be combined with hydrogen peroxide to tackle complex wastes, providing several mechanisms for generating oxidative radicals. In some cases, the UV/ozone system is more effective than the UV/hydrogen peroxide system, e.g. for the oxidation of 4-chloronitrobenzene and nitrobenzene, due to the higher rate of hydroxyl radical generation by ozone photodecomposition.

Oxidative degradation of pollutant organic compounds by heterogeneous photocatalysis using semiconductor particles, such as titanium dioxide has been the main subject of numerous recent studies. Heterogeneous photocatalysis is a process in which the illumination of an oxide semi-conductor, usually anatase or rutile, produces photoexcited electrons (e^-) and positive charged holes (h^+). The photoexcitation of the semi-conductor particles by UV light changes the energy state of the electrons from the valence band of the solid to the conduction band [102]. When a solution containing suspended n-type semi-conductor particles is properly illuminated with UV light, the solid surface is photoexcited, because the energy of the electrons may jump from the valence band of the solid to the conduction band. General equations for titanium dioxide in aqueous systems and the mechanism of the titanium dioxide-photocatalyzed oxidative degradation are outlined below (eq. 49-55):

$$TiO_2 + h\gamma \longrightarrow h^+_{VB} + e^-_{CB} \qquad (49)$$

$$h^+_{VB} + e^-_{CB} \longrightarrow \text{heat} \qquad \text{(recombination)} \qquad (50)$$

$$TiO_2h^+_{VB} + \text{compound} \longrightarrow \text{products}_{ox} \qquad (51)$$

$$TiO_2h^+_{VB} + H_2O_{ad} \longrightarrow TiO_2 + HO^{\cdot}_{ad} + H^+ \qquad (52)$$

$$TiO_2h^+_{VB} + HO^-_{ad} \longrightarrow HO^{\cdot}_{ad} + TiO_2 \qquad (53)$$

$$TiO_2e^-_{CB} + O_2 \longrightarrow O_2^{\cdot-} + H^+ \longrightarrow HO_2^{\cdot} \qquad (54)$$

$$HO^{\cdot}_{ad} + \text{compound} \longrightarrow \text{product}_{ox} \qquad (55)$$

ad.=adsorbed species on the titanium dioxide surface

e^-_{CB}= conductive band electrons

h^+_{VB}= positive charged holes on the titanium dioxide surface

When titanium dioxide is irradiated by UV (λ<390 nm), it generates h^+_{VB}/e^-_{CB} pairs and these species migrate to the solid surface. The surface of the semi-conductor becomes so strongly oxidizing that it can initiate the oxidation of organic pollutants at the solid-liquid surface in water by converting dissolved dioxygen (eq. 54), water (eq. 52) or hydroxyl$^-$ ions (eq. 53) to hydroxyl radicals and other radicals, such as $O_2^{\cdot-}$ and $HO_2^{\cdot}$. The formation of hydroxyl radicals in aqueous titanium dioxide suspension was proved by EPR measurements [103]. Although there is supportive evidence about the formation of hydroxyl radicals, the controversy still exists as to whether h^+_{VB} or $HO^{\cdot}$ radicals are responsible for the oxidation process as the dominant species. It is known that oxidation by holes occurs because trichloroacetic acid and oxalic acid were observed as intermediates during the oxidation of chlorinated ethanes in the presence of hydroxyl radicals (UV/titanium dioxide system) [104]. Studies on titanium dioxide-assisted photodegradation of pollutants to inorganic products were extensively reviewed by Venkatadri and Peters [2]. All kinetic studies showed that titanium dioxide-assisted photooxidation of pollutants follows Langmuir-Hinshelwood kinetics where the initial rate of the disappearance of pollutant can be described in terms of its concentration and its absorption and reaction characteristics as follows [105]:

$$\frac{-dC}{dt} = \frac{k\,KC}{1 + KC} \tag{56}$$

C= Concentration of pollutant in solution
k= rate constant
K= Absorption equilibrium constant of the pollutant on the titanium dioxide surface.

The effectiveness of the titanium dioxide-assisted photodegradation process largely depends on the nature of the substrate. For example, while shorter illumination times are required (20-40 min.) for the complete oxidation of colored compounds, 24 hours are required for chlorophenols. Also the formation of different intermediate products revealed differences between direct and titanium dioxide-assisted photolysis. Direct photolysis of 4-chlorophenol at 290 nm or longer wavelength yielded twelve primary intermediates. On the other hand, only six intermediate products were observed when titanium dioxide was present in the same system [106]. The rate of degradation is also influenced by several other factors, such as *p*H, titanium dioxide concentration, temperature, quantity of dissolved oxygen, light intensity and type, and the presence of dissolved anions and cations [107]. All studies, in particular, suggested that the optimum titanium dioxide concentration for oxidation is 2.0 g/L, since a higher titanium dioxide concentration could cause lower light penetration resulting in lower oxidation rates. The optimization of all factors rigorously depends on the chemical character of the substrate. The effect of loading and thermal pretreatment of the semi-conductor catalyst as well as the influence of added chloride ions have been examined by Barbeni *et al.* in the photodegradation of 2,4,5-trichlorophenoxy acetic acid and 2,4,5-trichlorophenol on titanium dioxide [99]. It was shown that pretreatment of titanium dioxide, such as preheating or loading with platinium, either decreased or did not affect the rate of photodegradation, respectively. Conversely, it was also shown that loading titanium dioxide with platinum increased the generation of carbon dioxide, by almost two fold, in the photocatalytic oxidation of benzene (0.38 mmol carbon dioxide per mmol benzene was generated with anatase and 0.72 mmol carbon dioxide was generated with 10 % platinizated anatase). In the oxygen-saturated system the carbon dioxide concentration rose up to 1.85 mmol per mmol of benzene after 40 hours illumination in the titanium dioxide and 10% platinium system. It is clear that platinized anatase has a higher efficiency than plain anatase powder [108]. Furthermore the catalytic activity of the titanium dioxide in the degradation of urea was increased by loading silver (at 1.0 % w/w proportion rate) and under these conditions, 83 % of this compound was destroyed, compared with only 16 % using pure anatase [109]. An extensive comparison was made in Mathews and McEvoy's study involving the photocatalytic degradation of phenol and the following results were observed under identical illumination conditions [110]:-

a) a free suspension of titanium dioxide is ca. 2.6 times more effective than an immobilized catalyst, but this difference is smaller when higher waste flow rates were used;
b) direct sunlight and UV light exhibited a similar degradation effect;

c) varying the *p*H of the solution between 3.5 and 8.5 did not have a dramatic effect on the degradation.

Photodegradation has also been studied with other semi-conductors, such as ZnO, CdS, WO_3 and SnO_2, but titanium dioxide seems to be the most efficient [111] and reusable several times without any significant change in the activity [112].

Solar energy is a renewable, cheap, and excellent resource for the future. Other waste treatment techniques, such as adsorption and air stripping only transfer the contaminants from water to the adsorbents or air and further treatments are required. However, photocatalytic decontamination achieves complete degradation on a laboratory and small plant scale for dilute solutions (e.g. 10^{-5}-10^{-6} M) and the low cost makes this process very attractive. New process designs and further developments of photochemical technologies will be great steps forward for this environmentally friendly cleaning up process.

1.4. Purpose of the Present Study

The wet air oxidation (WAO) of alkyl pyridines commonly found in effluents from coking plants, involving the application of high pressure and temperature for the destruction of organic wastes, was the subject of a recent study [23]. As an extension of this study, it was thought that sulphur-containing heterocyclic compounds require investigation under these conditions, since these compounds are also found in effluent from coal and petrochemical plants. The aim is to achieve the destructive oxidation of sulphur-containing heterocyclic compounds and also to explore the selective oxidative functionalisation of these systems using metal ion-hydrogen peroxide reagents. Therefore, thiophene and its derivatives were chosen, since thiophene itself is the simplest aromatic sulphur heterocycle and its simple alkyl derivatives are readily accessible.

These compounds have been of great interest in the last decade following the realization of the deleterious effect that sulphur dioxide formed by burning of, e.g. organically bound sulphur, can have in the form of acidic rain. Polycyclic aromatic sulphur heterocycles (PASH) are one of the major classes of by-products in coal and petrochemical feedstock conversions, and studies of the oxidation of simple thiophenes will be of value in developing treatment processes for more complex systems. The oxidation of thiophenes has been investigated by several researchers. Iovel and Shymantskaya [113] found that oxidation of 2-methylthiophene with molecular oxygen on a vanadium-molybdenum oxide catalyst gave thiophene-2-aldehyde, thiomaleic anhydride and maleic anhydride. Again oxidative coupling of thiophene on palladium catalyst was studied by Kozhevnicov and Matweev [114], and bithiophenes were found to be the main products.

As far as can be ascertained from a survey of the literature, only a few studies have been reported on the oxidation of thiophenes and related systems with hydrogen peroxide. Gvozdetskaya [115] show that oxidation rates increased in the order pyrrole < cyclopenta diene< furan < thiophene, and also studied the effect of the nature and position of substituents. Although the parent ring system is fairly stable to oxidation, substituted thiophenes can be oxidised more easily. The oxidation of 3-methylthiophene was found to be considerably slower than that of 2-methylthiophene and the oxidation products are oxo-acids, diacids and other ring decomposition products. Another study was carried out by Jennings [116] in which the rate of oxidation of 2-methylthiophene with hydrogen peroxide was investigated, but no information was given on the nature of the products formed. Thus, there is a need for further investigations on the oxidation of thiophene and its derivatives, with particular reference to oxidative destruction and the identification of the oxidation products. A deeper understanding of the reaction mechanisms and the optimization conditions would be useful for waste treatment. In the present work, the oxidation of thiophenes with oxygen-containing compounds and catalyst systems, e.g. Fenton chemistry, Gif chemistry and titanium dioxide-assisted photocatalytic oxidation has been studied.

The aims of this study can be summarised as follows:

1.) To investigate the course of oxidation of thiophene, and 2- and 3-methylthiophenes, and benzo-[b]-thiophene under Fenton-related and Fenton-like oxidation conditions.

2.) To investigate the kinetics associated with the oxidation of methyl-substituted thiophenes using Fenton-type reagents as the oxidation system.

3.) To investigate new oxidation methods, such as the titanium dioxide-assisted photocatalytic oxidation process which involves use of natural sunlight.

4.) To gain a better understanding of the possible involvement of free radical species in such oxidation reactions.

5.) Assess the importance of the metal ion in such reactions.

In chapter 2, the study of the oxidation products derived from the oxidation of simple thiophenes with various metal ion-hydrogen peroxide systems is reported.

Chapter 3 reports quantitative studies of some of these reactions.

The synthesis of some oxidation products, not readily available from commercial supplies, is discussed in chapter 4. Literature references are listed at the end of each chapter.

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CHAPTER 2

THE FENTON-RELATED, FENTON-LIKE AND PHOTO-CATALYSED OXIDATIONS OF THIOPHENES AT AMBIENT TEMPERATURE AND ATMOSPHERIC PRESSURE

CHAPTER 2

THE FENTON-RELATED, FENTON-LIKE AND PHOTO-CATALYSED OXIDATIONS OF THIOPHENES AT AMBIENT TEMPERATURE AND ATMOSPHERIC PRESSURE

The catalytic oxidative degradation of thiophene and 2- and 3-methylthiophene has been studied at room temperature and atmospheric pressure using various catalytic systems. The catalyst systems were all metal ion-containing and were related to the Fenton oxidation system. The use of metal ions other than Fe(II) may change the oxidation rates and the nature of the degradation products in Fenton-like oxidations. Fenton-related and Fenton-like oxidations were carried out using the general procedure described by Ito *et al.* [1] for the hydroxylation of benzene using Fenton's reagent. In this thesis, the use of the term "Fenton-related" implies a reagent system involving iron(II), iron(III) or iron(II)+copper(II) in the presence of hydrogen peroxide, and "Fenton-like" implies the use of other metal ions in combination with hydrogen peroxide. Ito *et al.* established optimum conditions for the effective formation of phenol from benzene and the conditions established were adopted in this study.

2.1. Experimental

The optimized Fenton oxidation procedures were used under conditions proposed by Ito *et al.*[1] and Morris [2]. Thiophenes are water-insoluble and would normally require a water miscible co-solvent. Therefore, the oxidation reactions of thiophene and 2- and 3-methylthiophene were carried out in acetonitrile/water, methanol/water, acetic acid/water or solely in water. Oxidation products in water were essentially the same as in methanol and acetic acid both under nitrogen atmosphere and in open systems. The reactions were found to be vigorously exothermic when an organic co-solvent was used, so oxidation reactions were carried out solely in water for quantitative scale studies. However, the use of acetonitrile as co-solvent resulted in the formation of additional products which are described individually in the results. Each catalyst system was prepared by first taking the appropriate amount of metal salt and dissolving it in dilute sulphuric acid. The thiophene (0.01 mol) was suspended in water (50 cm^3) and if necessary, a co-solvent (50 cm^3). The metal salt (0.01 mol) was added to this solution, dissolved in sulphuric acid (1 mol L^{-1}, 50 cm^3), followed by the dropwise addition of the hydrogen peroxide solution in water 27 % w/v [0.05 mol (6.15 cm^3) or 0.2 mol (24.8 cm^3)] while the reaction vessel was cooled in ice. The reactions were repeated under a nitrogen sealed system and in an open system respectively, but both systems showed the same oxidation products. Therefore, all subsequent reactions were carried out in an open system involving the same volume of solvent so that the results might be more comparable. After the addition of hydrogen peroxide solution, the reaction mixture was stirred at room temperature for varying periods of time (from 1 hour to 24 hours).

2.1.1. Catalysed Oxidation Reactions

Various catalyst systems used in this study will be discussed in this Chapter. Generally, Fenton and related oxidation of thiophenes was carried out under the above conditions in laboratory-scale reactions. Fenton-related catalyst systems comprise mixtures that have been suggested in the literature and they have been discussed in section 1.3.2.1. Additionally, other catalytic systems that have also been suggested in the literature as having potential were studied.

The catalyst systems used in this study are as follows;

Iron(II) sulphate / hydrogen peroxide
Iron (II) sulphate and Cu(II) sulphate / hydrogen peroxide
Iron(III) sulphate / hydrogen peroxide
Vanadium(IV) sulphate / hydrogen peroxide
Copper(II) sulphate / hydrogen peroxide
Copper(II) chloride / hydrogen peroxide
Copper(I) chloride / hydrogen peroxide
Titanium(III) chloride / hydrogen peroxide

All chemicals were purchased from Aldrich and Lancaster (U.K.) as analytical grade. The oxidation of each of the thiophenes was studied using each of the catalysts stated above. The results, together with the information from the literature, led to the investigation of other oxidation reactions. These included carrying out the Fenton catalysed oxidation reactions of thiophene, 2- and 3-methylthiophene and benzo-[b]-thiophene in the presence of TEMPO, a radical trap, and EDTA, a complexing agent, respectively. The Fenton oxidation of some possible reaction intermediates derived from the parent thiophenes was also studied so as to gain further information about the origin of end-products. The results of these latter reactions will be discussed in sections 2.3.3. and 2.3.4., but sample preparation and analysis were the same for all catalysed oxidation reactions considered.

As discussed in the introduction, Gif chemistry may involve the formation of high oxidation state iron complexes rather than free radicals. The oxidation of thiophenes was carried out using Fenton's reagent under Gif conditions and the results were compared with those from Fenton-related conditions, to determine whether free radical species are involved in the latter.

It is well-known that Fenton-related reagents generate powerful oxidizing species usually assumed to be hydroxyl radicals ($HO^{\cdot}$). In the present study other hydroxyl radical generating systems were explored, e.g. the titanium dioxide assisted photocatalytic oxidations of thiophenes. Although the oxidation reaction conditions are completely different, sample preparation and analysis were the same as for the above Fenton-catalysed oxidation reactions. The results of this work will be discussed in a separate section (2.3.5) in this Chapter.

2.1.2. Sample Preparation

After the reaction was completed, sample preparation involved the extraction of organic products into an organic solvent. The aqueous reaction mixture was extracted with 4x100 cm^3 of dichloromethane. The organic layers were combined and dried using magnesium sulphate, and the extract was evaporated to 2 cm^3 under reduced pressure.

The dichloromethane-insoluble polar products remaining in the aqueous phase were then isolated by removing the excess water on a rotary evaporator. The residue that then remained was extracted with methanol. A cleaning up procedure was employed for samples using microfilters which allow only organic compounds to be filtered and trap inorganic compounds thus avoiding blockage of HPLC column and LC/MS interfaces.

2.1.3. Sample Analysis

Gas chromatography (GC) techniques have some advantages as compared to the other techniques in terms of the analysis of organic mixtures and are applicable for almost all types of organic compounds. Using different types of column gives great opportunities for simple separation and analysis. Especially, capillary column technology achieves better separation for complex mixtures because of specific coating materials and the length of the column. Combined techniques, in particular gas chromatography-mass spectrometry (GC-MS), provide a means of “fingerprinting” components of a sample mixture. Since the thiophenes are volatile enough to be detected by GC, the analysis of the oxidation products generated from these precursors initially involved GC techniques using capillary column chromatography.

GC-MS and HPLC

Both the dichloromethane and methanol extracts were analysed using a capillary column gas chromatograph coupled to a mass spectrometer. The instrument used was a VG Trio 1 Mass Quadrupole Spectrometer (Manchester, U.K.) coupled to a 5890 Hewlett-Packard Gas Chromatograph (Avondale, PA, USA). The conditions used involved a ramp program and due to the polarity of the system being used, an Econo-Cap Capillary SE-54 (immobilized 5 % diphenyl, 95 % dimethylpolysiloxane) column was used. The instrument was operated under the following conditions;

Column:	30m SE-54
Carrier gas:	Helium
Temperature program 1:	40 (5 min)-250 (5 min) at 5 $^{\circ}$C min^{-1}
Temperature program 2:	30 (5 min)-250 (5 min) at 30 $^{\circ}$C min^{-1}
Injection volume:	1 mm^3 splitless
Ion source:	Electron impact (70 eV)
Source temperature:	150 μA
Scan rate:	1s scan^{-1}
Scan range:	20-500 Daltons

After detection on GC/MS, appropriate standard compounds were analysed under the same conditions or spiked into the reaction mixtures. Both retention times and mass spectral fragmentations of products were compared with those of the standards.

The High Performance Liquid Chromatography (HPLC) technique was used for the analysis of non-volatile products which may not have been detected by GC. The methanol extract did not give rise to any peak on GC. A methanol-water mixture was used as mobile phase and instrument conditions were optimized for the best detection. The conditions used in the analysis of methanol-soluble oxidation products were as follows;

Injection volume:	20 μL (fixed injection loop)
Column type:	C-18
Detector:	Philips Pye Unicam LC-UV detector
Data collection;	HP340 desk top integrator
Flow rate:	2 ml. min^{-1}
Wavelength:	254 nm
Mobile phase:	MeOH/H_2O (1:4)

The liquid chromatography-mass spectrometry (LC-MS) technique was used for the determination of the identity of sample components, but problems arose as a result of blocking of the interface between the Liquid Chromatograph and the Mass Spectrometer and also detector poisoning.

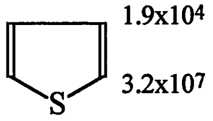
The Fenton-related and Fenton-like oxidation reactions of thiophenes considered in this Chapter mainly resulted in the complete destruction of thiophene ring when excess hydrogen peroxide was used. This shows the effectiveness of the process for the oxidative destruction of this type of substance. Reduced quantities of hydrogen peroxide were therefore employed so as to achieve better understanding of reaction pathways. In GC/MS analysis, the oxidation products that were formed in each reaction were either identified by comparison with authentic substances, or possible structures were suggested from the molecular ions and fragmentation patterns observed in their mass spectra. The observations made for each of the reactions are summarised and discussed in the subsequent sections of this Chapter.

GC temperature program 1 and the same instrument conditions were used for the investigation of these oxidation reactions and for confirmation with the authentic substances. Temperature program 2 was only used for the quantitative-scale determination which provided quicker results for hundreds of samples. Therefore, any difference noted in retention time values for the same compounds may have to be considered with reference to the precise analytical conditions used in the analysis of each of the samples.

As oxidation reactions were carried out with other oxidizing reagents, such as m-chloro perbenzoic acid, hydrogen peroxide and sodium perborate, direct comparisons could be made with oxidation products observed in each case. An extensive study was also done with a range of substituted thiophenes to investigate how substitution affects the route of the oxidation, with respect to oxidation in the ring, in the side chain or at sulphur.

2.2. The Catalysed Oxidation of Thiophenes

Fenton-related and Fenton-like oxidation of a range of thiophenes were investigated under the conditions mentioned above in details. Thiophene itself was chosen as a model compound and later its alkyl and aryl substituted derivatives were studied. The reactivity of thiophenes changes with substitution pattern. For example, oxidative degradation of 2-methylthiophene can be easier than that of 3-methyl thiophene [3]. In addition, the reactivity of the 2- and 3-positions of the thiophene ring towards electrophiles is quite different. Thus, e.g., partial rate factors (reactivities relative to benzene) for tritium exchange with trifluoroacetic acid for thiophene are as follows;



Because of this high reactivity, even mild electrophiles suffice to cause electrophilic substitution predominantly at the α-position yielding 2- (or α) substituted thiophenes [3]. It may be expected that the reaction of thiophenes with free radical species are similar to electrophilic substitution reactions.

Fenton-related oxidation products of thiophene, 2-methylthiophene, 3-methylthiophene and further oxidation of intermediate products (e.g. 5-methyl-2-hydroxythiophene, and thiophene-2-aldehyde) and benzo-[b]-thiophene are given below. The Fenton-like oxidizing systems like copper(I) copper (II), vanadium(IV) and titanium (III) will also be discussed in a separate section.

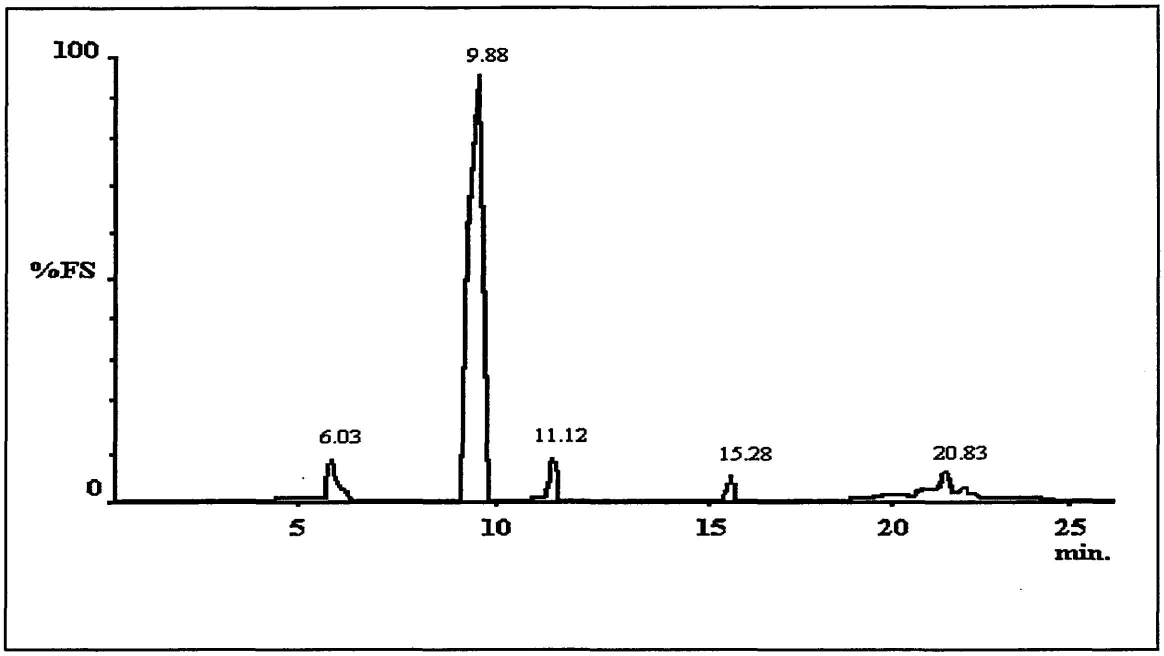
2.2.1. Fenton's reagent and Fenton-related Reagents

2.2.1.1. Thiophene

a) Analysis by GC/MS

The oxidation of thiophene **(11)** led to the formation of the hydroxylated thiophene **(12)** as major oxidation product, together with the some minor species. The gas chromatogram of the Fenton oxidation of thiophene is given in Figure 2.1.

Figure 2.1. GC chromatogram of the Fenton-catalysed oxidation of thiophene



All species formed in the oxidation have been identified by either spiking with an authentic sample, (commercially available or prepared by a synthetic method), or by deducing the structure from mass spectral and retention time (t_R) data. The resulting oxidation products which were identified by GC/MS analysis using temperature program 1 and instrument conditions given in section 2.1.3 are summarised in Table 2.1. and the possible pathway for their formation is summarised in Scheme 2.1.

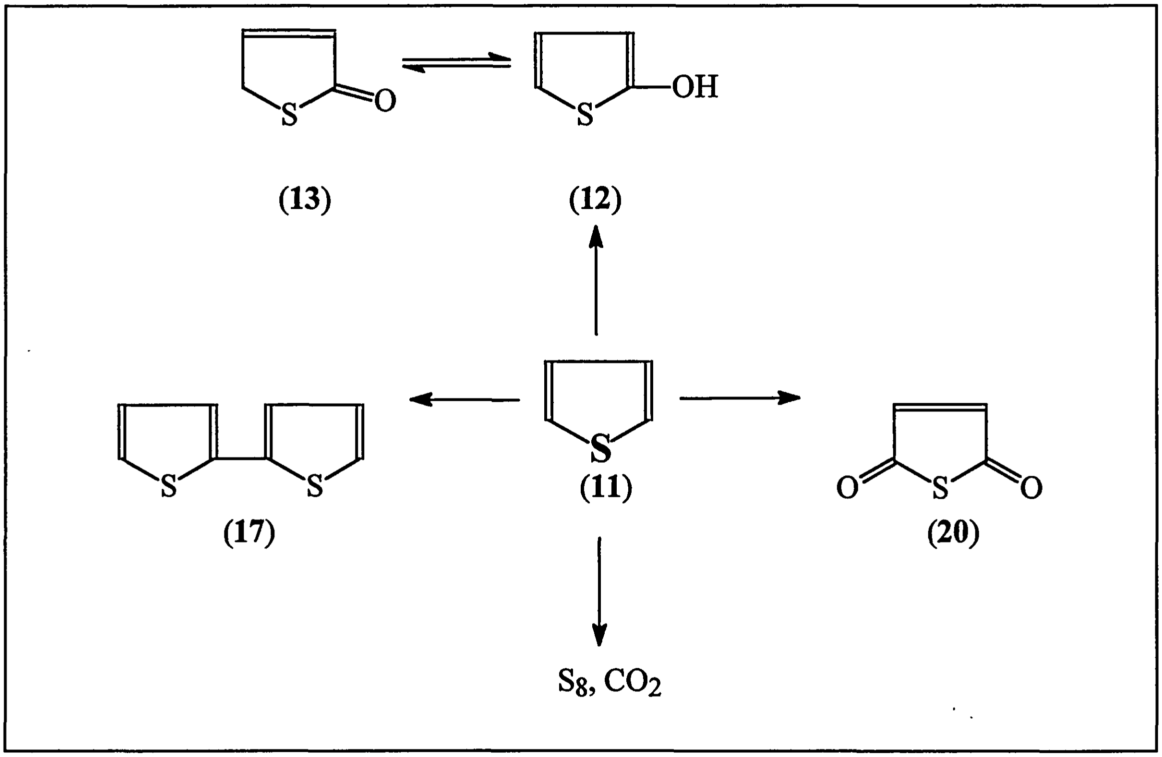
Table 2.1. Oxidation products arising from the Fenton-related oxidation of thiophene.

Comp. No	t_R 1 hr	t_R 24 hr	Apparent RMM	Solvent	Proposed structure
13	9.50	9.88	100	H_2O, CH_3COOH/H_2O $MeCN/H_2O$ $MeOH/H_2O$	(5H)-thiophen-2-one
17	-	20.83	166	H_2O, $MeCN/H_2O$	2,2'-bithiophene
20*	-	6.03	114	$MeCN/H_2O$	thiomaleic anhydride
21*	11.12	11.12	116	H_2O, $MeCN/H_2O$	unknown

Oxidation systems: $Fe(II)/H_2O_2$, $Fe(II) + Cu(II)/H_2O_2$, $Fe(III)/H_2O_2$.

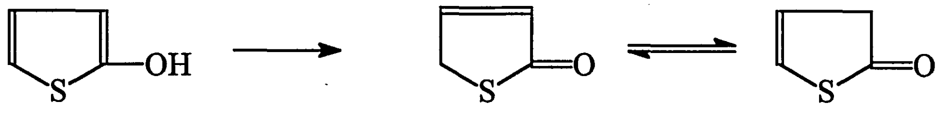
* Indicates that proposed structure has not been proved by comparison with the authentic substance.

Scheme 2.1.



It appears that allowing the reaction to continue for just over one hour takes the reaction almost to completion in that the only oxidation products observed are S_8 generated from the cleavage of heterocyclic ring and gases such as hydrogen sulphide, sulphur dioxide and carbon dioxide in all solvent systems. When more concentrated hydrogen peroxide was employed (0.2 mol, 24.8 cm^3, 27 % H_2O_2) all thiophene was immediately fully oxidized by the addition of oxidant. The use of dilute hydrogen peroxide (0.05 mol, 6.15 cm^3) enabled the isolation of a range of oxidation products which gave useful information about the reaction pathway (Scheme 2.1).

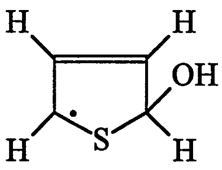
The formation of 2-hydroxythiophene **(12)** as a major product, indicates the probable involvement of a radical reaction pathway via the formation of hydroxyl radicals. Reactions of thiophene with radiolytically produced hydroxyl radicals have been shown to result mainly in the formation of 2-hydroxythiophene [4]. In earlier studies, the reaction of hydroxyl radicals with thiophenes has been investigated by Safarov in oxygen- and air-saturated solutions and by Lilie in N_2O-saturated solutions. Both studies indicate that the hydroxyl radical attacks the 2-position in thiophene, the most reactive position, to give 2-hydroxythiophene [4]. It has been demonstrated that 2-hydroxythiophene exists almost exclusively in two keto-forms, namely (5H)-thiophen-2-one **(13)** and (3H)-thiophen-2-one **(14)** [5], of which the former is the more stable [6-9].



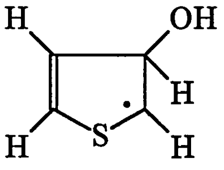
(12) **(13)** **(14)**

Proton-transfer in the 2-hydroxythiophene ring system gives rise to these three possible forms, and similar tautomeric forms were also observed in the case of alkyl-substituted hydroxythiophenes which will be discussed in sections 2.2.1.2 and 2.2.1.3..

Electron spin resonance spectroscopy has been used for the study of the reaction of thiophene with hydroxyl radicals, which were generated by pulse radiolysis of water, at different pH values [6]. When thiophene was oxidized at pH = 6.0, the radicals **(15)** and **(16)** were detected and these led to the formation of 2- and 3-hydroxythiophenes. The relative concentrations of **(15)** and **(16)** remained in a 4:1 ratio in the pH range 4.5-6.0. As the pH was lowered below 4.5, the signal due to **(15)** increased in intensity, and that of **(16)** decreased; below 2.5 only **(15)** was observed.

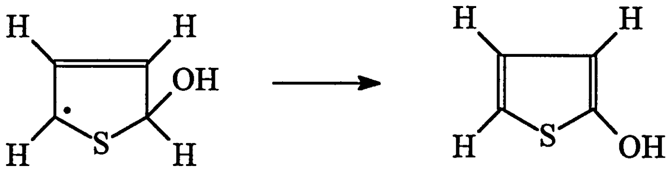


(15)



(16)

The Fenton oxidation was carried out at pH = 2.0 and this may explain the predominant formation of 2-hydroxythiophene.

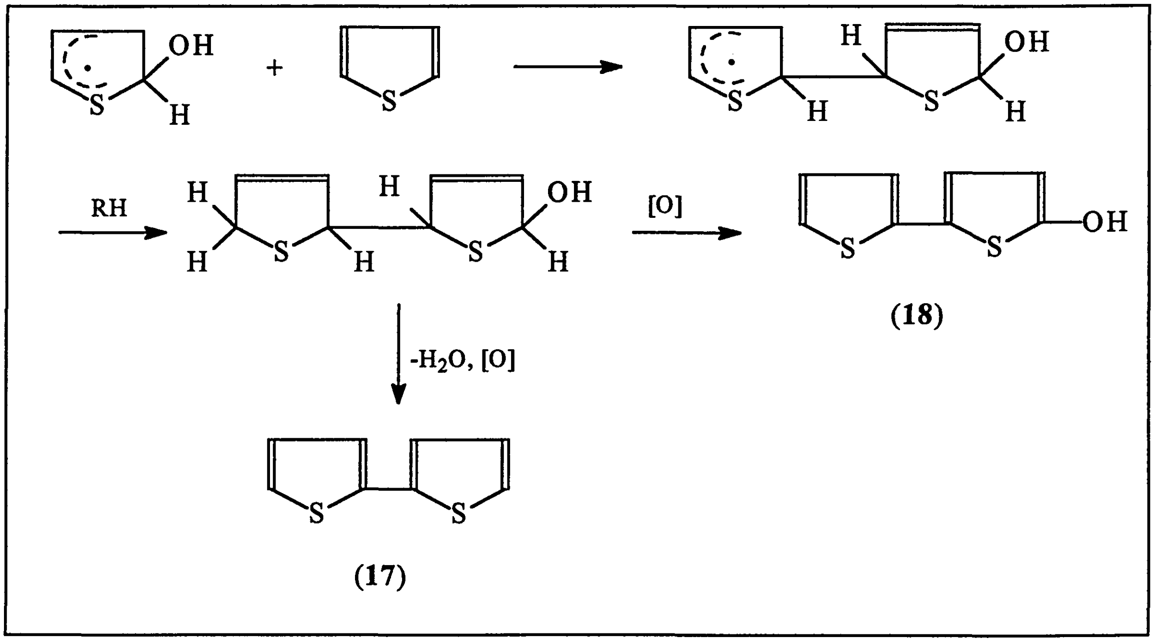


(1)

The $HO^{\cdot}$/ benzene system and the reactions of the resulting hydroxycyclohexadienyl radical **(1)** have been studied by several workers [8,9]. The formation of the hydroxycyclo hexadienyl radical (1) and its further dimerisation have also been observed in the Fenton oxidation of benzene; this has been discussed in section 1.3.2.1. This mechanism has been considered as a possibility for the related thiophene system, but an important distinction is that in the case of benzene very little phenol and biphenyl are directly produced by the hydroxycyclohexadienyl radical.

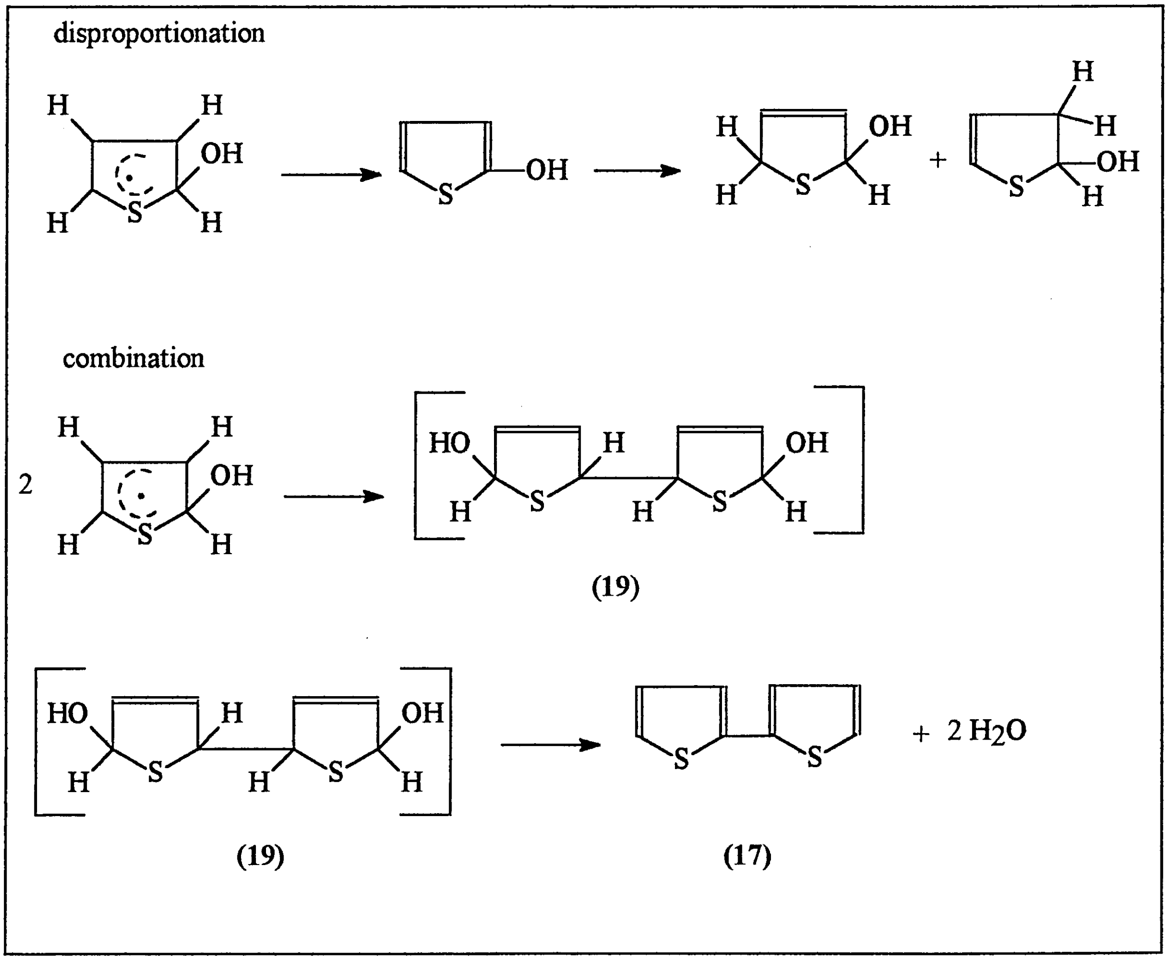
In the radiolytically generated HO/thiophene system, the major product is 2-hydroxythiophene, (in mainly the (5H)-thiophen-2-one form) and minor ones are 2,2'-bithiophene (17) and hydroxylated 2,2'-bithiophene (18) [4]. A radical species might have been generated similar to hydroxycyclohexadienyl radical (1) which attacks any unreacted thiophene to give (17) and (18) (Scheme 2.2).

Scheme 2.2.



A recombination-disproportion mechanism can also be described for these radical-radical reactions. It is quite conceivable that both of these radical-radical reactions go through the formation of a dimeric intermediate similar to **(19)** in Scheme 2.3, from which the most stable products are derived.

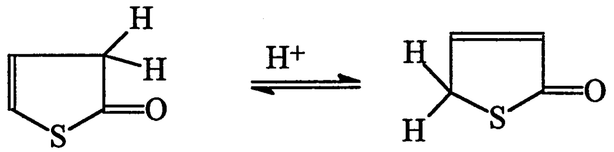
Scheme 2.3.



(19)

(19) (17)

Combination at the 5 position and the formation of **(19)** indicates that the 5 position of the 2-hydroxythienyl radical is the position of greatest electron density [4]. In the case of the Fenton oxidation of thiophene the same products as discussed above were observed under the acidic reaction conditions (pH < 2.0) and (3H)-thiophen-2-one being readily converted to (5H)-thiophen-2-one.

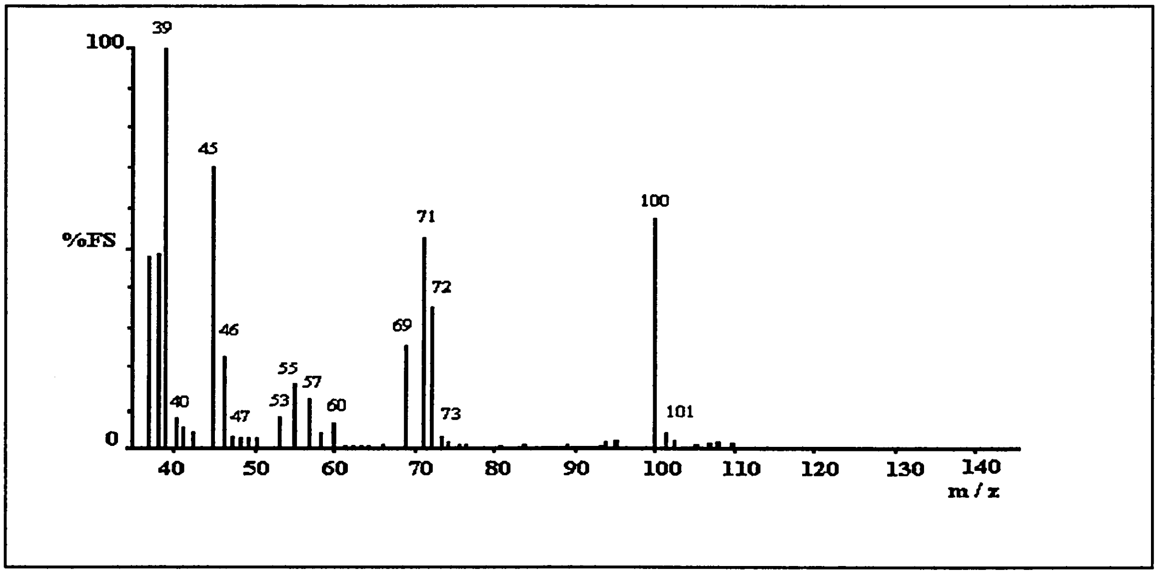


(2)

(14) (13)

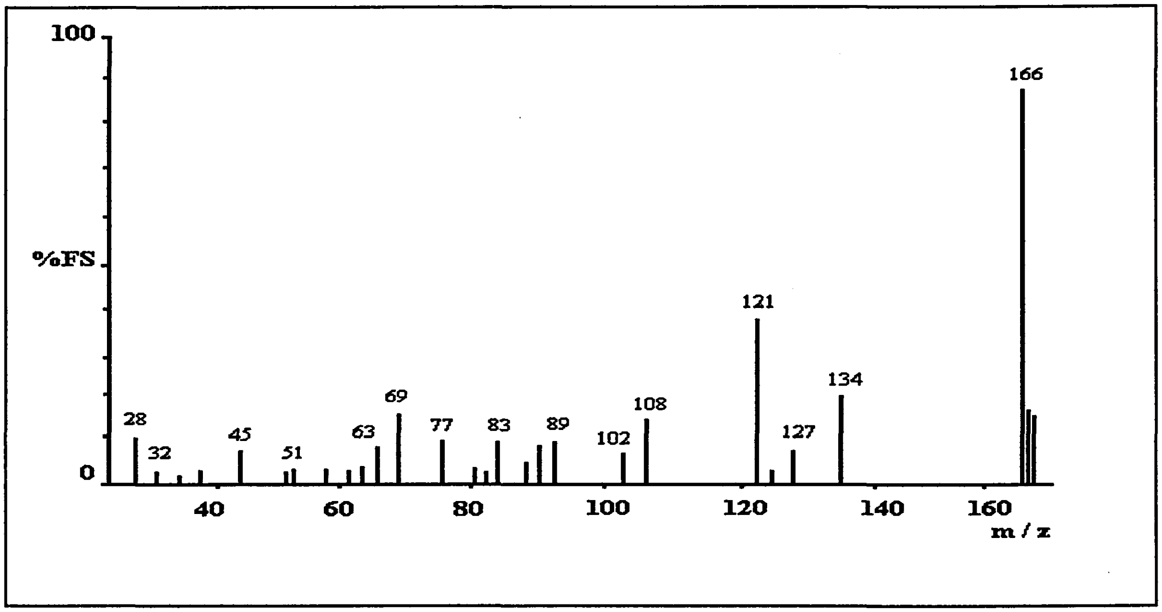
Components (13) and (17) were identified by making comparisons with the authentic commercially available standard. The formation of (5H)-thiophen-2-one was observed in both the presence and absence of air and all co-solvent systems (acetonitrile, methanol acetic acid). Comparison with the authentic sample gave the same mass spectral fragmentation pattern and same retention time on GC. This oxidation product was also isolated from the reaction mixture by flash column chromatography by using a dichloromethane/petroleum ether (3:7) solvent system. Its NMR spectrum showed exactly the same pattern as observed in the authentic sample. A broad peak was observed on GC due to its keto ⇌ enol tautomeric properties. The mass spectral fragmentation of (5H)-thiophen-2-one is given in Figure 2.2.

Figure 2.2. Mass spectrum of (5H)-thiophen-2-one

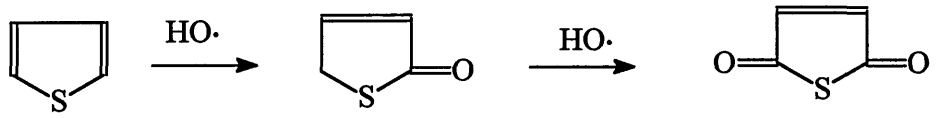


2,2'-Bithiophene was detected in the copper-containing catalyst systems, Fe(II) + Cu(II), in both the presence and absence of co-solvent acetonitrile and its mass spectrum is shown in Figure 2.3.

Figure 2.3. Mass spectrum of 2,2'-bithiophene



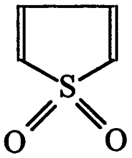
The diketo system (**20**) was detected only in the presence of an acetonitrile co-solvent containing system. It might arise from multiple hydroxylation of thiophene similar to those demonstrated in the Fenton oxidation of benzene [10a]. The relative mass of this product is 114 and the compound is described in the literature [10b] but all attempts to prepare it failed. Since it is a minor component, it could not be isolated from the reaction mixture. A comparison with the mass spectrum fragmentation of similar compounds resulted in some useful information in support of its possible structure. Maleic anhydride and thiotetronic acid show similarities to this product with a mass fragmentation pattern that includes a stable molecular ion at *m/z* 114 and fragment ion at *m/z* 86(the loss of CO) and *m/z* 54.



(3)

(13) **(20)**

Component **(21)** exhibited an apparent molecular ion at *m/z* 116 and it was detected in all iron containing systems (Fe(II)/H_2O_2, Fe(III)/H_2O_2, and Fe(II) + Cu(II)/ H_2O_2) in water. Some possible structures were suggested, one possibility being the sulphone **(22)**.

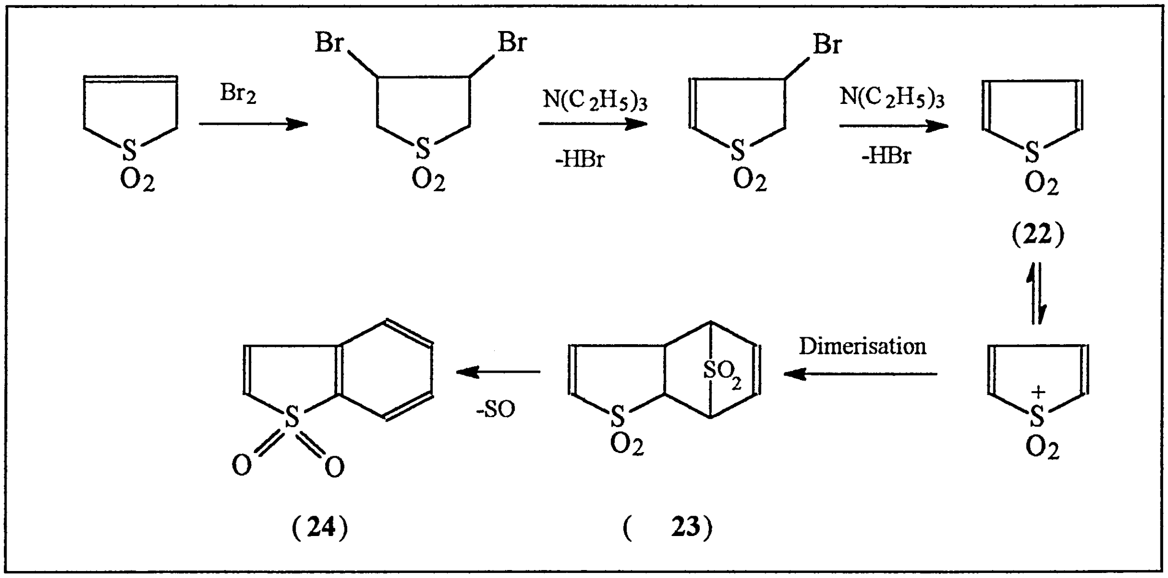


Thiophen-S,S-dioxide **(22)**

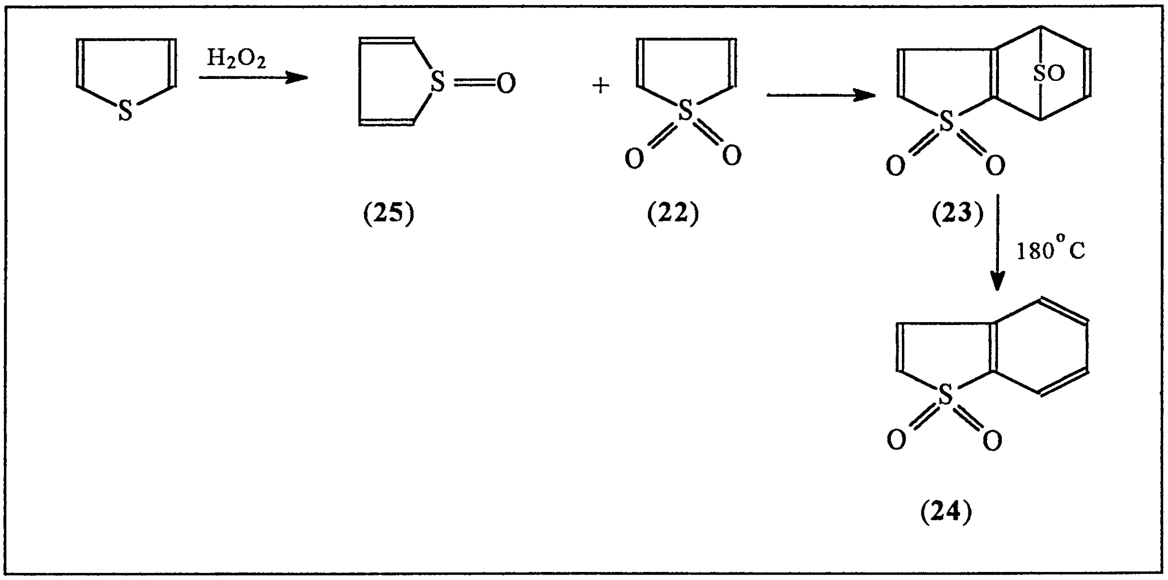
Extensive literature work showed that this sulphone is extremely unstable and undergoes spontaneous dimerisation, resulting in the formation of benzo-[b]-thiophen-S,S-dioxide **(24)** [10-14] and thiophen-S,S-dioxide itself cannot be isolated due to this dimerisation [11,12]. Since the aromatic character of thiophene is destroyed by its conversion into the S,S-dioxide, which then behaves like a cyclic diene [13-15]. This reaction pathway is shown in Scheme 2.4 and the reaction leads to the formation of benzo-[b]-thiophen-S,S-dioxide.

It is known that hydrogen peroxide [13] or sodium perborate [16] oxidize thiophene in the same manner as explained above to a product having the composition of a "sesquioxide" **(23)** which may arise by Diels-Alder combination of the sulphoxide **(25)** and sulphone **(22)** (Scheme 2.5).

Scheme 2.4.



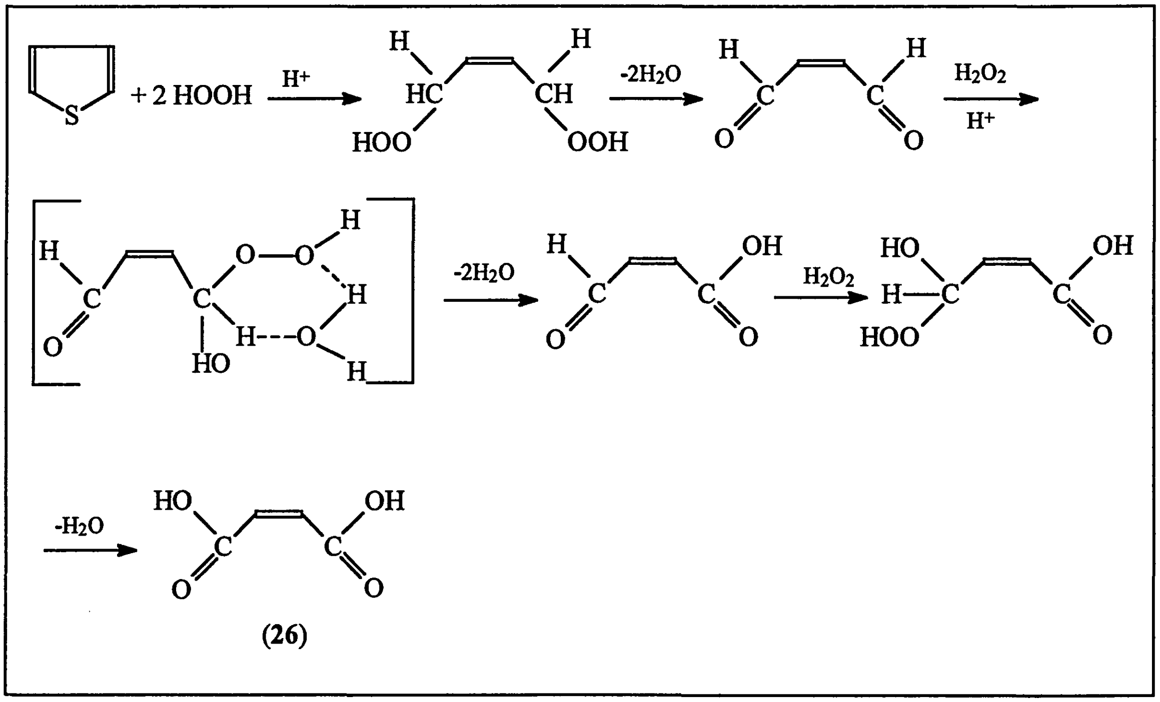
Scheme 2.5.



When thiophene was oxidized by sodium perborate, benzo-[b]-thiophene-S,S-dioxide was observed as the main product. This indicates the formation of sulphoxide and sulphone, but this dimeric product has never been observed in the oxidation of thiophene with the Fenton and related oxidation systems. Therefore, the possibility of oxidation at sulphur with the formation of sulphoxide and sulphone can probably be eliminated.

The second possibility is the formation of an organic acid which is formed by the splitting out of sulphur in the form of inorganic sulphur and/or sulphur dioxide. Such a compound was observed by Gvozdetskaya [17] in the oxidation of thiophene by hydrogen peroxide. According to this study, thiophene is oxidized by hydrogen peroxide in the presence of hydrochloric acid with opening of the ring, and the addition of barium chloride to the oxidation products results in the quantitative precipitation of barium sulphate, indicating that sulphur has been cleaved in the form of sulphur dioxide which is transformed to sulphate ions in the acidic medium. On the basis of the products formed the following mechanism can be postulated (Scheme 2.6).

Scheme 2.6.



Excess hydrogen peroxide oxidizes thiophene via splitting out sulphur and further oxidation in the presence of acid gives rise to maleic acid (**26**). However, both mass spectral fragmentation and retention time of maleic acid did not show any similarity to those of component **(21)**, so the chemical structure of **(21)** remains unknown.

The gaseous product carbon dioxide was trapped by precipitation into barium hydroxide solutions. Sulphur dioxide was mainly left in the aqueous phase in the form of sulphate ions and could not be determined quantitatively since sulphuric acid was already used for keeping the pH of the reaction mixture at 2.0. Carbon dioxide was precipitated as barium carbonate and the amount of gas liberated was calculated. The amount of detected carbon dioxide, which depends upon the reaction time, is given in section 3.4.2.1. The sulphur allotrope (S_8) was detected by GC/MS analysis and confirmed by comparison with an authentic sample.

b) Analysis by HPLC

The non-volatile oxidation products which might be formed in the Fenton and related oxidation of thiophene were investigated by using HPLC techniques. The HPLC method outlined in section 2.1.3 was employed for the analysis of the above reactions, conducted over 1 hour and 24 hours respectively. As explained before, the aqueous phase was first separated and then evaporated to dryness and the residue was finally dissolved in methanol. After a careful cleaning process, e.g. microfiltration, samples were run on the HPLC system, but acetic acid was the only product observed from the acetonitrile co-solvent system. This product does not arise from the Fenton oxidation of thiophene, but from the hydrolysis of acetonitrile;

$$CH_3CN + H_2O \xrightarrow{H^+} CH_3COOH \qquad (4)$$

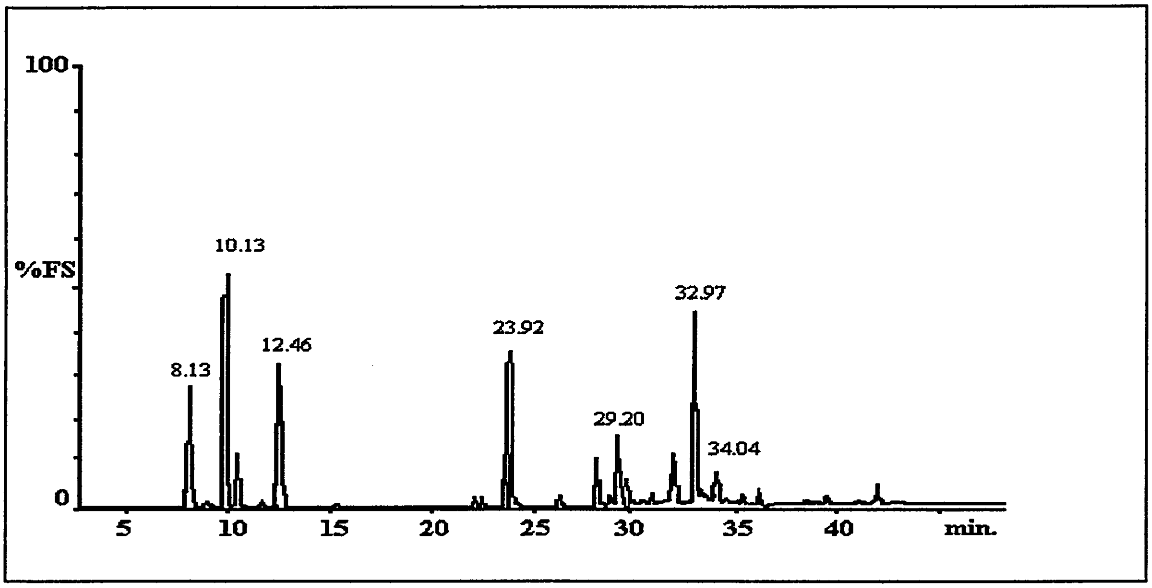
No other components were detected in the chromatogram of the aqueous phase. In addition, the dichloromethane extract containing all oxidation products was evaporated, the residue dissolved in methanol, and subjected to HPLC analysis. Again acetic acid was the only product observed. Polar oxidation products may not form due to ring cleavage or may be volatile and lost during the evaporation.

2.2.1.2. 2-Methylthiophene

a) Analysis by GC/MS

The oxidation of 2-methylthiophene was carried out using Fenton and related reagents and the reactions were monitored over time periods of 1 and 24 hour respectively. The reaction products were analysed using instrument conditions and temperature program 1 as described in section 2.1.3. The GC trace of the reaction mixture of 2-methylthiophene in water is depicted in Figure 2.4.

Figure 2.4. GC chromatogram of the Fenton-catalysed oxidation of 2-methylthiophene.



The oxidation products observed have been assigned structures by comparison with either authentic samples, or by consideration of mass spectral data. These products are summarised in Table 2.2. A possible pathway for the formation of these products is also presented in Scheme 2.7.

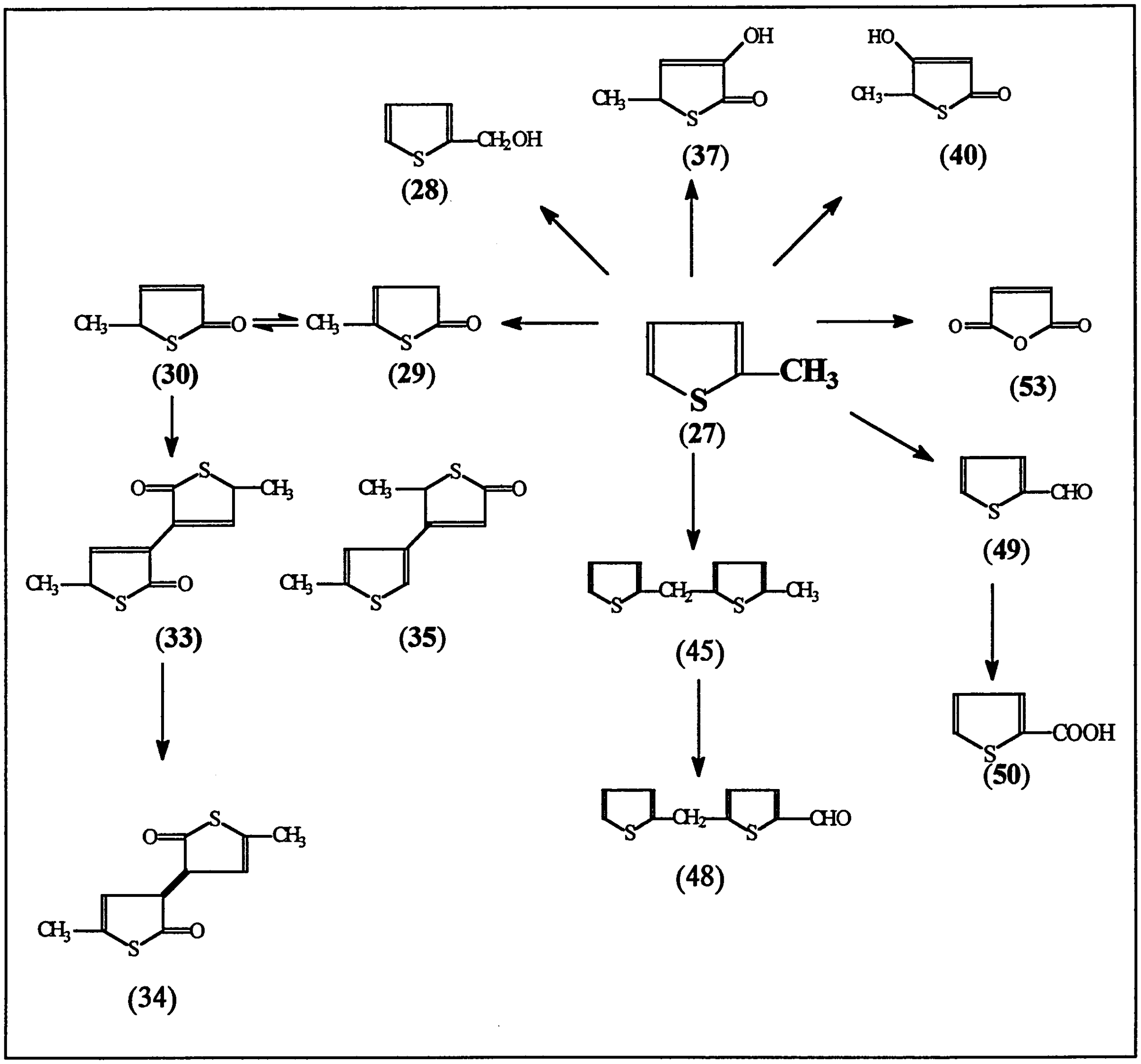
Table 2.2. Oxidation products arising from the Fenton-catalysed oxidation of 2-methylthiophene

Comp. No	t_R		Apparent RMM	Solvent	Proposed structure
	1 hr	24 hr			
28	12.46	12.46	114	H_2O, CH_3COOH/H_2O MeCN/H_2O MeOH/H_2O	2-hydroxymethylthiophene
29	9.92	-	114	H_2O, MeOH/H_2O	5-methyl-(3H)thiophen-2-one
30	10.10	10.13	114	H_2O, MeOH/H_2O	5-methyl-(5H)thiophen-2-one
33	29.20	29.20	226	H_2O , MeOH/H_2O	Indigoidal dimer
34	32.22	32.97	224	H_2O, MeOH/H_2O	Indigoidal dimer
35	31.88	31.88	210	H_2O, MeOH/H_2O	Indigoidal dimer
51*	-	9.80	114	MeCN/H_2O	Unknown
52*	13.67	14.95	114	MeCN/H_2O	Unknown
53	3.70	-	98	MeCN/H_2O	maleic anhydride
37*	13.12	13.10	130	H_2O, MeOH/H_2O	5-methyl-2,3-dihydroxy thiophene
40*	11.05	11.53	130	H_2O, MeOH/H_2O	5-methyl-2,4-dihydroxy thiophene
45	23.91	23.92	194	H_2O, CH_3COOH/H_2O MeCN/H_2O MeOH/H_2O	2-methyl-5-(2-thienyl methyl)thiophene
48*	29.44	29.44	208	H_2O, CH_3COOH/H_2O MeCN/H_2O MeOH/H_2O	5-(2-thienylmethyl) thiophene-2-aldehyde
49	8.13	8.13	112	H_2O, CH_3COOH/H_2O MeCN/H_2O MeOH/H_2O	thiophene-2-aldehyde
50	-	9.15[1]	128	H_2O, MeOH	thiophene-2-carboxylic acid

* Indicates that proposed structure has not been proved by comparison with the authentic substance

[1] HPLC analysis was performed by using methanol/water (1:4) at 2 ml/min.

Scheme 2.7.

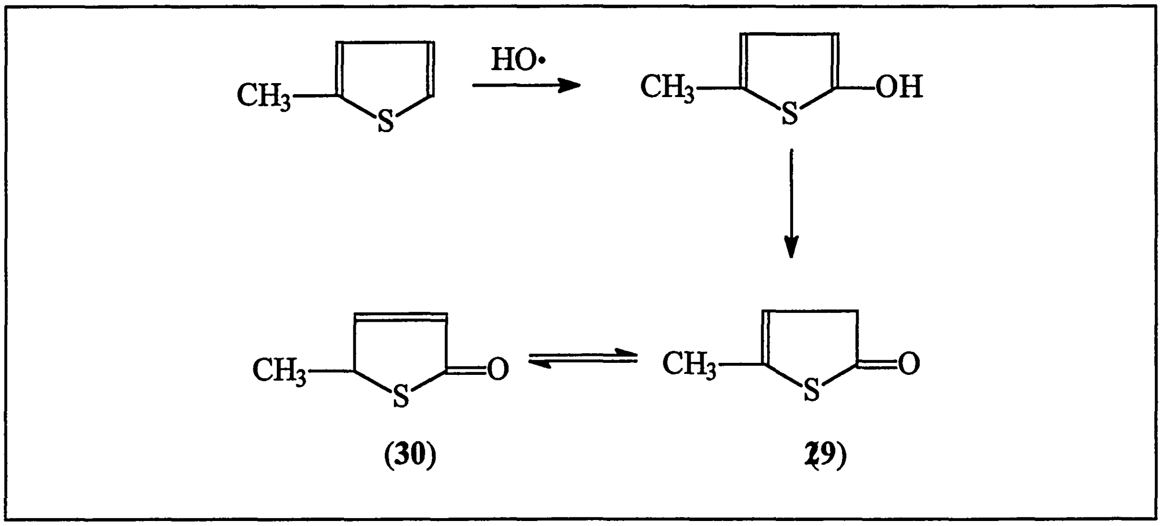


Fenton catalysed oxidation of 2-methylthiophene did not show any significant effect on the range of oxidation products formed when the oxidation process was allowed to continue for more than 1 hour; only a few additional compounds, such as thiophene-2-carboxylic acid, were observed after a 24 hour reaction period. The use of dilute hydrogen peroxide (0.05 mol, 6,15 cm^3) enabled the isolation of an extensive range of oxidation products shown in Scheme 2.7. Mono and dihydroxylated methyl thiophenes were observed as main oxidation products.

The structure of component **(28)** was confirmed as 2-hydroxymethylthiophene by comparison with the authentic substance. Hydroxylation of the 5-position of 2-methylthiophene resulted in the formation of 5-methyl-(5H)thiophen-2-one **(30)** and possibly further hydroxylation of this gave the dihydroxylated thiophenes **(37)** and **(40)**. Although **(30)** 5-methyl-(5H)thiophen-2-one was confirmed by using the authentic substance, all attempts failed to identify the structure of **(37)** and **(40)**, therefore only possible structures were proposed from their mass spectral fragmentations.

Thiophenes bearing such electron-donating substituents such as alkyl or aryl can be easily oxidized by hydroxyl radicals [13]. When thiophene is substituted with a methyl group at the 2-position (2-methylthiophene), the 5-position becomes more active for hydroxylation rather than 4-position, and 5-methyl-2-hydroxythiophene was obtained. A similar range of tautomeric structures are also valid for 5-methyl-2-hydroxythiophene as discussed in section 2.2.1.1, and these structures are shown in Scheme 2.8.

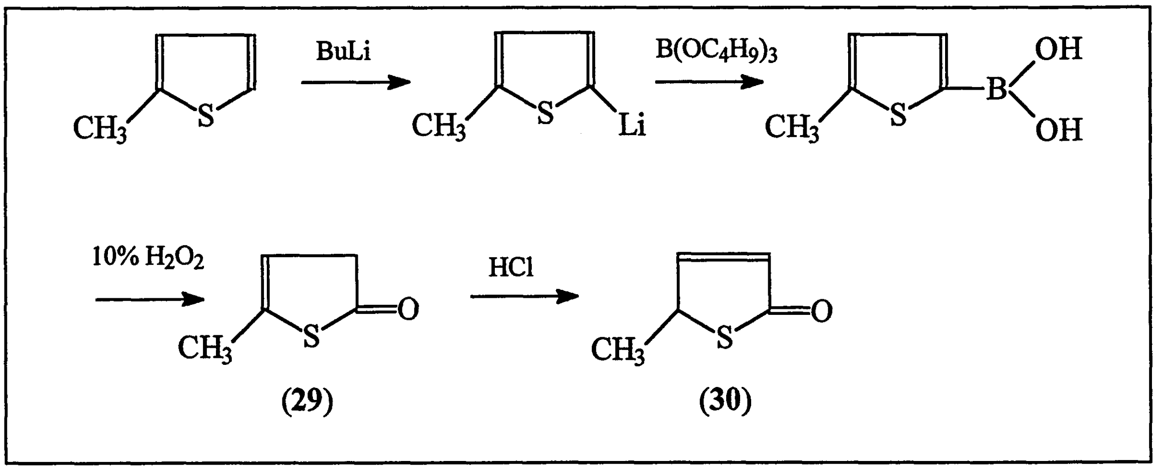
Scheme 2.8.



(30) **(29)**

Components (29) and (30), namely 3H- and 5H- thiophen-2-one respectively, were prepared by following the method as described by Hörnfeldt [18]. The preparation of these two compounds required a three step reaction pathway as outlined in Scheme 2.9 and experimental details are given in section 4.2.

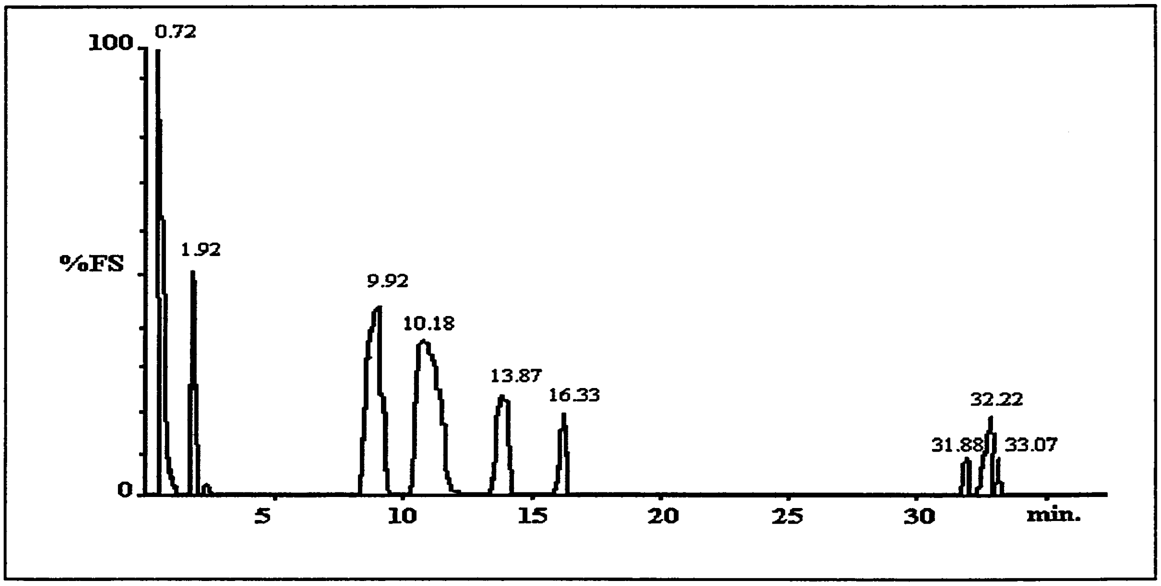
Scheme 2.9.



The GC chromatogram of this reaction mixture is shown in Figure 2.5 and comparison with the products observed in the Fenton-catalysed oxidation of 2-methylthiophene showed a perfect match.

It is known that (29) is easily converted to (30) in the presence of acid and this may explain the formation 5-methyl-(5H)-thiophen-2-one as one of main products from the Fenton-catalysed oxidation of 2-methylthiophene and observed 1 and 24 hour reaction times.

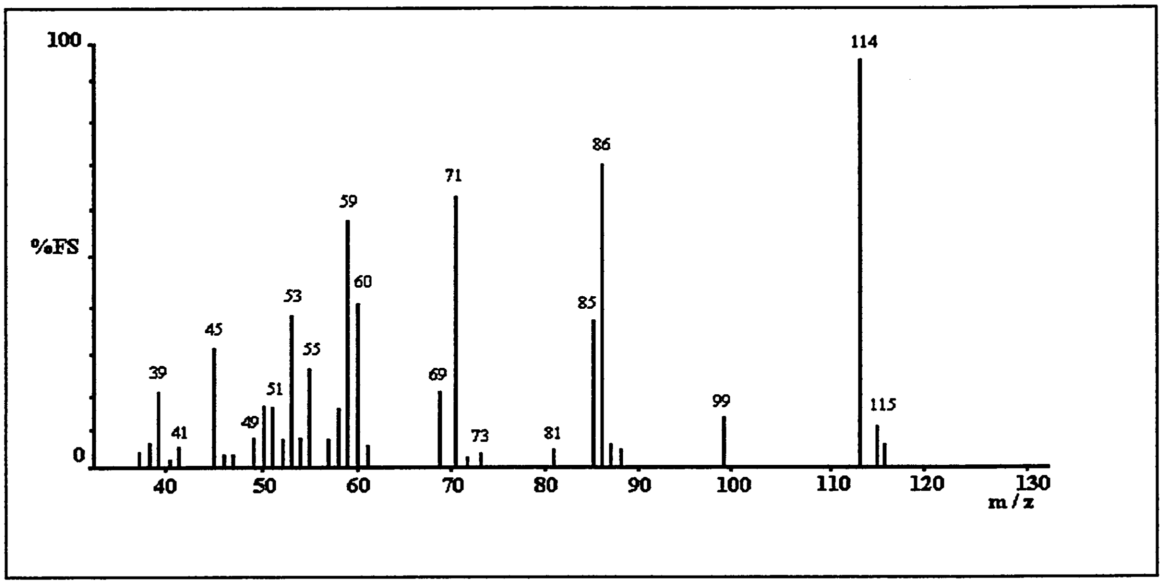
Figure 2.5. The GC chromatogram of the reaction mixture of prepared components (**29**) and (**30**).



The reaction of 2-methylthiophene with radiolytically produced hydroxyl radicals also resulted in the formation of (**30**) [4]. The formation of this component is evidence for the involvement of hydroxyl radicals (HO$^{\bullet}$) as the oxidizing species under Fenton-catalysed oxidation conditions.

All Fenton-related systems gave a small amount of 5-methyl-(3H)-thiophen-2-one (**29**) and 5-methyl-(5H)-thiophen-2-one (**30**) as the main product. Additionally, (**30**) was isolated in approximately 10% yield from the oxidation mixture of 2-methylthiophene in a preparative scale reaction and experimental details are given in section 4.2. Both (**29**) and (**30**) exhibited an apparent molecular ion at *m/z* 114 and a fragment ion at *m/z* 99 indicating the loss of $-CH_3$ (Figure 2.6).

Figure 2.6. Mass spectrum of 5-methyl-(5H)-thiophen-2-one.

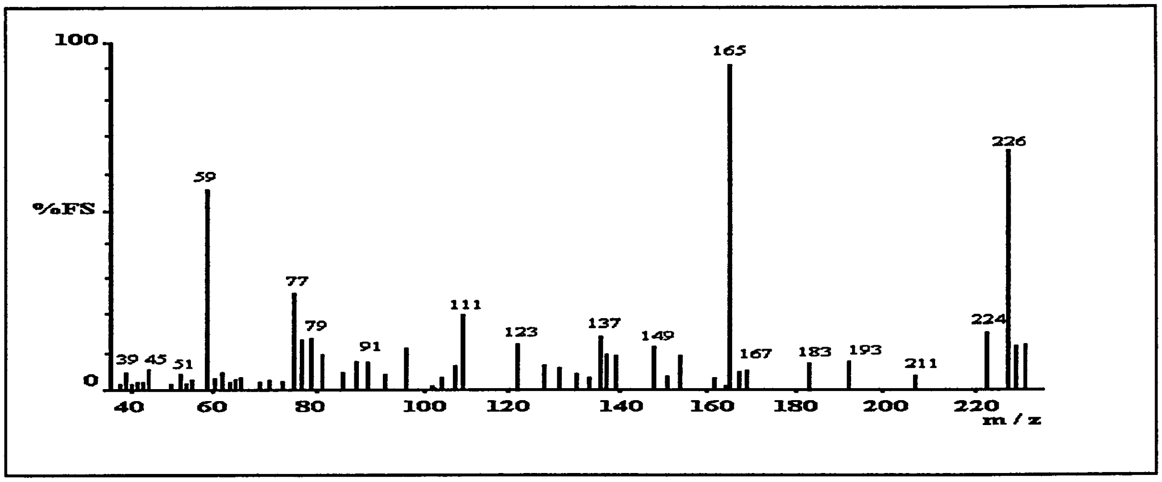


The above methyl substituted thiophene-2-one tautomers are known to undergo oxidative conversion to the dimeric systems giving components (33), (34) and (35) (*m/z* 226, 224 and 210 respectively) [4, 19, 20] and these were also detected in the Fenton-related oxidations of 2-methylthiophene. The mass spectral fragmentations of dimeric structures (33), (34) and (35) are shown in Figure 2.7.

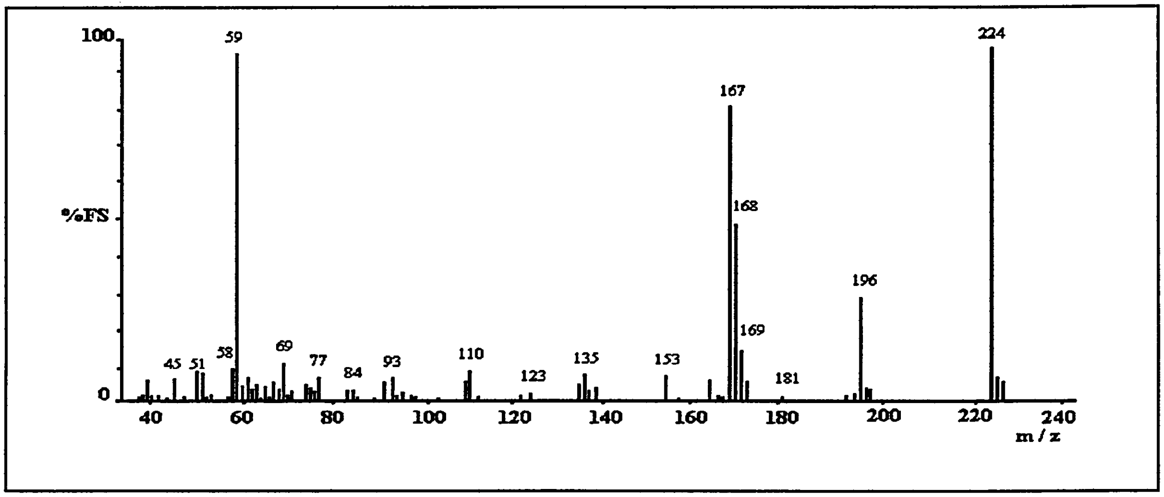
According to Hörnfeldt, alkylhydroxythiophenes undergo oxidative dimerisation to form such indigoidal structures [20], and the structures of the dimeric products obtained in the synthesis of the 5-methyl-(5H)-thiophen-2-one were elucidated by Hörnfeldt. When this procedure was repeated in our study, the same dimeric products were also observed which were identical with those components formed in the Fenton oxidation of 2-methylthiophene with respect to their retention time and mass fragmentations.

Figure 2.7. Mass spectrum of dimeric structures (33), (34) and (35).

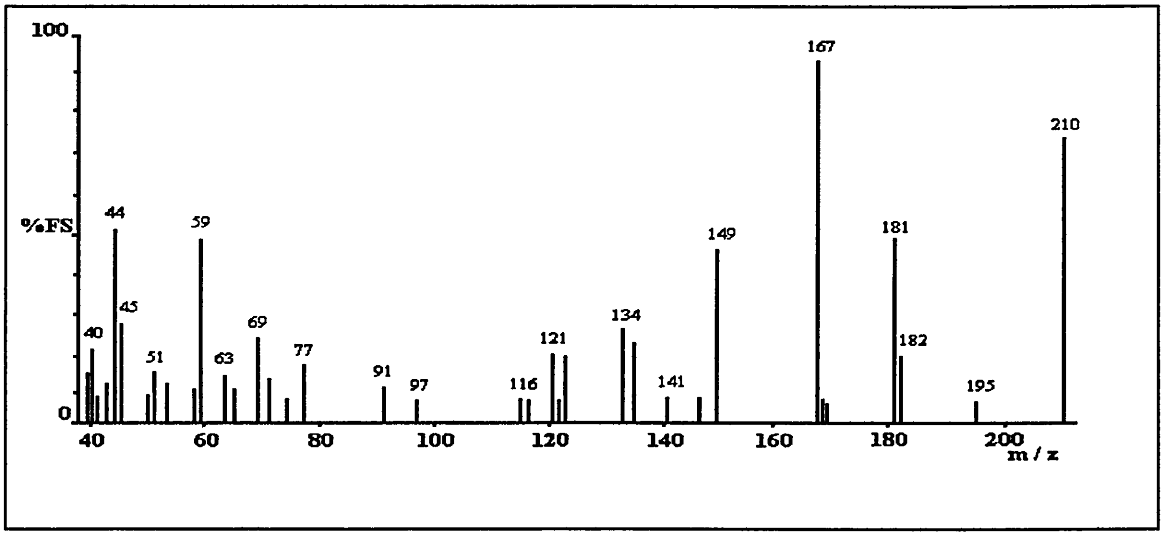
a) Component (33)



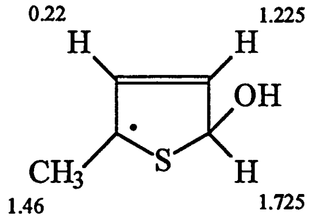
b) Component (34)



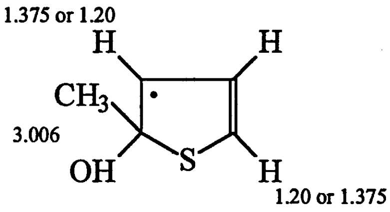
c) Component (35)



This side chain coupling is probably due to the formation of new radical species, depending on the pH. When 2-methylthiophene was oxidized by radiolytically produced HO˙ in the pH range 2.0-7.0, the radicals **(31)** and **(32)** were formed in a ratio ca. 4:1 [21].



(31)



(32)

When the pH value was lowered, the ESR signal due to **(31)** was increased while that due to **(32)** decreased. Coupling and rearrangement of this radical **(31)** may result in the formation of dimeric compounds called "indigoidal structures". It was also confirmed that ferric ion [Fe(III)] will increase the efficiency of this process. The 5-methyl-(3H)-thiophen-2-one system is quite reactive due to the α-hydrogens in the chain and indigoidal structures, e.g. quinone-like intermediates, are easily formed (Scheme 2.10) [4, 19, 20].

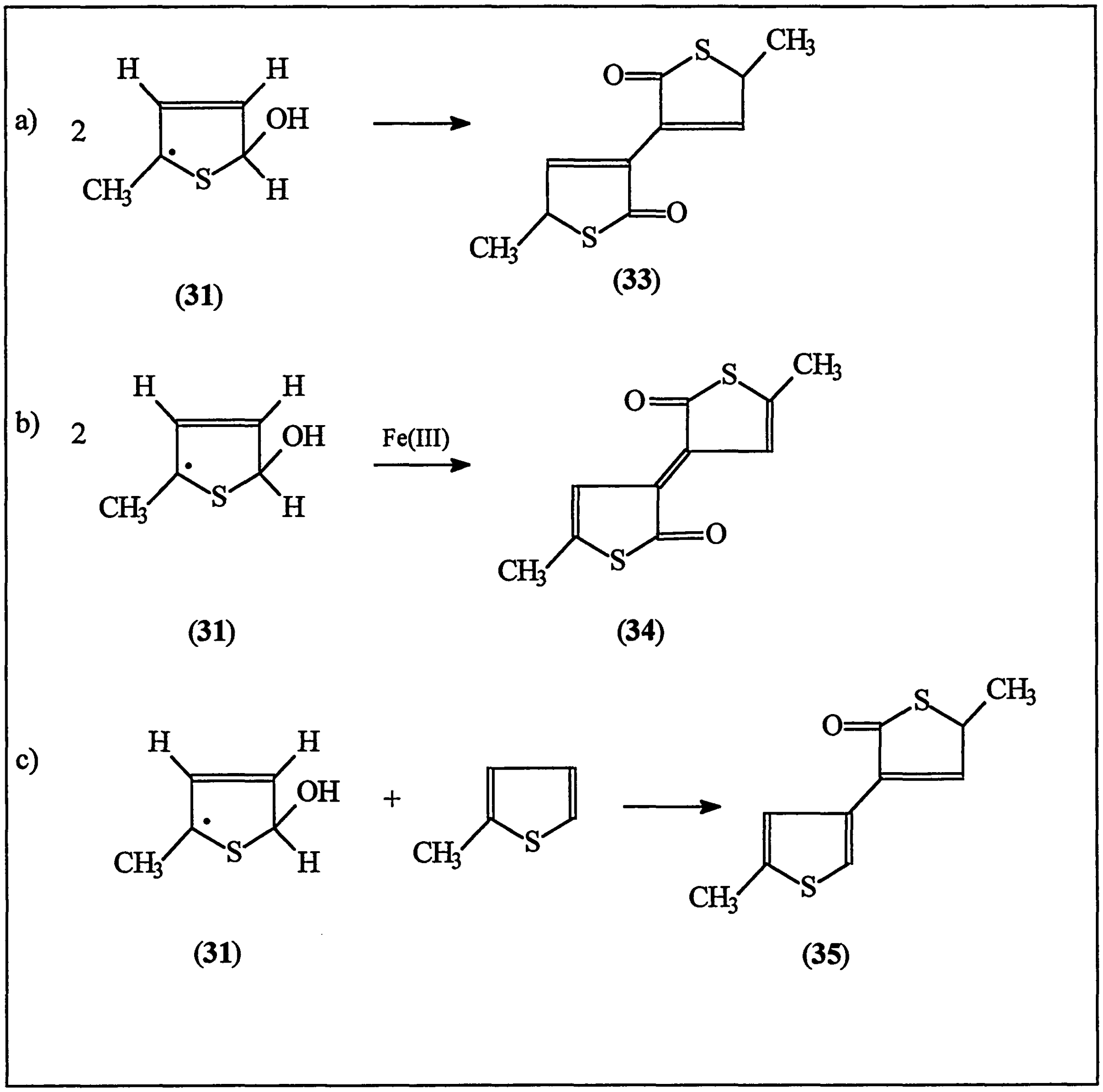
The origin of these dimeric structures is presumably as follows;

a) coupling of the two radicals **(31)**gives component **(33)** (Scheme 2.10a)

b)oxidative coupling of **(31)** in the presence of Fe(III) ions gives component **(34)** (Scheme 2.10b), or

c) radical attack of **(31)** on unreacted 2-methylthiophene gives component **(35)** (Scheme 2.10c).

Scheme 2.10.



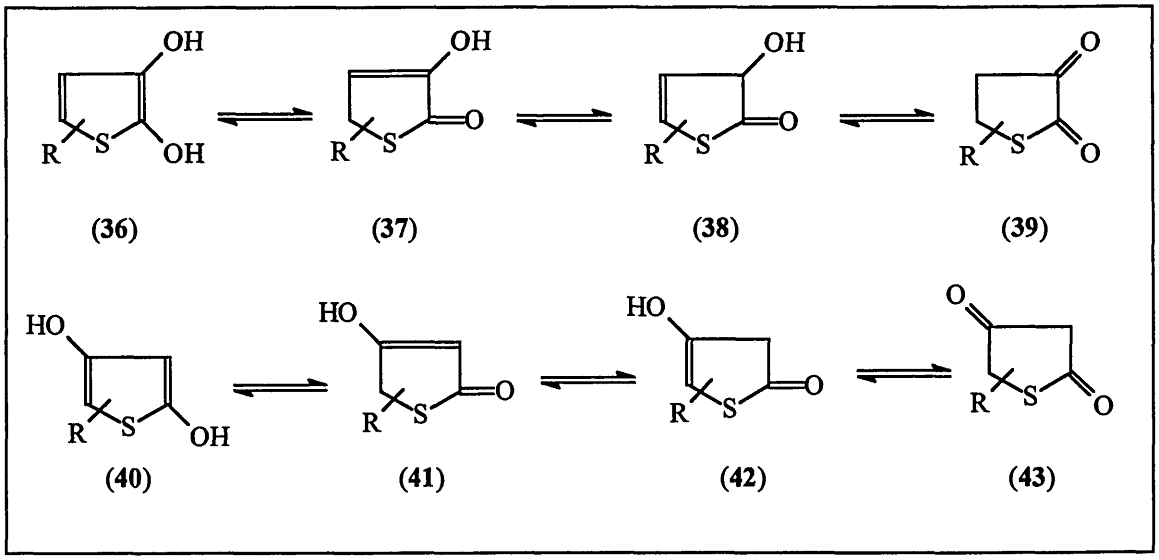
In the Fenton oxidation, Fe(III) already exists and therefore this oxidative coupling pathway may explain the formation of these indigoidal structures. Therefore the chemical structures of components (33), (34) and (35) were confirmed as these dimeric structures.

Multiple hydroxylation is common in Fenton related oxidations of aromatic systems and polyhydroxylated products have been identified in several cases [10a, 22-25]. Oturan and Pinson demonstrated the stepwise hydroxylation of benzoic acid to mono- and polyhydroxylated products with electrochemically generated hydroxy radicals [26]. They indicated that any process involving hydroxyl radicals shows a clear tendency to lead to multiple hydroxylation and this tendency increases with the number of hydroxyl groups already present on the aromatic ring.

Also characterized were the isomeric dihydroxythiophenes which presumably arise by attack of a second hydroxyl radical on the ring system of **(29)** and/or **(30)**. Two components were detected as products in all Fenton-related oxidation of 2-methylthiophene and each gave an apparent molecular ion at *m/z* 130.

2,3-, 2,4- and 2,5-Dihydroxythiophenes are known in the literature [27, 28]. Theoretically, 2,3- and 2,4-dihydroxythiophenes can exist in four tautomeric forms **(36-39** and **40-43** respectively), but Mortensen *et al.* [27] proved that dihydroxythiophene does exist as **(37)** (Scheme 2.11).

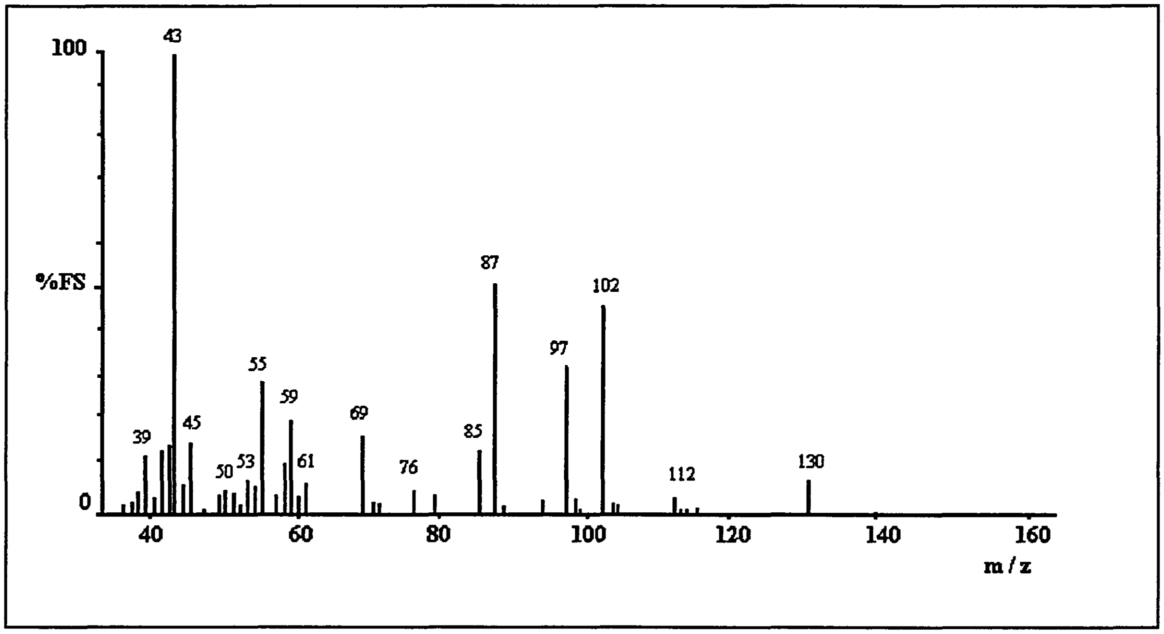
Scheme 2.11.



5-Methyl substituted 2,3-dihydroxy and 2,4-dihydroxy forms have been prepared by Mortensen *et al* [27] from di-t-butoxythiophenes via an organometallic reagent.

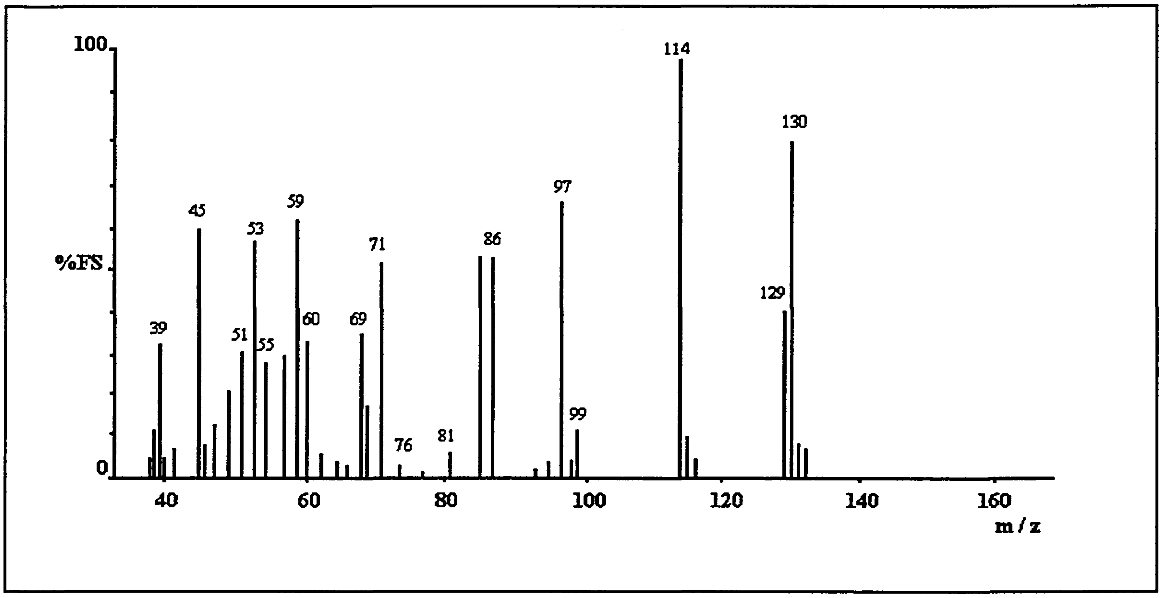
All attempts to prepare these two components following the method proposed by this group failed due to the rather complicated nature of the procedure and difficulties in isolation of the intermediate product in several cases. Possibly, 3-hydroxy-5-methyl-3-thienyl-2-one (**37**) can be suggested for the first component from the mass spectral fragmentation which is given in Figure 2.8.

Figure 2.8. Mass spectral fragmentation of component (**37**).



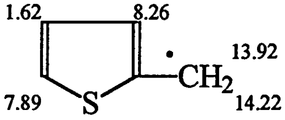
Additionally to this, one methyl-substituted dihydroxythiophene, an oxidation product of 3-methylthiophene which is discussed in section 2.2.1.3, was successfully prepared and its fragmentation pattern is very similar to that of component (**37**). A possible structure, 5-methyl-2,4-dihydroxythiophene (**40**), can be suggested for the second component giving an apparent molecular ion at *m/z* 130 but with a different mass spectral fragmentation from that of **(37)** (Figure 2.9). Presumably **(40)** may exist predominantly as any of the tautomers **(40-43)** as shown in Scheme 2.11.

Figure 2.9. Mass spectral fragmentation of component **(40)**



Isolation of **(37)** and **(40)** from the reaction mixture was not possible due to its complex nature and these structures have not been confirmed by NMR studies.

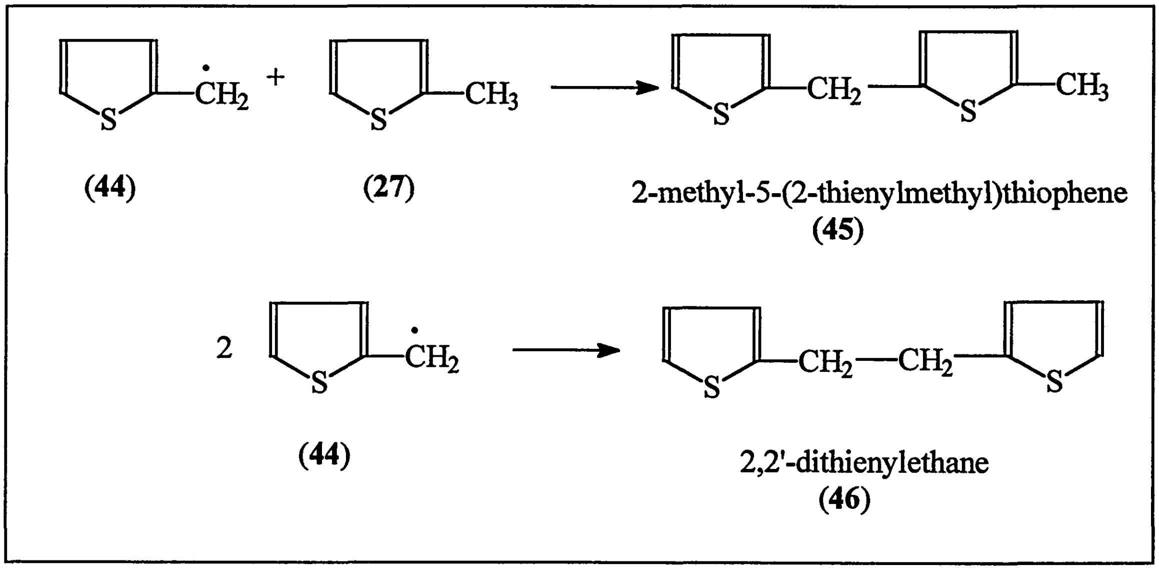
Another significant product was the dithienylmethane **(45)**, the origin of which is presumably attack of the initially formed 2-thienylmethyl radical at the 5-position of another 2-methylthiophene unit. It is well-known that thiophenes readily undergo substitution at a free alpha-position of the ring under free radical conditions [29]. The formation of 2-thienylmethyl radicals by hydrogen abstraction from the related methylthiophenes by the t-butoxy radical has been documented [30]. The simple 2-thienylmethyl radical **(44)** was observed by ESR spectroscopy by Hudson *et al* [31] who generated it by steady-state photolysis of dibenzoyl peroxide in 2-methyl thiophene and proton splitting for ring protons and methylene protons were calculated in gauss and methylene protons showing great activity.



(44)

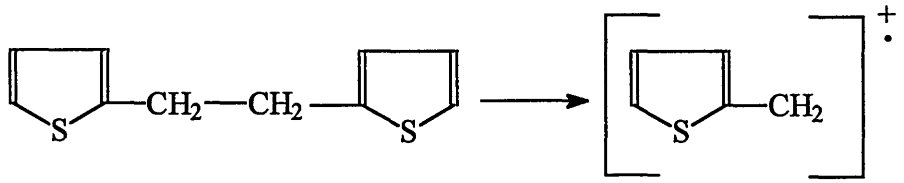
This high activity (spin population) results in the attack on unreacted 2-methylthiophene which generates the dithienylmethane (**45**) by radical substitution. Another possible product is the radical coupling product (**46**) (Scheme 2.12).

Scheme 2.12.



The compound observed in the Fenton-catalysed oxidation of 2-methylthiophene exhibited an apparent molecular ion at *m/z* 194 and a base peak at *m/z* 179 indicating the loss of the methyl group, together with fragments at *m/z* 111 and *m/z* 97 respectively.

This component is definitely not 2,2'-dithienylethane (**46**) since the mass spectral fragmentation pattern is completely different from that of the authentic compound, which was prepared by a synthetic method (section 4.1.1), even though their GC-retention times were similar. 2,2'-Dithienylethane exhibits a base peak at *m/z* 97 which could correspond to the formation of the stable fragment (**47**).

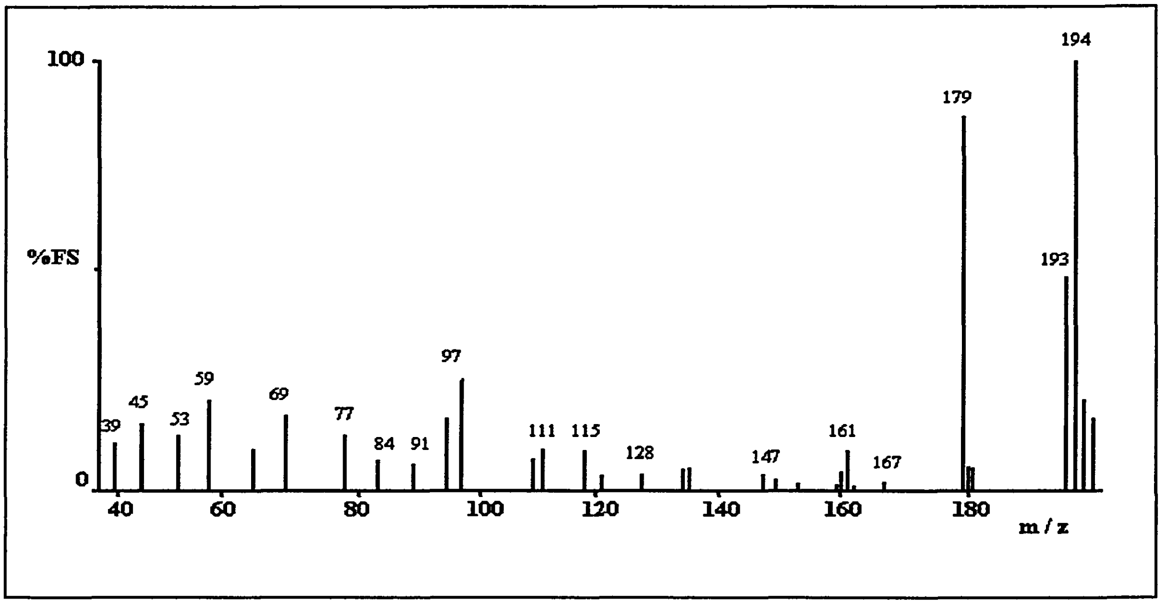


m/z 97

(**46**) (**47**)

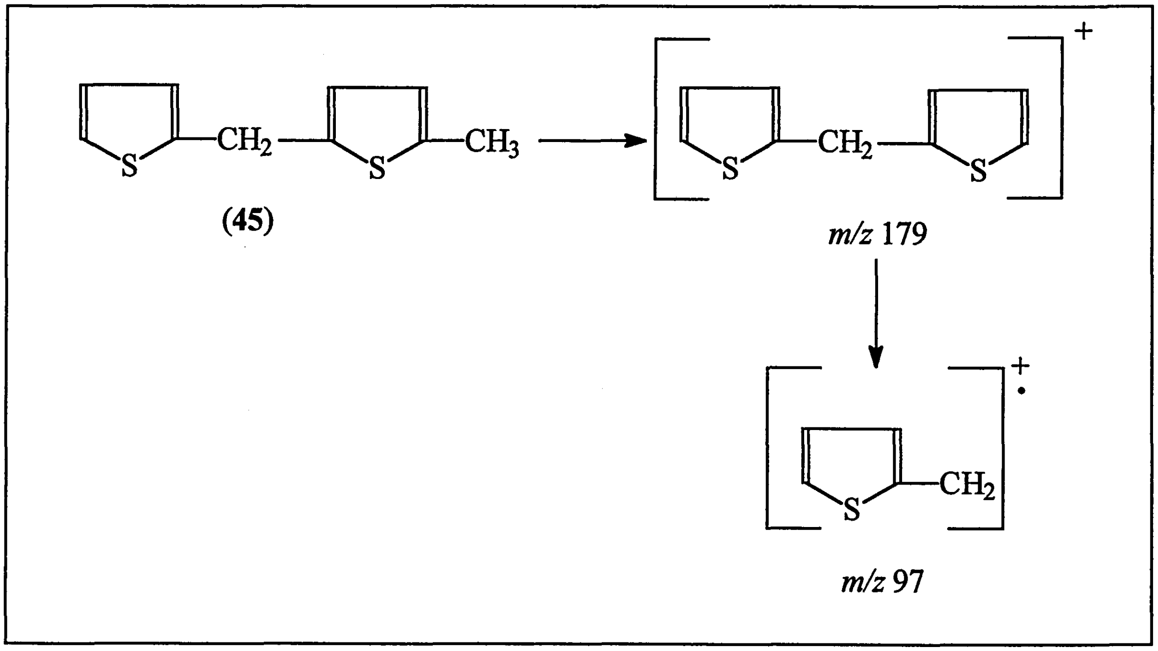
Therefore, the possible formation of the radical coupling product 2,2'-dithienylethane can be eliminated, and indeed the combination of such radicals is seldom seen in the Fenton reaction environment. Radicals will preferably attack on the active 5-position of unreacted 2-methylthiophene, present in excess. Component (**45**) was identified as 2-methyl-5-(2-thienylmethyl)-thiophene by comparison using the standard substance prepared from a synthetic method (Section 4.1.2.1), both mass spectral fragmentation patterns and retention time showing perfect match with those from (**45**). The mass spectral fragmentation of the standard substance 2-methyl-5-(2-thienylmethyl)-thiophene is given in Figure 2.10.

Figure 2.10. Mass spectral fragmentation of 2-methyl-5-(2-thienylmethyl)-thiophene



A possible fragmentation pattern of component (**45**) is shown in Scheme 2.13.

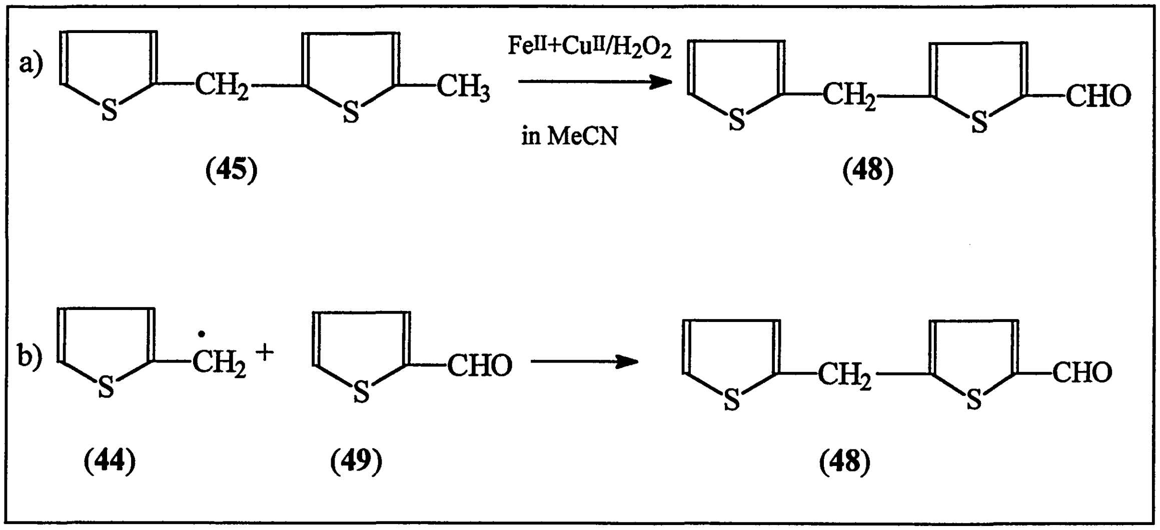
Scheme 2.13.



As a dithienylmethane component (**45**) could be expected to be quite reactive and can undergo further oxidation reactions. A small peak was seen on GC having a molecular ion at *m/z* 208 and a stable ion at *m/z* 179 possible from loss of -CHO that is characteristic for aldehydes. Component **(48)** was assigned as 5-(2-thienylmethyl) thiophen-2-aldehyde produced by further oxidation of the methyl group of **(45)** to an aldehyde under Fenton oxidation conditions (section 2.2.1.5.4) (Scheme 2.14a).

However, **(48)** may also formed from attack of the 2-thienylmethyl radical **(44)** on one of the most abundant compounds thiophene-2-aldehyde **(49)**, generated as an oxidation product from the Fenton oxidation of 2-methylthiophene (Scheme 2.14b).

Scheme 2.14.



Also detected among the oxidation products of 2-methylthiophene were the simple aldehyde **(49)** and a minor amount of the carboxylic acid **(50)** and they were confirmed by comparison with commercially available authentic samples. Significantly these were also formed when the oxidation reactions were conducted in the presence of radical trap, suggesting that their formation is non-radical in origin. Thiophene-2-aldehyde is observed as one of the major products with all types of catalyst and solvent system.

Additionally, other oxidation products were determined when reaction was carried out in the acetonitrile/water solvent system. Although hydroxylated methylthiophenes were not observed in this system, three new components **(51)**, **(52)** and **(53)** along with **(28)**, **(45)**, **(48)** and **(49)** were determined.

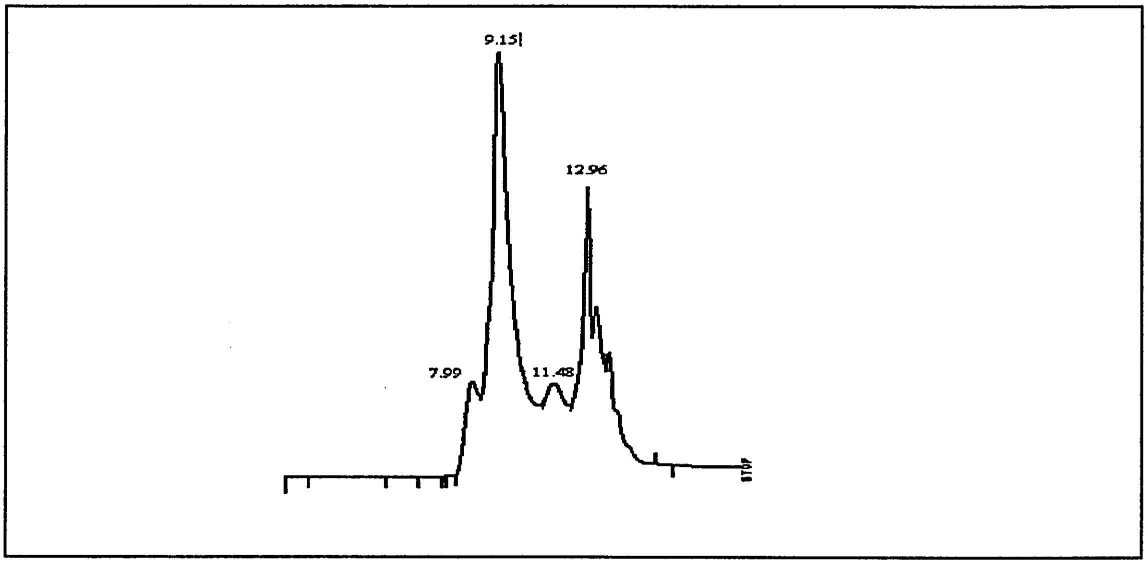
The mass spectra of components **(51)** and **(52)** exhibit an apparent molecular ion at *m/z* 114 and stable fragment ions at *m/z* 99 and *m/z* 43, indicating the loss of a methyl group followed by complete destruction of the ring. The one possible structure for these components is 2-methylthiophene-S-oxide. When applied to 2-methylthiophene, general S-oxidation methods (with sodium perborate, m-chloroperbenzoic acid or hydrogen peroxide-acetic acid) did not give a S-monoxide. An extensive literature search showed that, attempts to prepare the S-monoxide of mono-substituted thiophenes have been unsuccessful in several cases [11,16]. Thus it was not possible to prepare the authentic 2-methylthiophen-S-monoxide and chemical structures of **(51)** and**(52)** have not been identified yet, but component **(53)** was identified as maleic anhydride by comparison with the authentic substance. In the literature [32a] maleic anhydride has been generated in the oxidation of 2-methylthiophene with oxygen on vanadium-molybdenum oxide catalyst system.

Inorganic oxidation products, mainly volatile inorganic gases such as carbon dioxide, were the major decomposition products, formed from the complete destruction of the heterocyclic ring when excess hydrogen peroxide was employed. The ring cleavage resulted in S_8, and volatile sulphur dioxide and carbon dioxide. The sulphur species was observed in the dichloromethane extract, giving a relative molecular ion at *m/z* 256 (S_8). Carbon dioxide was easily determined by absorption into barium hydroxide solution and precipitated as barium carbonate. The quantitative yield of carbon dioxide is given in section 3.4.2.2.

b) Analysis by HPLC

Thiophene-2-carboxylic acid (**50**) was detected by the GC/MS technique, but is insufficiently volatile for accurate determination. Even concentrated samples of thiophene-2-carboxylic acid gave a broad peak. The identification of involatile oxidation products that are formed in the Fenton-catalysed oxidation of 2-methylthiophene requires the use of the HPLC technique involving development with a polar solvent system (methanol/water) at different ratios. The HPLC method outlined in section 2.1.3. was used for the analysis of the 24 hour reactions and the sample preparation method was also described in the same section. The chromatogram obtained displayed only one small peak (t_R = 9.15) on elution with a solvent mixture of methanol/water (1:4) at 2cm^3/min rate, indicating a low yield of thiophene-2-carboxylic acid (<1%). The HPLC chromatogram is shown in Figure 2.11. This was also confirmed by spiking the sample with a small amount of the standard substance. The formation of thiophene-2-carboxylic acid as an oxidation product is due to further oxidation of thiophen-2-aldehyde. This was implied since Fenton-catalysed oxidation of thiophen-2-aldehyde (**49**) resulted in the formation of thiophene-2-carboxylic acid along with the other oxidation products (section 2.2.1.5.1).

Figure 2.11. HPLC chromatogram of methanol extract of 2-methylthiophene Fenton oxidation reaction mixture.

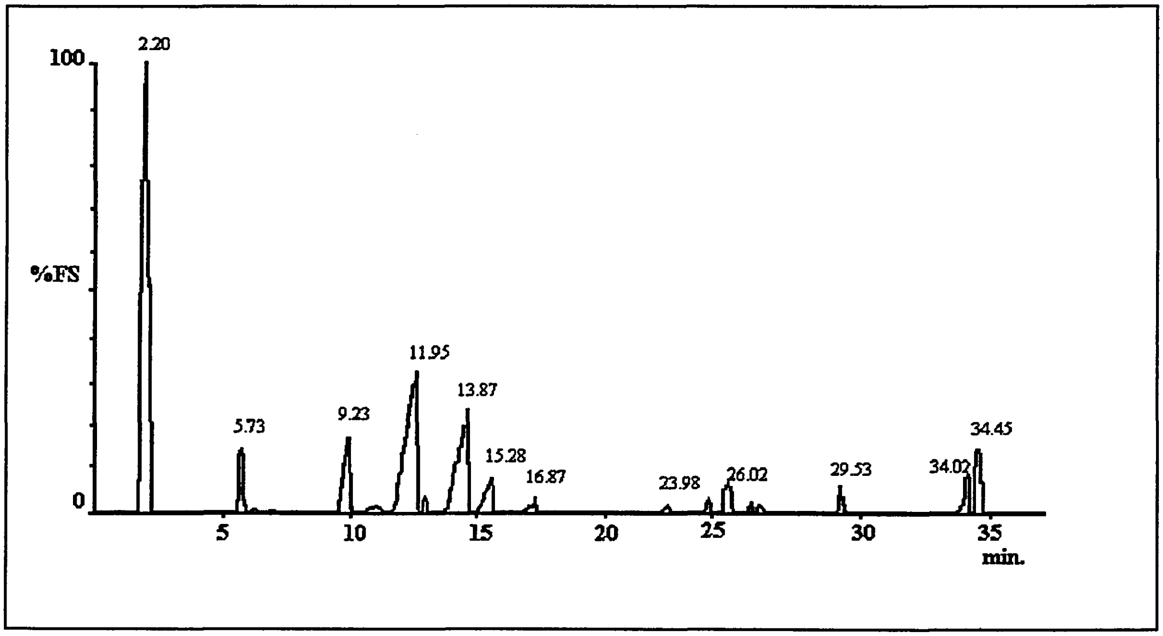


2.2.1.3. 3-Methylthiophene

a) Analysis by GC/MS

The course of Fenton-related oxidations of 3-methylthiophene (**54**) followed a similar pattern, although 3-methylthiophene had a lower oxidation rate. The Fenton- related oxidations of 3-methylthiophene was carried out over two time periods, 1 hour and 24 hour respectively. Both reactions were analysed using instrument 1 and temperature program 1 and a GC trace of the resulting reaction mixture is shown in Figure 2.12.

Figure 2.12. GC chromatogram of the Fenton-catalysed oxidation of 3-methylthiophene.



The oxidation products have been assigned structures by comparison with the authentic standard or by consideration of mass spectral data. All data obtained are summarised in Table 2.3 and Scheme 2.15 represents possible pathways for their formation.

Table 2.3. Oxidation products arising from the Fenton-catalysed oxidation of 3-methylthiophene.

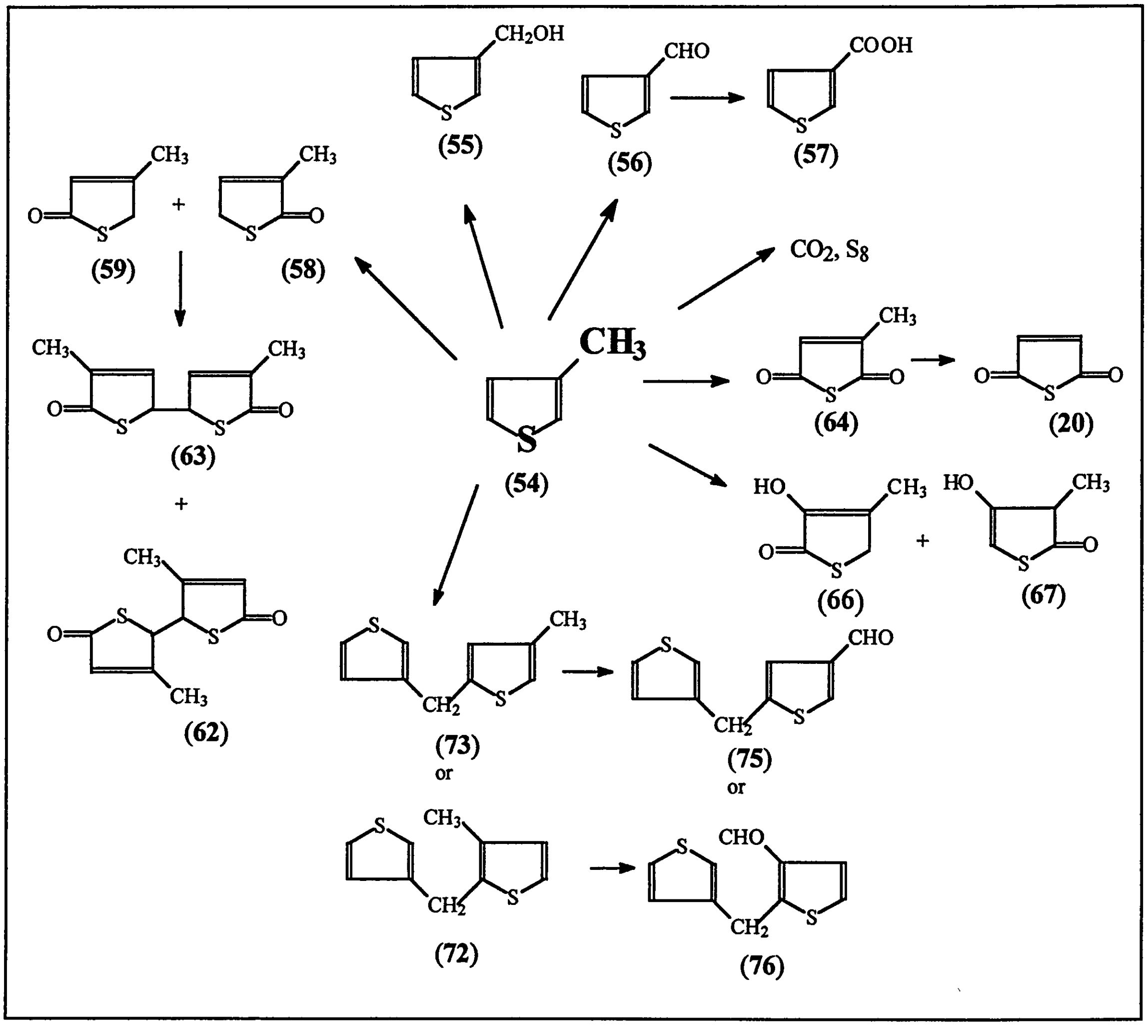
Comp. No	t_R 1 hr	t_R 24 hr	Apparent RMM	Solvent	Proposed structure
55	-	11.91	114	$MeCN/H_2O$	3-hydoxymethylthiophene
58	11.93	11.95	114	H_2O, $MeCN/H_2O$	3-methyl-(5H)thiophen-2-one
59	13.82	13.87	114	H_2O, $MeCN/H_2O$	4-methyl-(5H)thiophen-2-one
62	29.50	29.53	226	H_2O, $MeCN/H_2O$	Indigoidal dimer
63	34.00	34.02	226	H_2O, $MeCN/H_2O$	Indigoidal dimer
64	9.78	9.23	128	H_2O, $MeCN/H_2O$	3-methylthiomaleic anhydride
20*	-	5.73	114	H_2O, $MeCN/H_2O$	thiomaleic anhydride
66	-	16.87	130	H_2O, $MeCN/H_2O$	4-methyl-2,3-dihydroxy thiophene
67*	-	15.28	130	H_2O, $MeCN/H_2O$	3-methyl-2,4-dihydroxy thiophene
72 or 73	-	23.98	194	H_2O, $MeCN/H_2O$	3-methyl-2-(3-thienylmethyl) thiophene or 3-methyl-5-(3-thienylmethyl) thiophene
75 or 76*	-	26.08	208	H_2O, $MeCN/H_2O$	2-(3-thienylmethyl)thiophen-3-aldehyde or 5-(3-thienylmethyl)thiophen-3-aldehyde
56	-	9.43	112	$MeCN/H_2O$	thiophen-3-aldehyde
57	-	8.43[1]	128	$MeCN/H_2O$	thiophene-3-carboxylic acid

* Indicates that proposed structure has not been proved by comparison with the authentic substance

[1] HPLC analysis was performed by using methanol/water (1:4) at 2 ml/min.

From Table 2.3, it can be seen that allowing the oxidation of 3-methylthiophene to proceed for a long reaction period produces all oxidation products due to the relatively slow oxidation process.

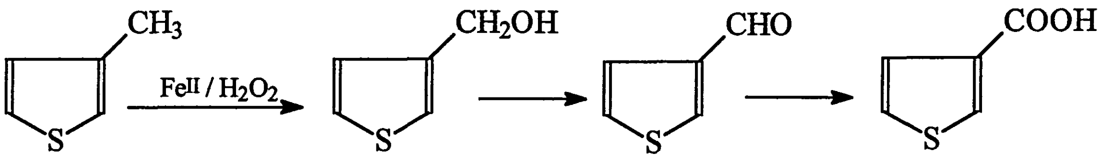
Scheme 2.15.



Again, inorganic oxidation products were mainly volatile inorganic gases, e.g. carbon dioxide and they were the major decomposition products formed from the complete destruction of heterocyclic ring, as happened with 2-methylthiophene. The ring cleavage resulted in the formation of S_8 and carbon dioxide. Sulphur was observed in the dichloromethane extract giving a molecular ion at *m/z* 256. Carbon dioxide was determined in the same way described earlier in section 2.2.1.2 and the relative amounts of generated carbon dioxide are discussed in section 3.4.2.3.

Oxidation at the methyl group gave (55), (56) and (57) as minor products and were confirmed by comparison with the authentic standard materials . A possible pathway for their stepwise oxidation is shown in Scheme 2.16.

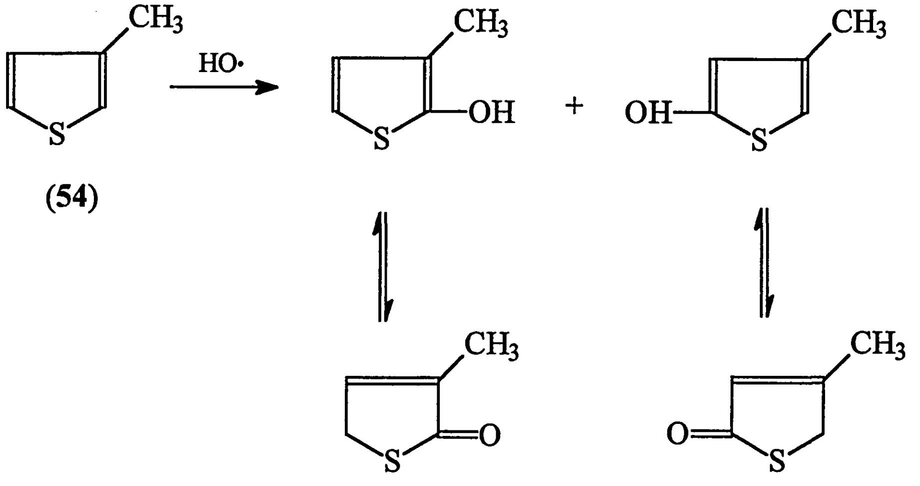
Scheme 2.16.



(54) (55) (56) (57)

Two monohydroxylated 3-methylthiophenes were observed as the main products from the Fenton-related oxidations of 3-methylthiophene; the formation of these two hydroxylated products and stable keto tautomers are outlined in Scheme 2.17.

Scheme 2.17.



(54) (58) (59)

Both of these hydroxy-3-methylthiophenes form tautomers (**58**) and (**59**) as a result of hydroxyl substitution at the thiophene ring, and exist predominantly as the keto tautomers (see discussion in section 2.2.1.1).

As indicated earlier for the hydroxylation of 2-methylthiophene, the position and nature of the substituent influence the position of the hydroxylation. In the case of 3-methylthiophene both the 2- and 5-positions of the thiophene system can react with the hydroxyl radicals, usually leading to the formation of hydroxythiophenes, namely 3-methyl-(5H)thiophen-2-one (**58**) and 4-methyl-(5H)thiophen-2-one (**59**).

The components observed in the Fenton-related oxidation of 3-methylthiophene both have the same apparent molecular mass of 114, but have different retention times (t_R = 11.95 and 13.87 respectively). The authentic substances (**58**) and (**59**) were prepared for comparison as described by Hörnfeldt and Gronowitz [18]. The GC/MS properties of the standards were identical with those of the products detected in the oxidation of 3-methylthiophene (Figures 2.13 and 2.14).

Both substances gave rise to molecular ion at *m/z* 114 and stable fragment ions at *m/z* 85 and *m/z* 71 respectively. The mass spectral fragmentation of component (**58**) is given in Figure 2.14.

Figure 2.13. GC chromatogram of mixture of the standard substances (58) and (59).

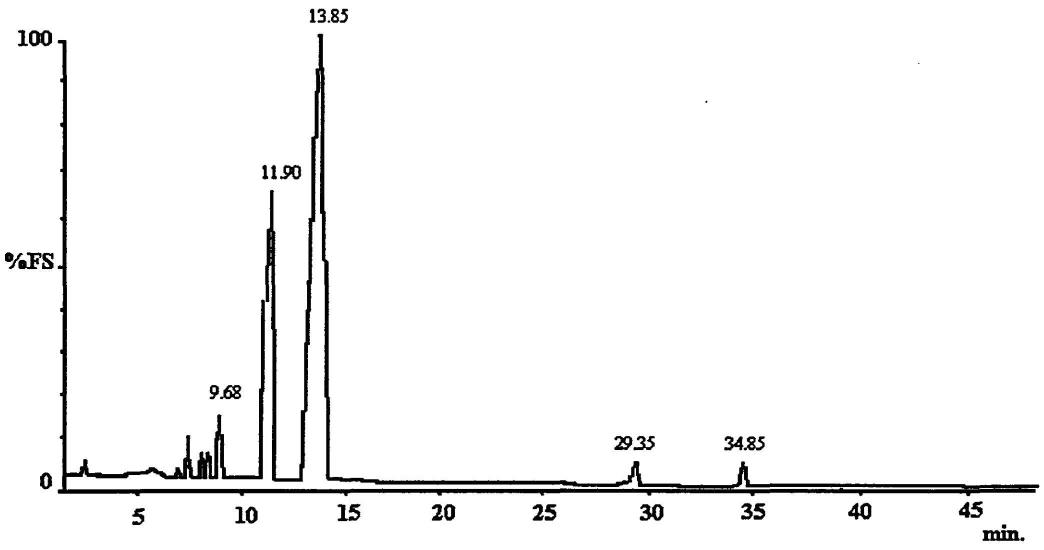
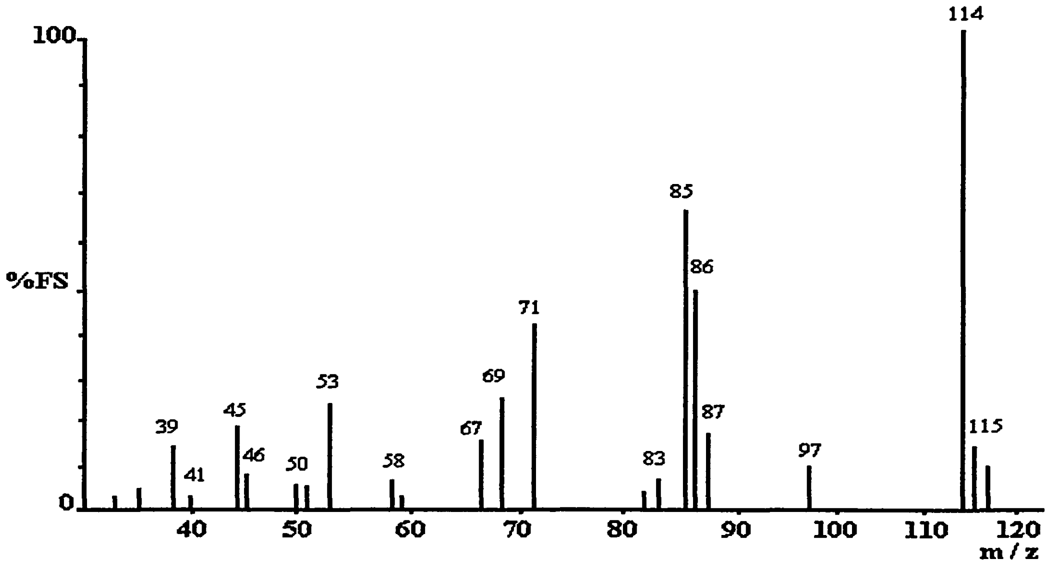
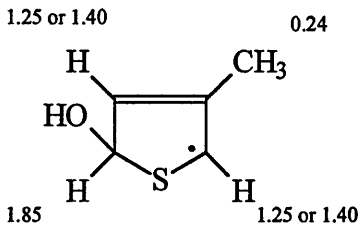


Figure 2.14. Mass spectrum of 3-methyl-(5H)thiophen-2-one (58).

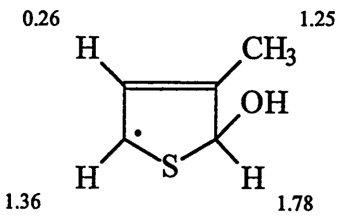


In the presence of copper(II) ions the rate of reaction was slightly decreased but the yields of components **(58)** and **(59)** increased. This phenomenon made possible the isolation of the products by using flash column chromatography. Both components were successfully isolated from the reaction mixture and their complete chemical structures were evaluated by using ^{1}H NMR. The preparation and structural elucidation of these components is given in section 4.2.1.3 in detail.

Dimerisation products, e.g. components **(62)** and **(63)** were observed as expected. In the reaction of 3-methylthiophene with radiolytically generated hydroxyl radicals, signals from the radicals **(60)** and **(61)** were observed by ESR spectroscopy [21].



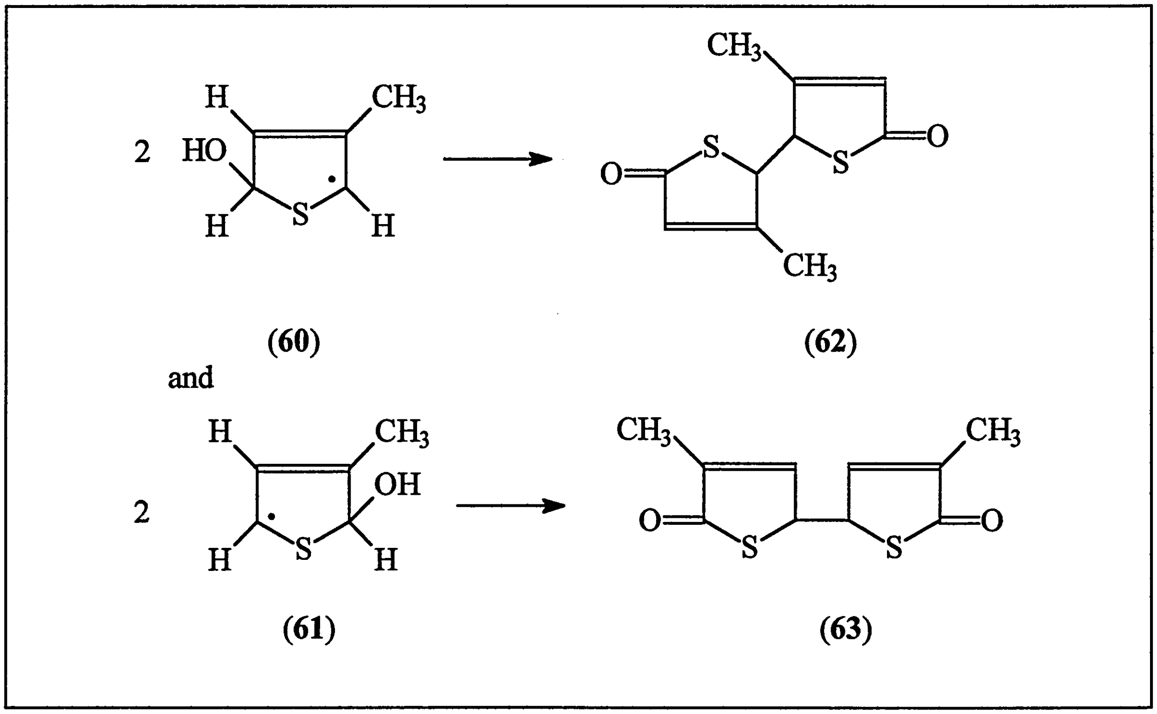
(60)



(61)

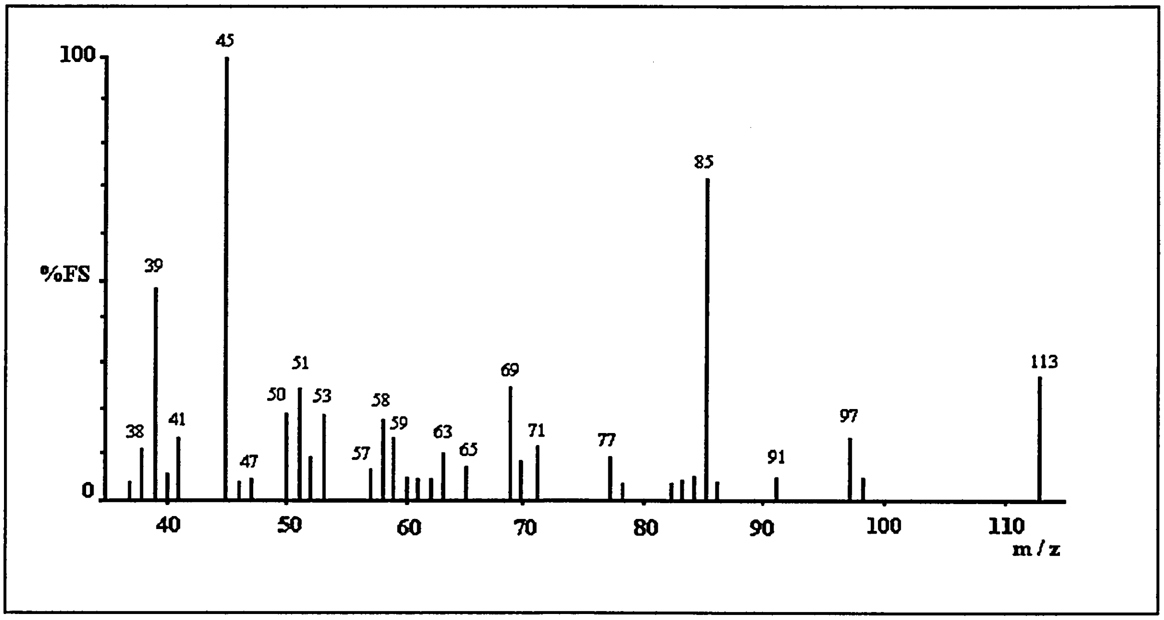
Coupling of these radicals may lead to the formation of the dimeric indigoidal structures as in the case of 5-methyl-2-hydroxythiophene. A radical coupling mechanism is shown in Scheme 2.18.

Scheme 2.18.



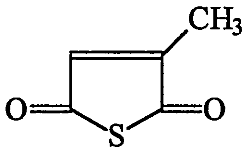
Components (**62**) and (**63**) did not give the expected molecular ion at *m/z* 226, but gave the same stable fragment ions at *m/z* 113 (Figure 2.15), whereas their retention times were different (t_R = 29.53 and 34.02 respectively).

Figure 2.15. Mass spectrum of the dimerisation product of 3-methyl-(5H)-thiophen-2-one.



The same compounds were detected by GC/MS in the synthesis of components **(58)** and **(59)**, and their GC/MS properties exhibited an excellent match with those of the above dimeric Fenton-catalysed oxidation products.

A range of dihydroxylated products was also detected in the Fenton- related catalysed oxidation reaction. Dihydroxylation led to the formation of components **(20)**, **(64)**, **(66)** and **(67)**, the structure of each of which was elucidated by comparison with standard substances or consideration of mass spectral data. Component **(64)**, thought to be 3-methylthiomaleic anhydride, was observed as a main oxidation product in all catalytic systems, but when the reaction was carried out in only water (no co-solvent used), its formation was significantly reduced. Although this compound was not prepared individually, it was also formed as a by-product in the preparation of components **(58)** and **(59)**. It is possible that 3-methylthiophene may undergo 2,5-dihydroxylation and lead to the formation of **(64)**.



3-methylthiomaleic anhydride **(64)**

Again, component **(20)** may be formed from the same reaction pathway and oxidative cleavage of methyl group. It is interesting to relate these findings to Jenning's work[32b] in which treatment of 3-methylthiophene with oxygen at elevated temperature in the presence of a catalyst of a Group Va oxide, such as vanadium, antimony or phosphorus oxides, gave 3-methylthiomaleic anhydride and thiomaleic anhydride.

Two other components, (**66**) and (**67**), giving the same apparent molecular mass of *m/z* 130 with different mass spectral fragmentation were also detected. Component (**66**) was confirmed as 4-methyl-3-hydroxy-thiophen-2-one by comparison with an authentic standard substance. This compound was prepared from the degradation of an antibiotic called cephalexin [28]. The reaction pathway and mass spectral fragmentation is given in Scheme 2.19 and Figure 2.16 respectively.

Scheme 2.19.

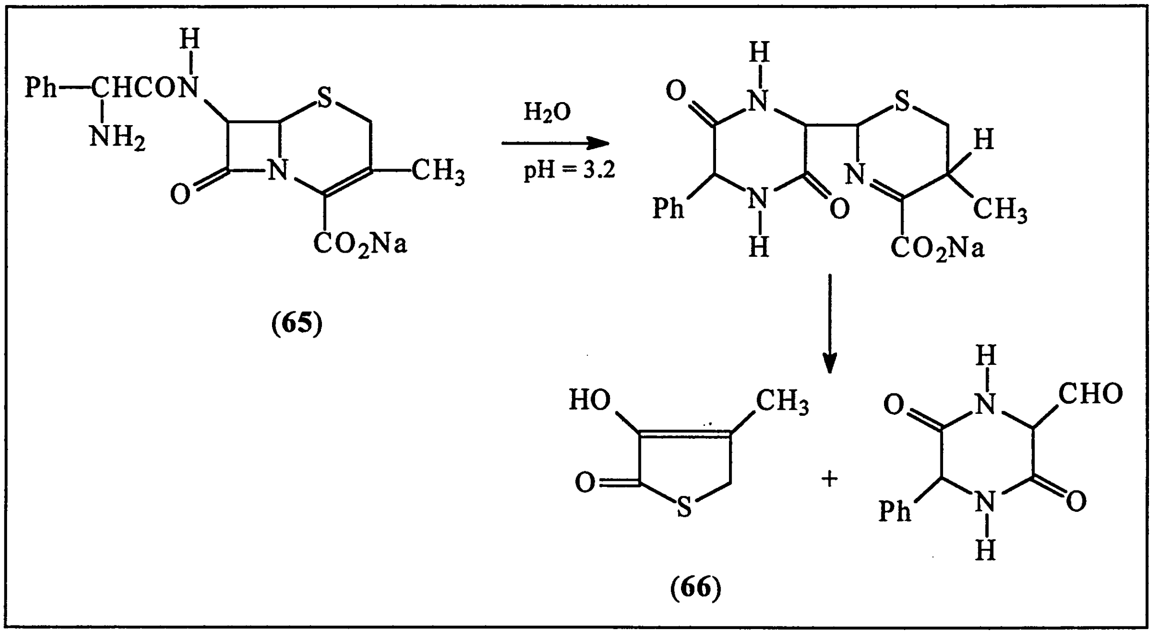
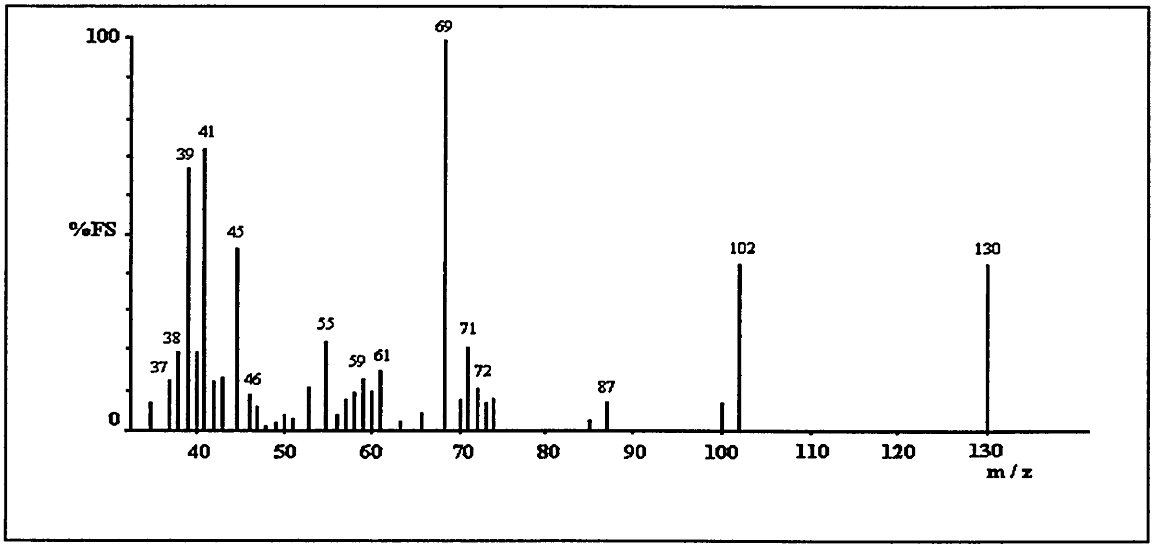
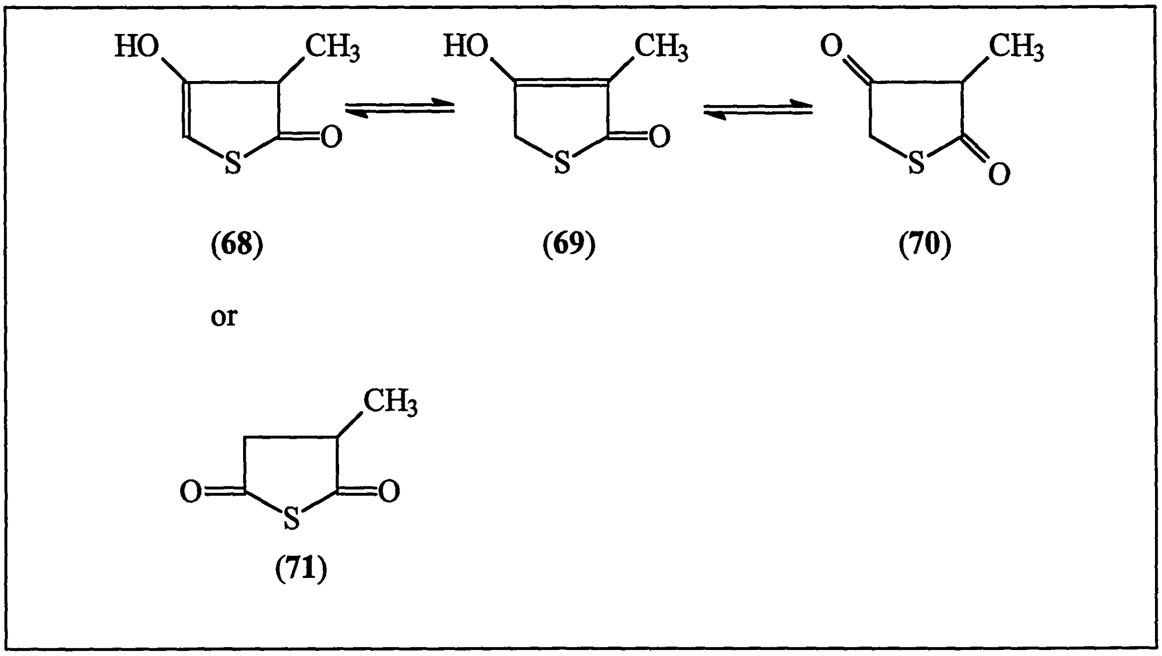


Figure 2.16. Mass spectrum of 4-methyl-3-hydroxy-thiophen-2-one.

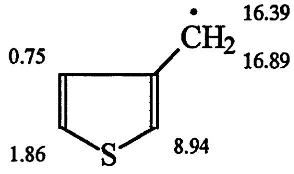


Component (**67**), on the other hand, had a different fragmentation pattern to component (**66**), showing a molecular ion at *m/z* 130 and fragment ions at *m/z* 114 and *m/z* 97 respectively. Although 2,4-dihydroxythiophenes are known in the literature [27], attempts to prepare (**67**) failed. Component (**67**) is likely to exist in several tautomeric forms (**68-70**) or the isomer (**71**) as shown in Scheme 2.20.

Scheme 2.20.



A dithienylmethane system was also formed in the Fenton and related oxidations of 3-methylthiophene. Although almost certainly (**73**) (on the basis of an hindered attack by the 3-thienylmethyl radical at the free 5-position of 3-methylthiophene), it was not possible to rule out structure (**72**) for this product. ESR studies indicate the formation of 3-thienylmethyl radical (**74**) was observed in the steady-state photolysis of dibenzoyl peroxide in 3-methylthiophene [31]. This radical (**74**) has greater spin population and is 2.2. fold less reactive than the 2-thienylmethyl radical (**44**) [21, 31], so the 3-thienylmethyl radical is more reluctant to be involved in further reactions.



(74)

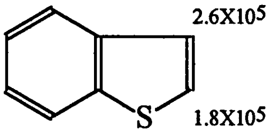
As a result of this reduced activity, dithienylmethane systems are formed in low yields. A synthetic approach to these systems gave a mixture of the isomeric dithienylmethanes, **(72)** and **(73)** which could not be separated on a preparative scale (see section 4.1.2.2). GC/MS analysis revealed the presence of the two isomers having virtually identical retention times (t_R = 24.38 and 24.82) and mass spectral fragmentation patterns (apparent molecular ion at *m/z* 194 and fragment ion at *m/z* 179), making an unequivocal distinction between the alternative structures impossible. Again, further oxidation of component **(72)** or **(73)** gave an apparent aldehyde having a molecular ion *m/z* 208 for which structures **(75)** or **(76)** are possible as a result of further oxidation of a methyl group to the aldehyde.

b) Analysis by HPLC

The identification of involatile oxidation products formed in the Fenton-catalysed oxidation of 3-methylthiophene requires the use of the HPLC technique, with a polar solvent system, such as methanol/water (1:4, t_R = 8.43). The HPLC method outlined in section 2.1.3. was used for study of the products of the 24 hour reaction period and sample preparation method was also described in the same section. Trace amounts of thiophene-3-carboxylic acid **(57)** were detected. The structure of this component was confirmed by comparison with an authentic sample.

2.2.1.4. Benzo-[b]-thiophene

Aryl fusion weakens the aromatic character of the thiophene ring [13]. Benzo-[b]-thiophene is related to the monocyclic heterocycles in the same way that naphthalene is a benzo derivative of benzene. From a chemical standpoint, the chief effect of fusing the benzene ring onto the simple heterocycle is to increase the stability and to change the preferred orientation in electrophilic substitution from C-2 to C-3 [3]. Because of this stabilization, benzo-[b]-thiophene undergoes substitution reactions in the thiophene ring rather than benzene ring, but is still less reactive than thiophene itself. Partial rate factors for electrophilic substitution reactions indicate that the C-3 position is more reactive than the C-2 position.



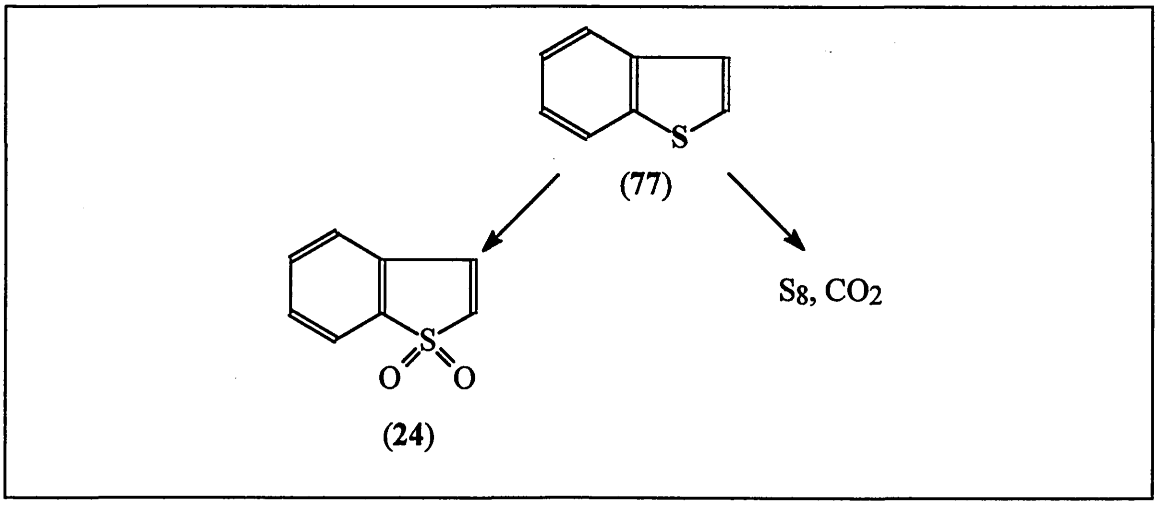
(77)

As described earlier, Fenton- related oxidation of simple thiophenes (thiophene and 2- and 3-methylthiophene) resulted in hydroxylation. It was interesting to see whether or not the fused aryl group would change the reaction pathway, decomposition mechanism and reaction intermediates. The oxidation of benzo-[b]-thiophene was carried out using Fenton-related catalytic systems for 1 hour and 24 hour reaction periods. An acetonitrile/water co-solvent system was employed in order to dissolve the benzo-[b]-thiophene and the reaction was always extremely exothermic at room temperature. The reaction was repeated using different solvent systems, e.g. methanol and glacial acetic acid. The Fenton-catalysed oxidation of benzo-[b]-thiophene was vigorously exothermic in acetonitrile and methanol, but was milder when acetic acid was employed as solvent. Reaction did not occur in the absence of co-solvent due to the insolubility of the substrate in water. The dichloromethane extracts were analysed using instrument 1 and temperature program 1 as described in section 2.1.3. The oxidation reaction with iron(II) and copper(II) containing catalytic systems always led to complete oxidation of benzo-[b]-thiophene but only benzo-[b]-thiophen S,S dioxide (1,1 dioxide or sulphone) **(24)** was detected as the oxidation product. The structure of this oxidation product was confirmed by using an authentic standard and the results are summarised in Table 2.4 and Scheme 2.21.

Table 2.4. Organic oxidation product arising from the Fenton-catalysed oxidation of benzo-[b]-thiophene.

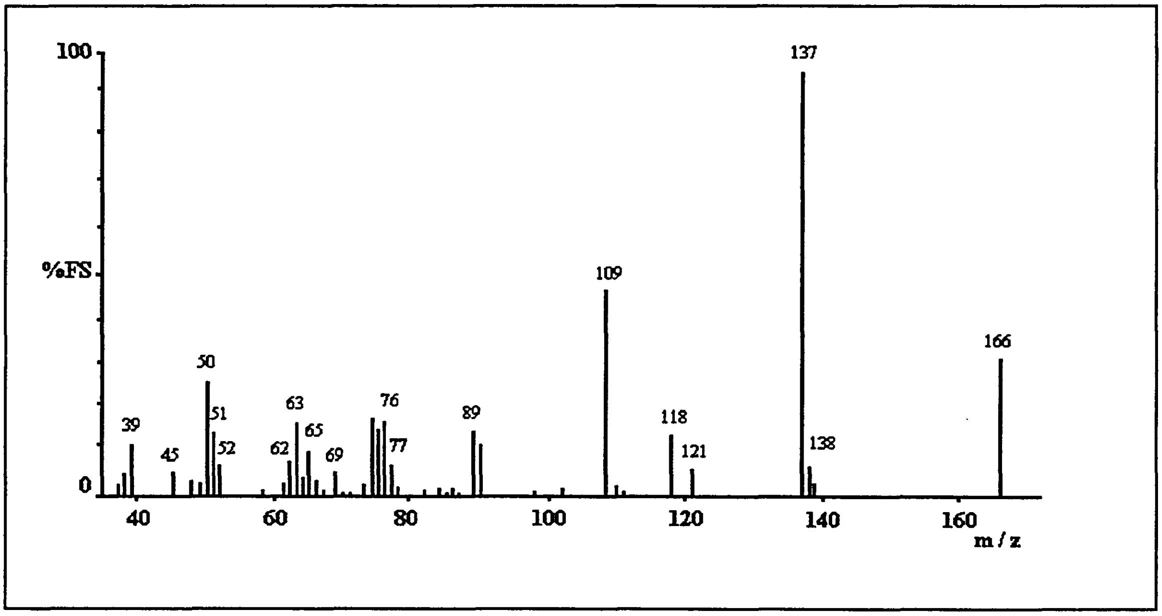
Comp. No	t_R 1 hr	t_R 24 hr	Apparent RMM	Solvent	Proposed structure
24	-	30.96	166	CH_3COOH/H_2O $MeOH/H_2O$ $MeCN/H_2O$	benzo-[b]-thiophen-S,S-dioxide

Scheme 2.21.



Benzo-[b]-thiophene S,S' dioxide (**24**), which was synthesized from a well-known oxidation process (see section 4.3), gave an apparent molecular ion at *m/z* 166 and a stable fragment ion at *m/z* 137 (Figure 2.17).

Figure 2.17. Mass spectrum of benzo-[b]-thiophene S,S' dioxide.



This result is very interesting compared with thiophene and its 2- and 3-methyl derivatives because the oxidation occurs at the sulphur atom and no hydroxylated product is observed.

Inorganic oxidation products, S_8 and carbon dioxide, also observed, were again derived from the main ring cleavage. Their determination has already been discussed in relevant sections related to thiophene and 2- and 3-methylthiophene.

2.2.1.5. Further Fenton-related Oxidation of Intermediate Products

Further Fenton-related oxidations of reaction intermediates were carried out in order to help understand whether the oxidation products described in section 2.2.1 are derived directly from the original compound or from further oxidation of a reaction intermediate.

Fenton-catalysed oxidations of thiophene-2-aldehyde (**49**), 2-hydroxymethylthiophene (**28**), 5-methyl-2-hydroxythiophenes (**29**) and (**30**) and 2-methyl-5-(2-thienylmethyl)-thiophene (**45**) were studied under the same conditions given in section 2.1.3 and were analysed using instrument 1 and temperature programme 1.

2.2.1.5.1. Thiophene-2-aldehyde (49)

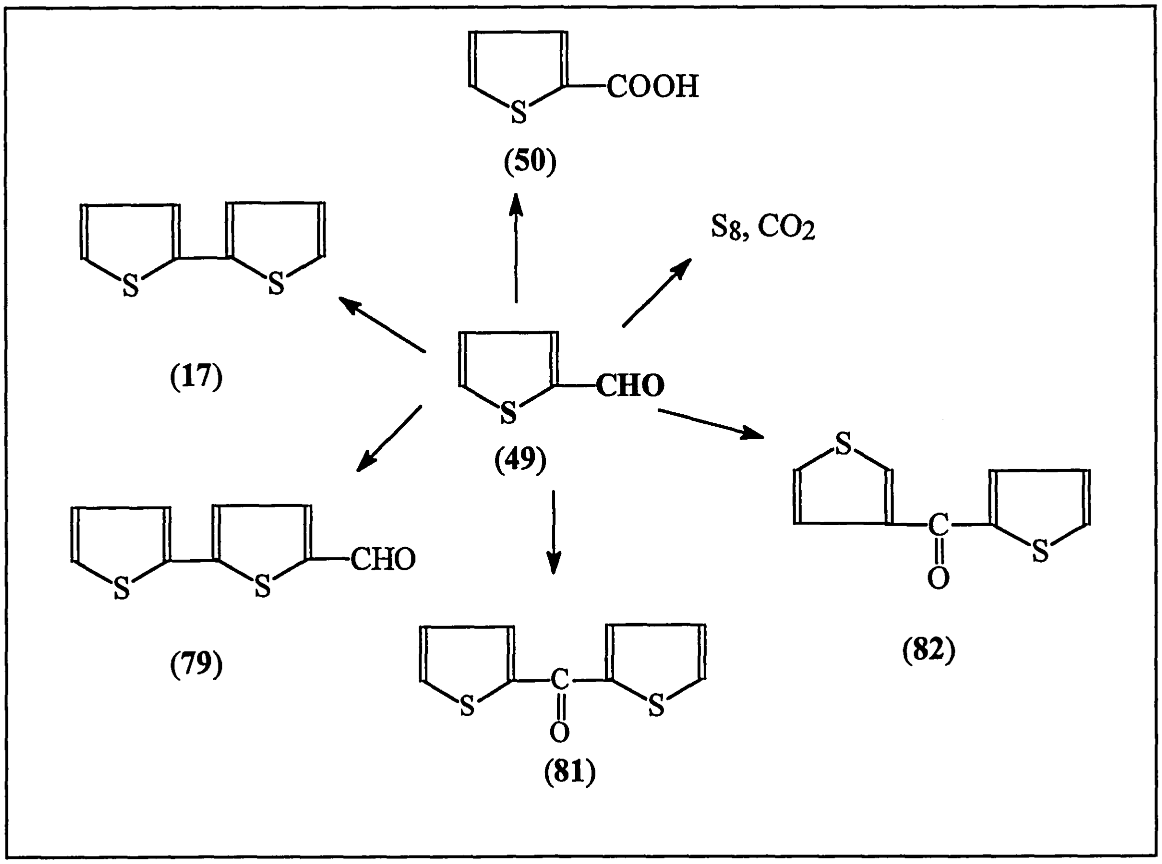
The oxidation of thiophene-2-aldehyde was carried out using Fe(II)/hydrogen peroxide and Fe(II)+Cu(II)/hydrogen peroxide systems in water. The oxidation was very effective and gave rise to complete oxidation of thiophene-2-aldehyde to ring cleavage products (e.g. S_8 and carbon dioxide) when the Fe(II)/hydrogen peroxide system was employed. On the other hand, the copper-containing system led to the formation of thiophene-2-carboxylic acid and some dimeric products, each of which had not been observed in the Fenton-related oxidation of parent substrate, 2-methylthiophene. This indicates that thiophene-2-carboxylic acid is probably derived from the further oxidation of thiophene-2-aldehyde. The identity of the oxidation products was confirmed by making a comparison with either standard samples or by consideration of mass spectral data.

The results are summarised in Table 2.5. Possible structures and reaction pathways are shown in Scheme 2.22.

Table 2.5. Oxidation products arising from the Fenton-catalysed oxidation of thiophene-2-aldehyde (49).

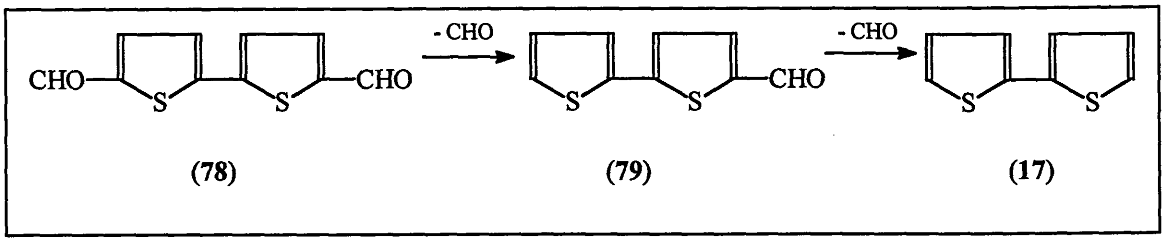
Comp. No	t_R (24 hr)	Apparent RMM	Solvent	Proposed structure
50	18.68	128	H_2O	thiophene-2-carboxylic acid
17	21.78	166	H_2O	2,2'-bithiophene
79	29.78	194	H_2O	2,2'-dithienyl-5-aldehyde
81	30.16	194	H_2O	2,2'-dithienylketone
82*	30.46	194	H_2O	2,3'-dithienylketone

Scheme 2.22.

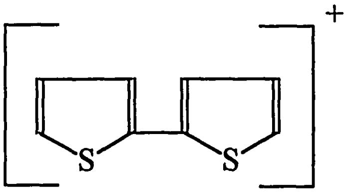


Component **(50)** was detected even with the GC/MS technique and confirmed by comparison with the authentic sample. The other three components were thought to have arisen as a result of the rearrangement of related dimeric structures. For example, 2,2'-bithiophene-5,5'-dicarboxaldehyde **(78)** was not observed as an oxidation product in the Fe(II) and Cu(II)-catalysed oxidation reaction, and it is suggested that formation of 2,2'-bithiophene-5-carboxaldehyde **(79)** occurs via rapid loss of an aldehyde group with loss of a second aldehyde group giving 2,2'-bithiophene **(17)**. Scheme 2.23 shows the possible pathway for their formation.

Scheme 2.23.



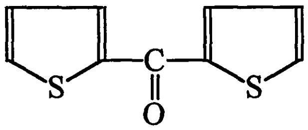
Components **(79)**, **(81)** and **(82)** possessed the same apparent molecular ion at *m/z* 194, but **(81)** and **(82)** had different mass spectral fragmentation patterns from **(79)** which exhibited aldehyde fragmentation, indicating the loss of -CHO, giving a stable ion at *m/z* 165 **(80)** as shown below.



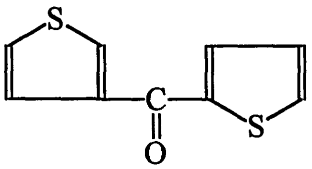
(80)

The authentic 2,2'-bithiophene-5-aldehyde was prepared from 2,2'-bithiophene and both retention time and mass spectral fragmentation showed a perfect match with the oxidation product of thiophene-2-aldehyde.

Components (**81**) and (**82**) had very similar retention times (t_R = 30.16 and 30.46 respectively) with identical fragmentation indicating that these are closely related isomers and 2,2'-dithienylketone and 2,3'-dithienylketone, respectively, were suggested as possible structures.



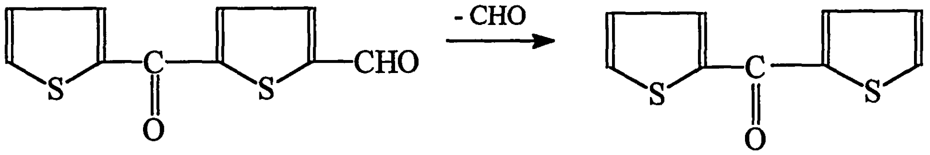
2,2'-dithienylketone



2,3'-dithienylketone

Component (**81**) was identified as 2,2'-dithienylketone by comparison with an authentic standard compound prepared using the method described in section 4.1.2.3.1a. Component (**82**) has not been prepared individually and its structure was assigned from the GC/MS similarities with component (**81**). The possible formation pathway for component (**81**) is shown in Scheme 2.24.

Scheme 2.24.

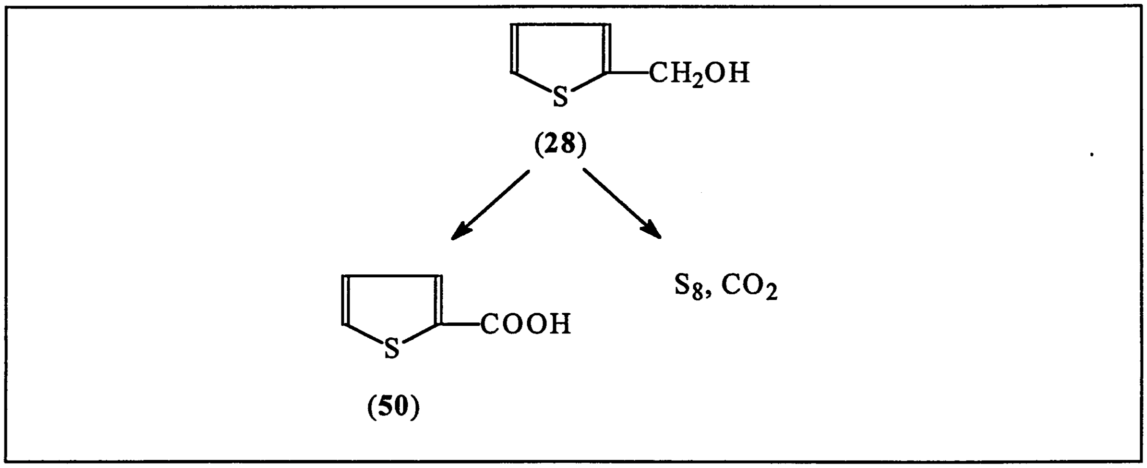


(**81**)

2.2.1.5.2. 2-Hydroxymethylthiophene (28)

Fenton-related oxidation of 2-hydroxymethylthiophene (**28**) was carried out in the presence of iron(II) and copper(II) ions, as described earlier in section 2.2.1.2 for the parent compound 2-methylthiophene. In contrast with the results obtained from thiophene-2-aldehyde, no dimeric products were observed and thiophene-2-carboxylic acid was the only product along with the inorganic decomposition products carbon dioxide and sulphur (Scheme 2.25).

Scheme 2.25.



The thiophene-2-carboxylic acid (**50**), which was produced in low yield, was determined by the HPLC technique using methanol/water (1:4) as mobile phase (t_R=9.15).

2.2.1.5.3. 5-Methyl-2-hydroxythiophenes (29) and (30)

A mixture of components (**29**) and (**30**) was oxidized with the Fe(II)+Cu(II)-containing catalysis system. The reaction was very effective and almost all the hydroxythiophene was oxidized giving mainly the indigoidal dimeric products and multiple hydroxylation products which had been observed in the oxidation of parent compound 2-methyl thiophene. The oxidation products are summarised in Table 2.6 and the possible structures and reaction pathways are shown in Scheme 2.26.

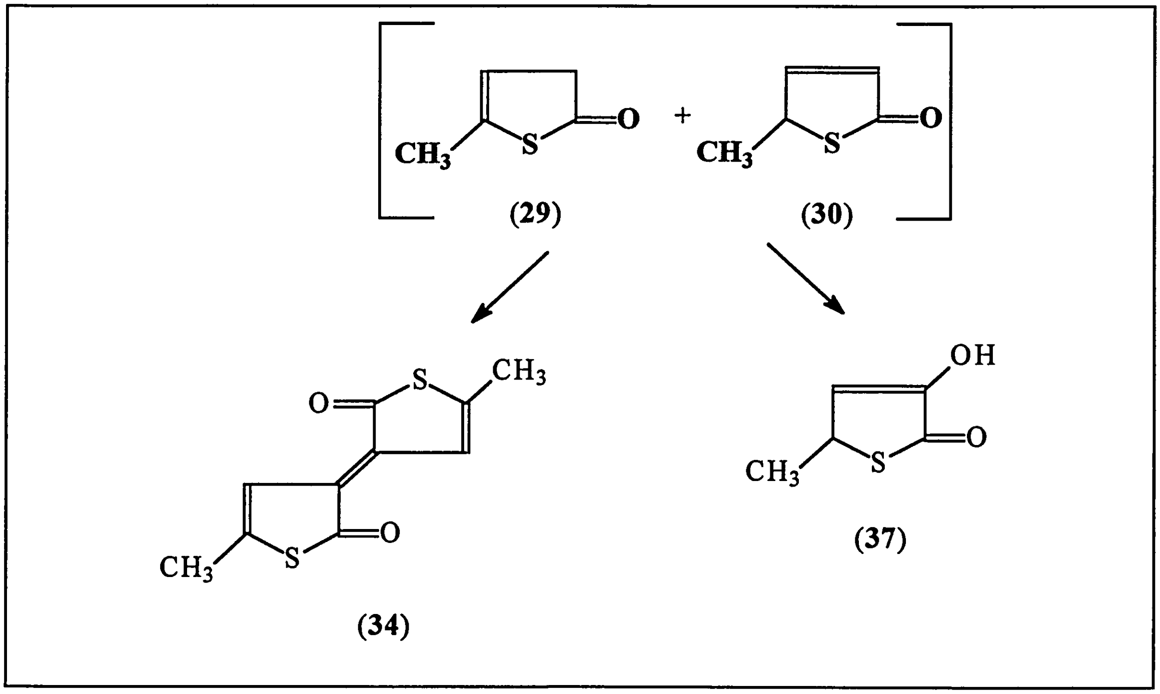
Table 2.6. Oxidation products arising from the Fenton-catalysed oxidation of 5-methyl-2-hydroxythiophenes.

Comp. No	t_R (24 hr)	Apparent RMM	Solvent	Proposed structure
37*	13.05	130	H_2O	5-methyl-2,3-dihydroxythiophene
34	33.02	224	H_2O	indigoidal structure

* Indicates that proposed structure has not been proved by comparison with the authentic substance

From Table 2.6, it may be seen that the further oxidation products from the Fenton-related oxidation of 5-methyl-(3H)-thiophen-2-one and 5-methyl-(5H)-thiophen-2-one are the same as the products observed in the oxidation of parent 2-methylthiophene.

Scheme 2.26.



Particularly, further hydroxylation gave component **(37)** and oxidative dimerisation resulted in the formation of component **(34)**. Some other minor products were also observed, but they were not related to the products of 2-methylthiophene, so they are not discussed here due to their complicated nature. Ring cleavage products S_8 and carbon dioxide were also observed.

As indicated in the literature, 2,5-disubstituted thiophenes can undergo oxidation at sulphur resulting in the S-monoxide or the S,S-dioxide [11,12,16]. It may be expected that 5-methyl-2-hydroxythiophenes behave like 2,5 disubstituted thiophenes and S-monoxide or S,S-dioxide may arise from the Fenton-related oxidation of components **(29)** and **(30)**. Metachloroperbenzoic acid (m-CPBA) oxidation of 2,5 disubstituted thiophenes gives S,S-dioxides in good yield. For example, when 2,5-dimethylthiophene was treated with m-CPBA, 2,5-dimethylthiophen-S,S-dioxide was obtained, but in contrast to this, oxidation of 5- methyl-2-hydroxythiophenes did not give S-monoxide or S,S-dioxide. The oxidation reaction of 5-methyl-2-hydroxythiophenes was repeated with hydrogen peroxide in acetic acid which gives the S,S-dioxide with 2,5-dimethylthiophene. However, no oxidation at the sulphur atom was observed. It can be concluded that the Fenton and related oxidation of hydroxythiophenes results in multiple hydroxylation rather than sulphur oxidation.

2.2.1.5.4. 2-Methyl-5-(2-thienylmethyl)thiophene (45)

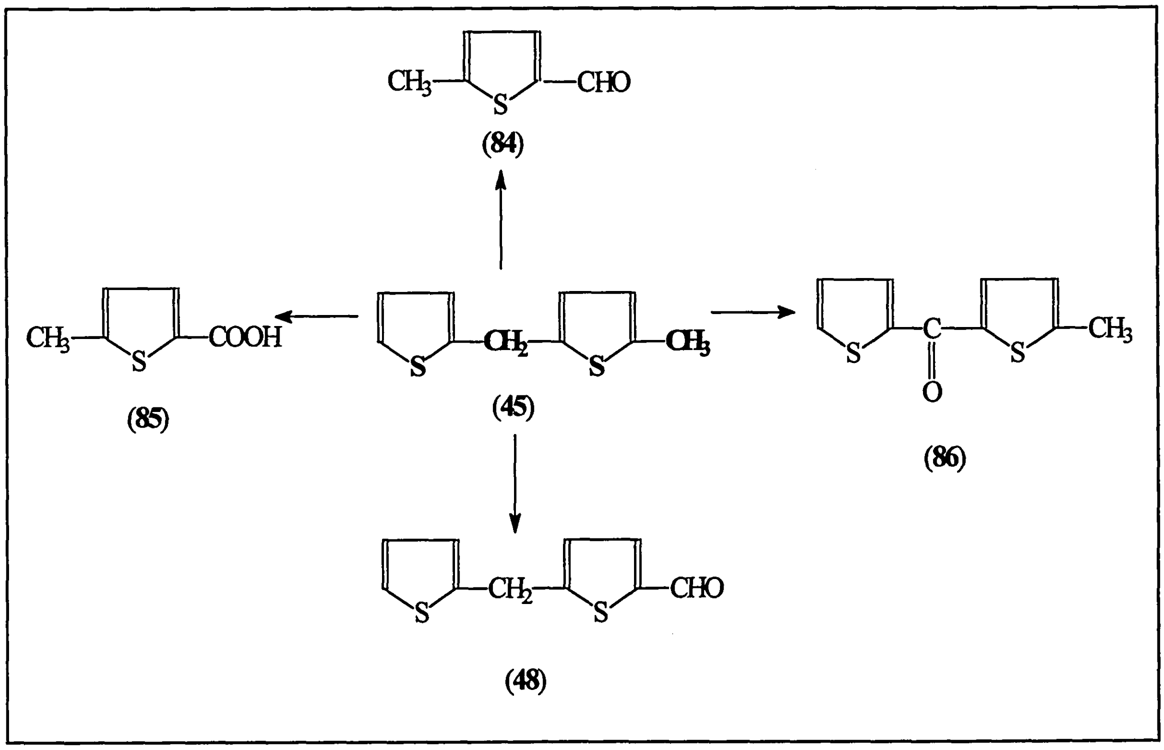
Synthetically prepared component **(45)** was treated with hydrogen peroxide containing the iron(II) and copper(II) catalytic system in acetonitrile, owing to its insolubility in water. The structures of the resulting products were confirmed either by comparison with an authentic sample or by consideration of mass spectral data. These results are summarised in Table 2.7. Scheme 2.26 represents possible pathways for their formation.

Table 2.7. Oxidation products arising from the Fenton-catalysed oxidation of 2-methyl-5-(2-thienylmethyl)thiophene

Comp. No	t_R (24 hr)	Apparent RMM	Solvent	Proposed structure
84	12.42	126	MeCN/H_2O	5-methylthiophen-2-aldehyde
85	18.25	142	MeCN/H_2O	5-methyl-thiophene-2-carboxylic acid
48*	30.09	208	MeCN/H_2O	5-(2-thienylmethyl)thiophen-2-aldehyde
86	31.39	208	MeCN/H_2O	2,2'-(5-methyl)-dithienylketone

* Indicates that proposed structure has not been proved by comparison with the authentic substance

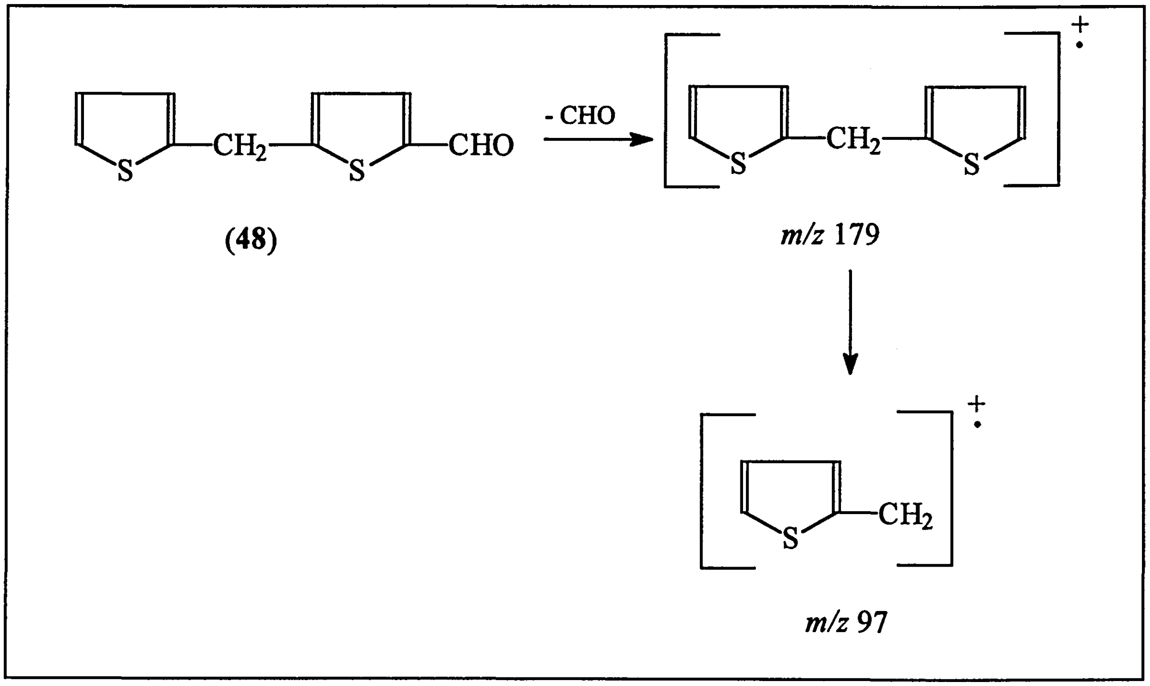
Scheme 2.26.



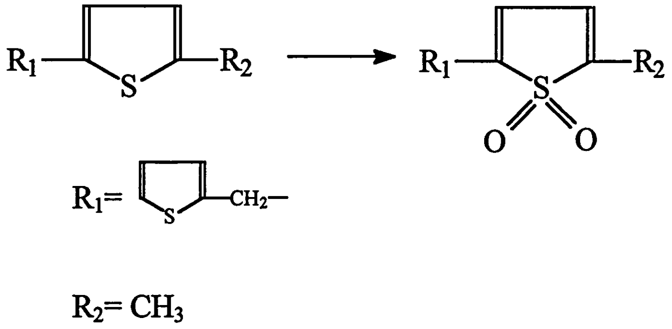
Component **(48)** is related to the oxidation products of parent 2-methylthiophene under the same conditions. Again, oxidation occurred on the methyl group rather than the sulphur and its possible formation pathways were discussed earlier in Scheme 2.14. Direct oxidation of **(45)** to **(48)** supports the proposed structure. The mass spectrum generated for component **(48)** contains stable fragment ions at *m/z* 179 and 97 respectively. The first fragmentation represents the loss of -CHO an indicative fragmentation pattern for aldehydes (Scheme 2.27).

Although components **(84)**, **(85)** and **(86)** were confirmed by comparison with authentic samples, they were not observed in the Fenton-related oxidations of 2-methylthiophene.

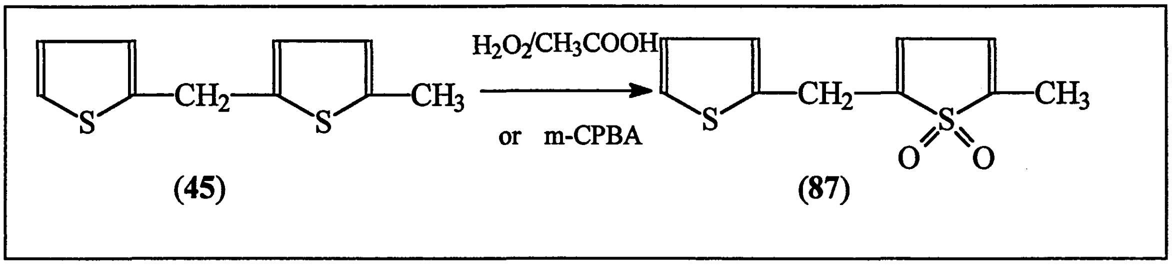
Scheme 2.27.



2-Methyl-5-(2-thienylmethyl)thiophene (**45**) behaves like 2,5-disubstituted thiophenes when oxidized with m-chloroperbenzoic acid or hydrogen peroxide/acetic acid systems (Scheme 2.28), but not with Fenton-related reagents.



Scheme 2.28.



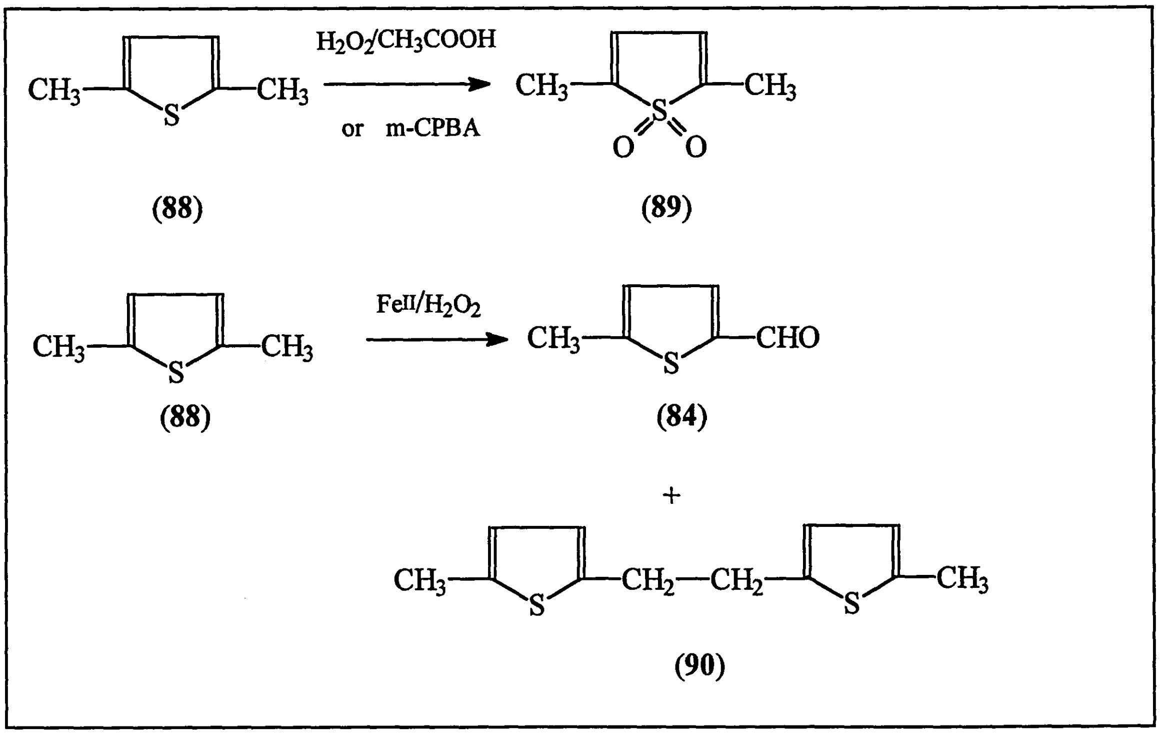
(**45**)

(**87**)

2-methyl-5-(2-thienylmethyl)thiophene S,S-dioxide (**87**) was prepared by using both methods shown above. This component was isolated and its structure was identified by NMR (see section 4.3). It is further evidence that Fenton-type oxidation occurs by a side-chain oxidation mechanism rather than sulphur oxidation.

Similar results were observed with 2,5-dimethylthiophene (**88**), where oxidation with the above systems gave 2,5-dimethyl-S,S-dioxide in both cases (section 4.3), but Fenton-catalysed oxidation resulted in the formation of 5-methylthiophene-2-aldehyde (**84**) and 2,2'-(5-methyldithienyl)ethane (**90**), with no S,S-dioxide (Scheme 2.29).

Scheme 2.29.



2.2.1.6. Summary

The oxidation of thiophenes, their methyl substituted derivatives and benzo-[b]-thiophene, using Fenton's reagent, generates an extensive range of oxidation products. The structures of the products indicate that thiophenes are oxidized effectively, achieving complete conversion to hydroxylated products, dimeric structures and ring cleavage products, such as carbon dioxide and, surprisingly, elemental sulphur. It would seem that the mechanism for the formation of many of these compounds involves free radical chemistry. This conclusion is largely based on the formation of a range of dimeric structures in each of the reactions studied here. The oxidation rate and the range of products showed differences depending on the position of methyl substitution. The Fenton-catalysed oxidation reactions do appear to be time-dependent, since allowing the reaction to proceed overnight produces a greater degree of destructive oxidation with fewer organic oxidation products being observed.

All of the Fenton-related oxidizing systems generated an extensive range of oxidation products. Especially, using copper(II) together with iron(II) increased the extent of formation of dimeric structures. However, in order to draw any comparison between each of them, quantitative analysis was carried out, following the decrease in concentration of the appropriate thiophene during each of the oxidation reactions as an indication of the effectiveness of the system used. Also, the isolation of some components from the oxidation mixture made it easier to obtain an approximate yield. All these findings will be given in Chapter 3.

2.3. Other Oxidizing Systems

2.3.1. Fenton-like Oxidizing Systems

The oxidation of thiophenes already described in this Chapter have involved the use of both iron- and copper-containing catalysts. However, it is known that there are several other metal ions which interact with hydrogen peroxide to produce reagents that are capable of oxidizing an organic system. The oxidation of a variety of organic substrates by a mixture of a low-valent transition-metal catalyst and hydrogen peroxide is commonly attributed to a "Fenton-like" mechanism [33]. Numerous metal ions and their complexes, in their lower oxidation states, for example Cu(I), Cu(II), V(IV), Ti(III), Cr(II) and Co(II), have been found to possess the oxidation features of the Fenton reagent. Therefore, combinations of these metals with hydrogen peroxide have been called "Fenton-like" reagents [33,34]. Some kinetic studies have shown that hydroxyl radicals are generated from mixture of hydrogen peroxide and metal complexes [35,36]. According to Norman [36], the interaction of titanium(III) ions and hydrogen peroxide generates free hydroxyl radicals which are the primary oxidizing agents. When iron(II) ions were replaced by titanium(III) ions, the same organic radicals were generated, although iron-containing reagents showed a greater degree of oxidation than titanium(III), probably due to the different nature of the metal complexes formed. There is some evidence in favour and some against the formation of hydroxyl radicals with the Fenton-like reagents and all these have been discussed earlier in section 1.3.2.1. Hence, the oxidation of the thiophene derivatives with Fenton-like reagents including vanadium(IV), titanium(III), copper(I) and copper(II) is of interest, since all of these metal ions appear to form hydroxyl radicals. Thus, the oxidation of thiophene and 2- and 3-methylthiophene was carried out using these catalyst systems. The systems used were as follows;

Vanadium (IV) sulphate / hydrogen peroxide
Copper(I) chloride / hydrogen peroxide
Copper(II) chloride / hydrogen peroxide
Copper(II) sulphate / hydrogen peroxide
Titanium(III) chloride / hydrogen peroxide

The experimental procedure for each of these oxidation reactions is outlined in section 2.1. and the GC/MS conditions are given in section 2.1.3. It is also suggested in the literature that titanium dioxide-assisted photocatalytic systems are involved in radical chemistry, in particular oxidation via hydroxyl radicals formed from the interaction of semi-conductor surfaces with light (section 1.3.3). The titanium dioxide-assisted photocatalytic reaction of 2-methylthiophene was carried out in an aqueous system and after particular time periods of illumination, the products were analysed. All these oxidation methods and oxidation products are discussed as separate sections in this Chapter.

2.3.1.1 Fenton-like Oxidation Reactions of Thiophene

The Fenton-like oxidation reactions of thiophene were carried out with vanadium(IV), copper(I), copper(II) and titanium(III) catalyst systems individually, using the same reaction conditions as described in section 2.1. The oxidation products observed were generally the same as in the Fenton-related reactions, although additional products were produced in the presence of titanium(III) catalyst system. The structures of the oxidation products have been assigned, either by comparison with authentic standards or by consideration of mass spectral data and they are summarised in Table 2.8. As the oxidation reactions proceed slower than Fenton-related reactions, the results shown here represent 24 hour reaction periods.

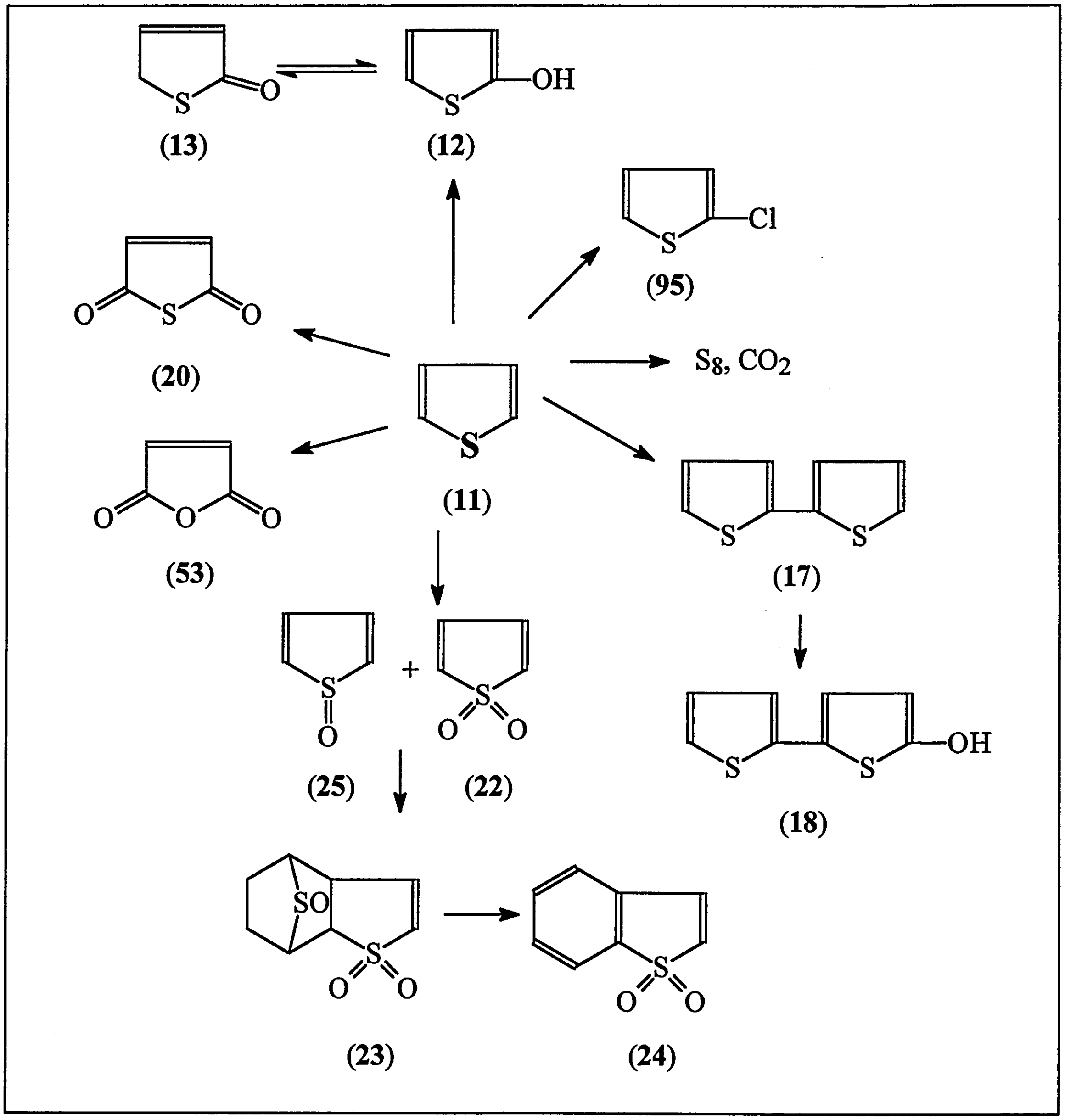
Table 2.8. Oxidation products arising from the Fenton-like oxidation of thiophene.

Comp. No	t_R 24 hr	Apparent RMM	Solvent	Catalyst	Proposed structure
20*	6.27	114	MeCN/H_2O, H_2O	V(IV), Cu(I), Cu(II), Ti(III)	thiomaleic anhydride
53	3.36	98	MeCN/H_2O	Cu(I), Cu(II)	maleic anhydride
13	9.92	100	MeCN/H_2O, H_2O	Cu(I), Cu(II), Ti(III)	(5H)-thiophen-2-one
21*	11.11	116	MeCN/H_2O	Cu(I), Cu(II)	Unknown
17	20.77	166	H_2O	Ti(III)	2,2'-bithiophene
92*	21.73	164	H_2O	Ti(III)	unknown
24	25.82	166	H_2O	Ti(III)	benzo-b-thiophen-S,S-dioxide
95	2.45	118	H_2O	Ti(III)	2-chlorothiophene

* Indicates that proposed structure has not been proved by comparison with the authentic substance

Although a strongly exothermic reaction occurred in the acetonitrile-water solvent system, no oxidation product was observed from vanadium(IV)-catalysed oxidation of thiophene with hydrogen peroxide except for the minor component (**20**) and inorganic ring decomposition products (e.g. S_8). The reaction was milder in the absence of acetonitrile co-solvent, but no organic oxidation product was found in the reaction mixture. The amount of unreacted thiophene is 22% of the starting amount (see section 3.4.2.1), and this indicates that oxidation did occur but led only to oxidative decomposition largely to give inorganic products.

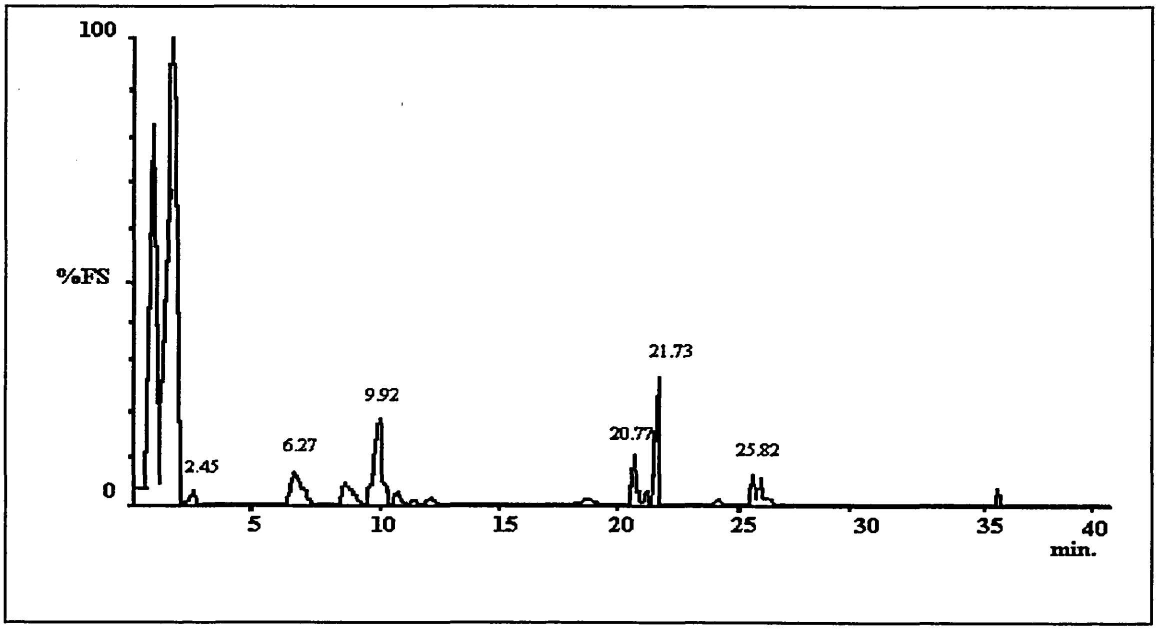
Scheme 2.30.



The oxidation reaction of thiophene was carried out using different copper salts; copper(II) sulphate, copper(II) chloride and copper(I) chloride as catalyst systems.

Using different copper(II) salts did not affect the product formation, but the solvent system used showed remarkable effects. (5H)-Thiophen-2-one (**13**) was the only major product in the absence of the co-solvent system, although its formation was significantly decreased in the presence of acetonitrile-water and components (**20**), (**21**) and (**53**) were also formed along with (5H)-thiophen-2-one. Although the same oxidation products were obtained from both Fenton-related and copper(I and II)-catalysed oxidation of thiophene, the latter catalyst system was completely ineffective over a short reaction period (1 hour). A long reaction period (24 hour), on the other hand, gave (5H)-thiophen-2-one in higher yield (59 %)[37] and details are given in section 3.4.2.1. The copper(II)-catalysed system looks very effective for the hydroxylation rather than the destructive oxidation of thiophene. The titanium(III)-catalysed oxidation of thiophene was investigated over only a 24 hour reaction period and this procedure generated a dark blue mixture of oxidation products. The GC trace of the dichloromethane extract is given in Figure 2.18.

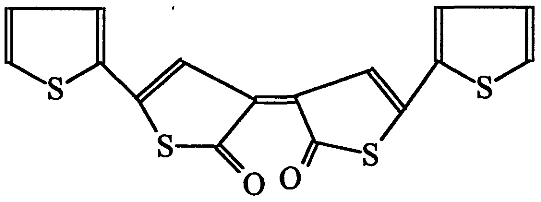
Figure 2.18. GC chromatogram of the titanium(III)-catalysed oxidation of thiophene.



As shown in Figure 2.18, titanium(III)-catalysed oxidation of thiophene generated a wide range of oxidation products some of which had not been observed before. Components **(13)**, **(17)** and **(20)** had already been seen in the Fenton-related oxidation of thiophene and their formation mechanisms have been discussed in section 2.2.1.1.

The formation of benzo-b-thiophen-S,S-dioxide **(24)** is interesting. It is known in the literature that hydrogen peroxide oxidizes thiophene to a product having the composition of a "sesquioxide" **(23)** arising from Diels-Alder combination of the sulphoxide **(25)** and sulphone **(22)** (Scheme 2.30)[38]. Unsubstituted thiophene sulphoxide and sulphone are unstable compounds and easily undergo further dimerisation products and it is thought that the benzo-[b]-thiophen-S,S-dioxide arises via the components **(25)** and **(22)**.

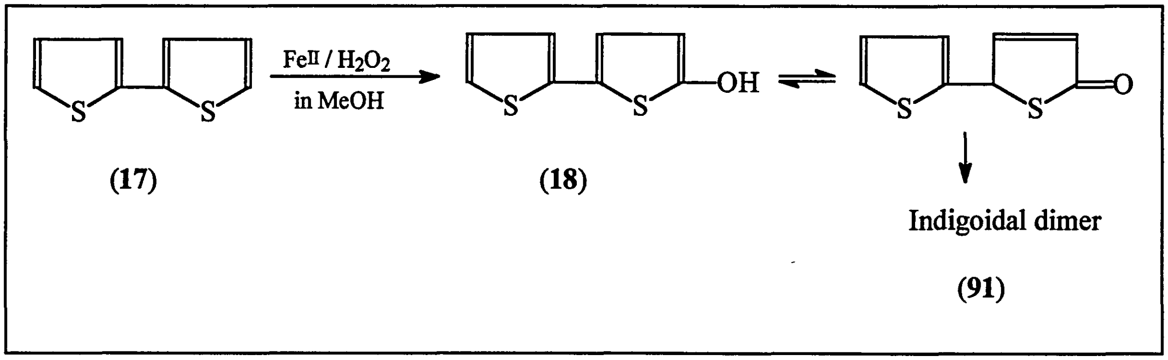
As described earlier in Scheme 2.2 and 2.3, component **(18)** is formed from a recombination-disproportion mechanism via 2,2'-bithiophene. When the reaction mixture was extracted with dichloromethane, a dark-blue organic phase was obtained. The crude mixture of oxidation products was fractionated by using flash column chromatography and a blue substance was separated. Some other coloured fractions were also obtained, along with the blue fraction, with colours ranging from blue to pink, yellow, green and brown. Although the blue and pink fractions were isolated, the peaks belonging to them did not appear on GC/MS and no information could be obtained since they decomposed easily. The same dark blue indigoid-like compound was reported by Hörnfeldt [39] and Saunders *et al.* [4]. The reaction of 2,2' bithiophene with radiolytically produced hydroxyl radicals gave a component which was thought to be **(18)**, but it was rapidly oxidized to a dark blue substance which is soluble in ether and water. The chemical structure of this compound could not be proved due to its unstable nature, but the suggestion is made of the dimeric compound **(91)** shown below;



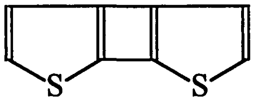
(91)

The same compound was obtained when 2,2' bithiophene was oxidized with hydrogen peroxide in the presence of Fenton's reagent and a possible pathway is shown in Scheme 2.31.

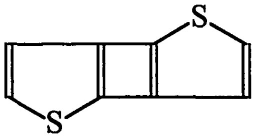
Scheme 2.31.



Also, component **(92)** gave a significant peak at t_R=21.73 having an apparent molecular ion at m/z 164 and fragment ions at m/z 136 and 104 respectively. Although its structure has not been identified, two possible structures may be suggested, **(93)** and **(94)**. 2-chlorothiophene **(95)** was also observed as a minor product in the titanium(III)-catalysed oxidation of thiophene and confirmed by comparison with an authentic sample.



(93)



(94)

The oxidation process does appear to be more effective when the titanium(III)-catalysed reaction was left for a 24 hour periods, but not as effective for complete destruction as compared to the Fenton-catalysed oxidation process.

2.3.1.2. Fenton-like Oxidation Reactions of 2-Methylthiophene

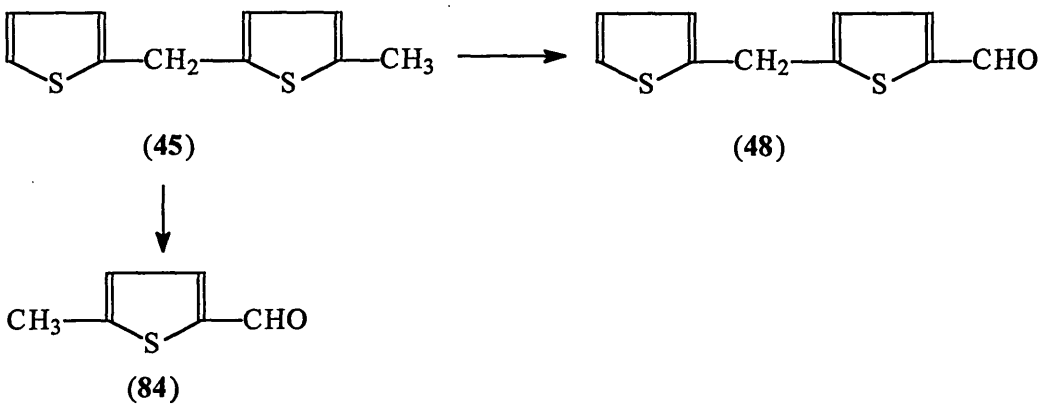
The oxidation of 2-methylthiophene was also carried out using the same conditions mentioned above (section 2.3.1.1.). The reaction was studied over time periods of 1 hour and 24 hour respectively and the reaction mixtures were analysed using GC/MS technique using the same instrument and temperature program 1 as outlined in section 2.1. The range of oxidation products using vanadium(IV), copper(I) and copper(II) catalyst systems resembles those seen earlier in the Fenton-catalysed oxidation of 2-methylthiophene. The resulting components are shown earlier in Table 2.2 and Scheme 2.7. This would seem to indicate that they may have been formed via the same mechanism, involving the intermediacy of hydroxyl radicals.

However, 5-methyl-2-hydroxythiophenes (components **(29)** and/or **(30)**) were not observed, but their dimerisation products, components **(33)** and **(34)** were observed together with polyhydroxylated products **(37)** and **(96)** as the main products in the reaction, presumably formed by further oxidation of **(29)** and/or **(30)** with the vanadium(IV) catalyst system.

A new component **(96)** giving an apparent molecular ion at *m/z* 146 (t_R=16.68) was formed which was assigned as 2,3,4-trihydroxy-5-methylthiophene based on the similarity of its mass spectral fragmentation to those of dihydroxythiophenes, but this component was generated only in vanadium(IV)-catalyzed oxidation of 2-methylthiophene.

However, an interesting observation was also made concerning the formation of 2-methyl-5-(2-thienylmethyl)thiophene **(45)**, since when the reaction was carried out with acetonitrile-water solvent system, **(45)** was the major product in an open system, but was not observed in a sealed system (nitrogen atmosphere) in a copper(II)-catalysed oxidation reaction. Possibly, **(45)** formed but rapidly underwent further oxidation giving the corresponding aldehyde **(48)** and its decomposition product 5-methyl-thiophen-2-aldehyde **(84)**. The detection of significant amounts of **(84)** (t_R=15.19, m/z 126) in a sealed system supports this pathway shown in Scheme 2.32.

Scheme 2.32.



Two chlorinated components (97) and (98) were observed as the major products when copper(I)chloride or copper(II)chloride were employed as catalyst. The compounds had t_R=5.50 and 5.72 and gave the same apparent molecular ions at *m/z* 132 and similar fragmentation. Component (97) was identified as 5-chloro-2-methylthiophene by comparison with the authentic substance and (98) is thought to be 3-chloro-2-methylthiophene but this has not yet been confirmed.

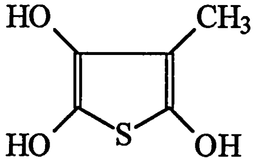
Although the titanium(III)-catalysed oxidation of 2-methylthiophene generated a mixture of oxidation products that include trace amounts of thiophene-2-aldehyde (**49**) and 2-methyl-5-(2-thienylmethyl)thiophene (**45**) along with the chlorinated 2-methylthiophenes (97) and (98), most of the 2-methylthiophene was left unreacted over a 24 hour period.

Consequently, the Fenton-like oxidation of 2-methylthiophene does not appear to be as efficient as the Fenton-catalysed oxidation reaction. Long reaction periods (24 hour) increased the extent of oxidation of 2-methylthiophene in the presence of vanadium(IV), copper(I) and (II) catalyst systems but the titanium(III)/hydrogen peroxide system seemed to be inefficient for the oxidation of 2-methylthiophene.

2.3.1.3. Fenton-like Oxidation Reactions of 3-Methylthiophene

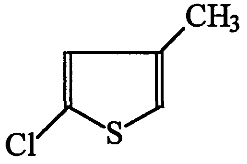
The Fenton-like oxidation reactions of 3-methylthiophene were also studied using vanadium(IV), copper(I), copper(II) and titanium(III) catalysts as discussed in section 2.3.1.1. The oxidation products formed here were almost the same as those identified in the Fenton-related oxidation reactions (Table 2.3 and Scheme 2.15).

The vanadium and copper-catalysed oxidations of 3-methylthiophene gave hydroxylated products via the same mechanism, presumably involving the intermediacy of hydroxyl radicals. Components **(20)**, **(58)**, **(59)**, **(62)**, **(63)** and **(66)** were observed in the presence of vanadium and copper catalysts systems along with the ring cleavage products S_8 and carbon dioxide. Dithienylmethanes (**72** or **73**) were not formed in the case of the vanadium(IV)/hydrogen peroxide system but a new component **(99)** which was thought to be a trihydroxythiophene appeared. The GC peak belonging to 4-methyl-2,3-dihydroxythiophene **(64)** significantly decreased in this reaction , probably due to further oxidation to give **(99)**.



(99)

It is noteworthy that the copper-containing catalyst systems significantly increased the formation of dimeric oxidation products, e.g. components **(62)**, **(63)** and (**72** or **73**). A chlorinated 3-methylthiophene was observed in the presence of copper chloride salts as one of the significant products and it was thought to be 5-chloro-3-methylthiophene **(100)** having an apparent molecular ion at *m/z* 132 and a stable ion at *m/z* 97.



(100)

Ti(III)-catalysed oxidation of 3-methylthiophene is the least effective system since no oxidation products were observed.

2.3.1.4. Summary

Fenton-like oxidation of the thiophenes gave similar oxidation products to the Fenton-related oxidation reactions. There is no fundamental difference between the Fenton-like and Fenton-related catalysed oxidations of thiophenes studied here. Only the titanium(III)/hydrogen peroxide system showed other oxidation products (e.g. benzo-b-thiophene) along with the Fenton-catalysed oxidation products. However, copper-containing reagents significantly increased the formation of hydroxylated products and dimeric compounds. It is obvious that the Fenton-related and Fenton-like catalyst systems showed different efficiencies for the oxidation of thiophenes presumably due to the formation of different metal complexes, and quantitative analyses provide evidence that they have different oxidation capacities. However, these catalyst systems seem to be less effective than the Fenton-related reagents for the oxidation of thiophenes.

2.3.2. Fenton-catalysed Oxidation of Thiophene and 2- and 3-Methylthiophene in the Presence of EDTA

In order to contribute to the debate regarding the oxidizing species responsible for the destruction of each of the thiophenes, the oxidation process was carried out in the presence of a complexing agent. It is well known that ethylenediaminetetraacetic acid (EDTA) generates a stable complex with iron(II) and increases the activity. Koppenol found that using EDTA as a complexing reagent in an iron(II)/hydrogen peroxide system, [involving ($Fe=O^{IV}$) containing intermediacy rather than hydroxyl radicals] increased the rate of oxidation [40], while others claimed the opposite [34]. Therefore, the Fenton-catalysed oxidation of thiophene and 2- and 3-methylthiophene was carried out in the presence of EDTA and a comparison made between the oxidation products which were formed in the presence and absence of complexing agent.

The oxidation reactions were carried out using the same experimental procedure as indicated in section 2.1. The EDTA (4.30 g, 0.01 mol) was initially added to the reaction mixture prior to the addition of hydrogen peroxide and an equimolar amount of thiophene. The oxidation reaction was investigated over periods of 1 and 24 hour. The oxidation products detected have been assigned structures by making a comparison with authentic standards or by consideration of their mass spectral data. The oxidation products from the Fenton-catalysed oxidation of thiophene and 2- and 3-methylthiophene in the presence of EDTA are summarised in Tables 2.9, 2.10 and 2.11 respectively.

Table 2.9. Oxidation products arising from the Fenton-catalysed oxidation of thiophene in the presence of EDTA.

Comp. No	t_R 1 hr	t_R 24 hr	Apparent RMM	Solvent	Proposed structure
13	9.50	9.80	100	H_2O	(5H)-thiophen-2-one
20*	-	6.04	114	H_2O	thiomaleic anhydride

* Indicates that proposed structure has not been proved by comparison with the authentic substance

Table 2.10. Oxidation products arising from the Fenton-catalysed oxidation of 2-methylthiophene in the presence of EDTA[1].

Comp. No	t_R 1 hr	t_R 24 hr	Apparent RMM	Solvent	Proposed structure
28	7.01	7.08	114	H_2O	2-hydroxymethylthiophene
30	6.60	6.70	114	H_2O	5-methyl-(5H)thiophen-2-one
34	11.09	11.18	224	H_2O	indigoidal dimer
53	4.50	4.57	98	H_2O	maleic anhydride
37*	7.50	7.68	130	H_2O	5-methyl-2,3 dihydroxy thiophene
40*	7.10	7.16	130	H_2O	5-methyl-2,4 dihydroxy thiophene
45	9.55	9.60	194	H_2O	2-methyl-5-(2-thienylmethyl) thiophene
48	9.91	9.93	208	H_2O	5-(2-thienylmethyl) thiophene-2-aldehyde
49	6.07	6.19	112	H_2O	thiophene-2-aldehyde

* Indicates that proposed structure has not been proved by comparison with the authentic substance

[1] Same instrument and temperature program 2 were used as outlined in section 2.1.

Table 2.11. Oxidation products arising from the Fenton-catalysed oxidation of 3-methylthiophene in the presence of EDTA[1].

Comp. No.	**t_R 1 hr**	**t_R 24 hr**	**Apparent RMM**	**Solvent**	**Proposed structure**
53	4.70	4.81	98	H_2O	maleic anhydride
58	7.56	7.65	114	H_2O	3-methyl-(5H)thiophen-2-one
59	7.89	7.96	114	H_2O	4-methyl-(5H)thiophen-2-one
64	7.01	7.08	128	H_2O	3-methylthiomaleic anhydride
66	7.30	7.34	130	H_2O	4-methyl-2,3 dihydroxy thiophene
67*	7.14	7.22	130	H_2O	3-methyl-2,4 dihydroxy thiophene
72 or 73	9.10	9.28	194	H_2O	3-methyl-2-(3-thienylmethyl) thiophene or 3-methyl-5-(3-thienylmethyl)thiophene
56	6.58	6.62	112	H_2O	thiophene-3-aldehyde

* Indicates that proposed structure has not been proved by comparison with the authentic substance

[1] Same instrument and temperature program 2 were used as outlined in section 2.1.

From the Tables above, it can be seen that there are some similarities between the oxidation products that were formed in the Fenton-catalysed oxidation reaction carried out in the presence and absence of EDTA. Using EDTA as a complexing agent seems to be slowing down the Fenton oxidation process of 3-methylthiophene while the oxidation of 2-methylthiophene seems to be accelerated. However, the oxidation products formed from all thiophenes did not show any difference from those formed from the reactions in the absence of EDTA. Therefore, it can be concluded that the presence of EDTA does not appear to have any effect on the oxidation mechanism for each thiophene.

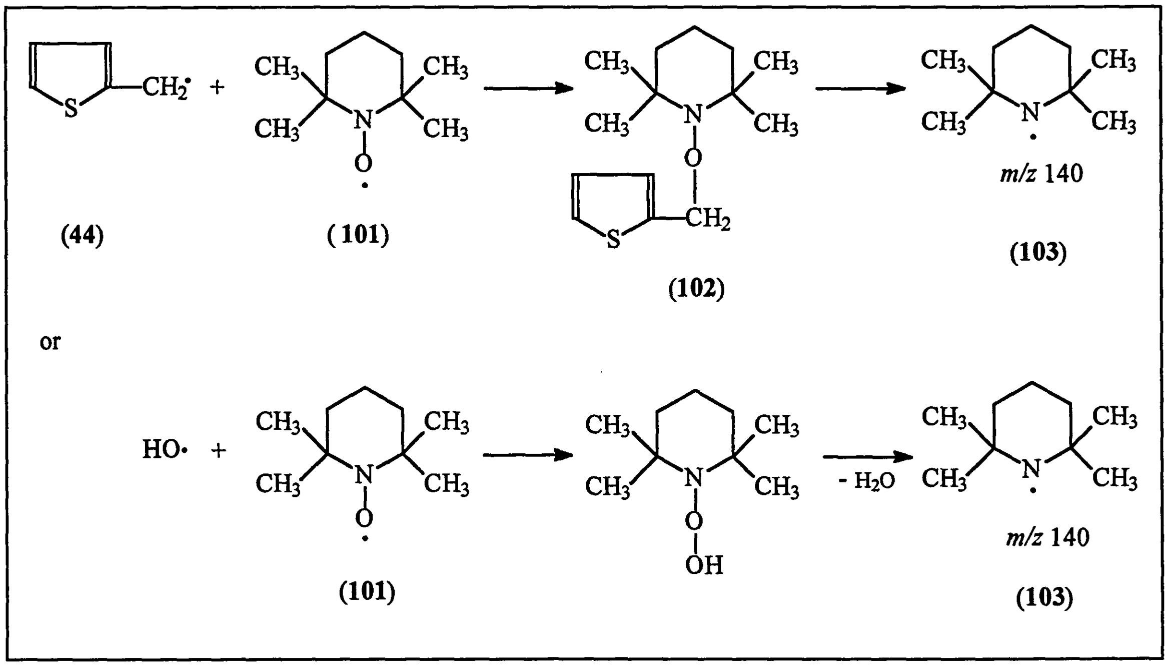
Particularly, the formation of hydroxylated products and dimeric structures still require the involvement of radical species.

2.3.3. Fenton-catalysed Oxidation of Thiophene and 2- and 3-Methylthiophene in the Presence of TEMPO

Spin trapping reagents are used for the identification of hydroxyl radicals ($HO^{\bullet}$) and free radicals derived from the substrate under oxidation conditions. The Fenton-catalysed oxidations of thiophene and 2- and 3-methylthiophene were carried out in the presence of a radical trap, 2,2,6,6,-tetramethyl-1-piperidinyloxy (TEMPO). It was expected that the radicals which were directly or indirectly formed from Fenton's reagent would be trapped by TEMPO and a comparison would lead to a conclusion about the formation of hydroxyl and other free radicals. Lunazzi *et al.*[30] showed that 2- and 3-thienyl radicals, generated through hydrogen abstraction by t-butoxyl radicals, were subsequently trapped by 2-methyl-2-nitrosopropane.

The products of Fenton-catalysed oxidation of 2- and 3-methylthiophene over a 24 hour reaction period in the presence of TEMPO (1.56 g, 0.01 mol) were analysed using the GC/MS technique and a significant difference was observed on comparison with those oxidation products detected in the absence of TEMPO. The oxidation reactions in the absence of TEMPO generated a range of oxidation products involving mainly 2-hydroxythiophene and dimeric structures which are all thought to arise via a free radical pathway. These products were not detected in the oxidation reaction in which TEMPO (**101**) was introduced; instead, a range of oxidation products was observed that have either apparent molecular ions of *m/z* 140 (**103**) or mass spectra that contain stable fragment ions at *m/z* 140. Hence, the components which contain a fragment ion at *m/z* 140 are thought to be the structures where the TEMPO has combined with a radical species, but decomposed to more stable structure as shown in Scheme 2.33.

Scheme 2.33.



The 2-hydroxythiophenes (components (**13**), (**30**), (**58**) (**59**) and their further oxidation and dimerisation products) and dithienylmethanes (components (**45**), (**72**) or (**73**)) were not formed in the oxidation reactions carried out in the presence of TEMPO. There was, however, evidence of ring destruction giving S_8 and carbon dioxide both in the presence and absence of TEMPO over a 24 hour period suggesting that the process of oxidative ring destruction is possibly non-radical in nature. Also detected among the oxidation products of 2- and 3-methylthiophene were the simple alcohols (**28**)and (**55**), aldehydes (**49**) and (**56**) and carboxylic acids (**50**) and (**57**) respectively. Significantly, these were formed when the oxidation reactions were conducted in the presence of the radical trap, TEMPO, suggesting that their formation is also non-radical in origin. Rather than free radicals, these non-radical oxidation pathways may involve the high oxidation state iron complexes which are analogous to Gif chemistry. The Fenton-catalysed oxidation of the thiophenes was studied to investigate the possible mechanism and reaction pathways under the Gif conditions and the results are described in the following section.

2.3.4. Fenton-catalysed Oxidation of Thiophene and 2-methylthiophene under Gif Conditions

It was thought that repeating Fenton-catalysed oxidation of thiophenes under Gif conditions might result in some useful information about the reaction mechanism. As discussed extensively in section 1.3.2.2., Gif chemistry is thought to involve high oxidation state iron complexes as the dominant species in the oxidation reactions. A pyridine-acetic acid mixture is used as the solvent system and oxidation reaction results in functionalisation, especially on secondary carbon. Gif chemistry was developed by Barton to provide a means of selectively generating functionalised systems from saturated hydrocarbons. The Fenton-catalysed oxidation of thiophene and 2-methylthiophene was conducted under Gif conditions to make a comparison between the free radical mechanism and the high oxidation state metal ion mechanism.

2.3.4.1. Experimental

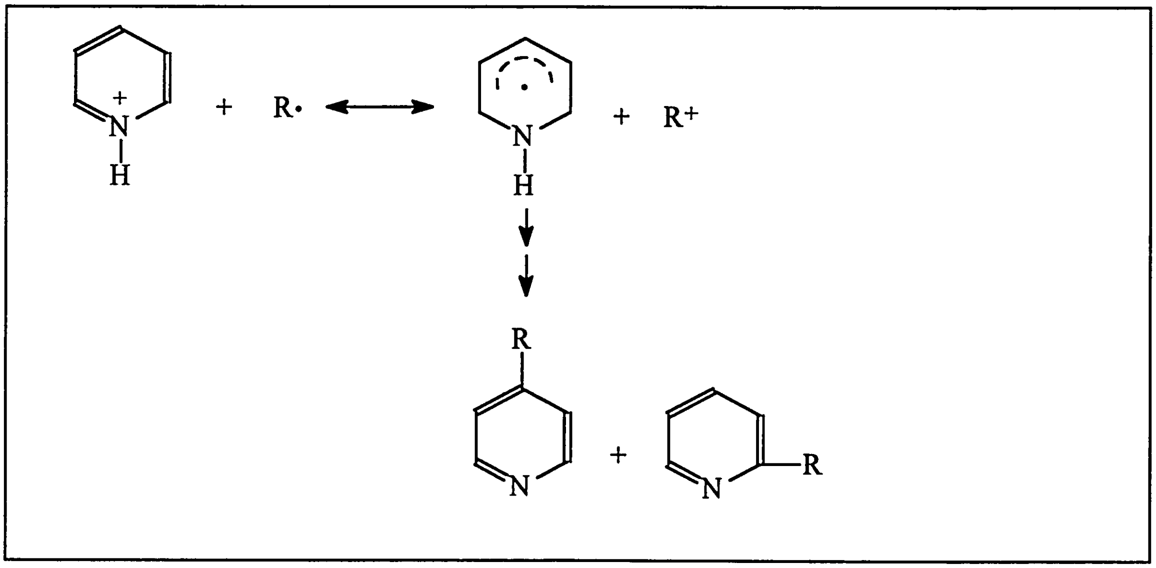
The thiophene (0.01 mol) was dissolved in a pyridine-acetic acid (28 cm^3) mixture and then added to the reaction flask together with Fe(II) salt ($FeSO_4$. $7H_2O$, 2.74 g, 0.01 mol) in sulphuric acid (50 cm^3, $1x10^{-3}$ mol dm^3). Aqueous hydrogen peroxide (6.15 cm^3,

5×10^{-2} mol) was added to the reaction while the flask was cooled in an ice bath and the reaction mixture was left for 24 hours. The reaction mixture was then poured into a large amount of water, neutralized with 0.1 M NaOH solution and extracted with dichloromethane. Finally, the extracts were combined, dried and evaporated to 2 cm^3.

2.3.4.2. Results

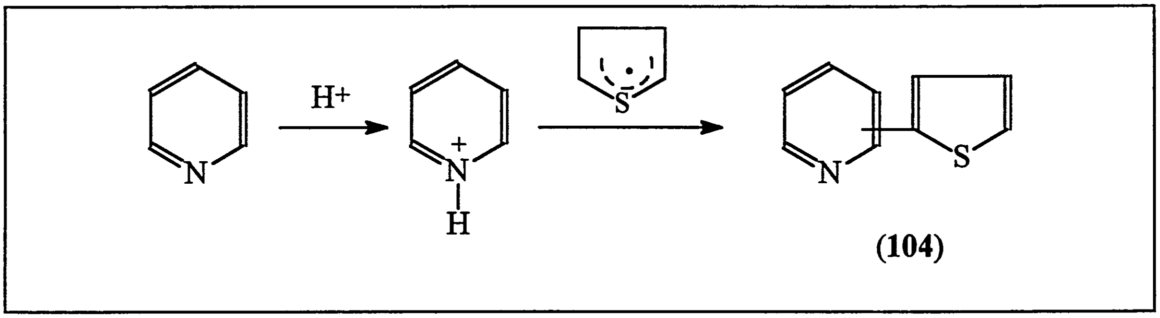
The resulting oxidation products were analysed by using the same instruments and method described in section 2.1. The Fenton-catalysed oxidation of thiophene under Gif conditions gave three oxidation products, each of which is different from those observed in the Fenton-catalysed oxidation of thiophene in both acetonitrile/water or water. These products comprised a pyridine-substituted thiophene, *m/z* 161 **(104)**, bipyridines, *m/z* 156 **(105)** and an unknown product that gives an apparent molecular ion at *m/z* 182 **(106)**. The alkylation of protonated pyridines was extensively studied by Minisci *et al* [41]. They suggested that pyridine alkylation occurs under Gif conditions as shown in Scheme 2.34.

Scheme 2.34.



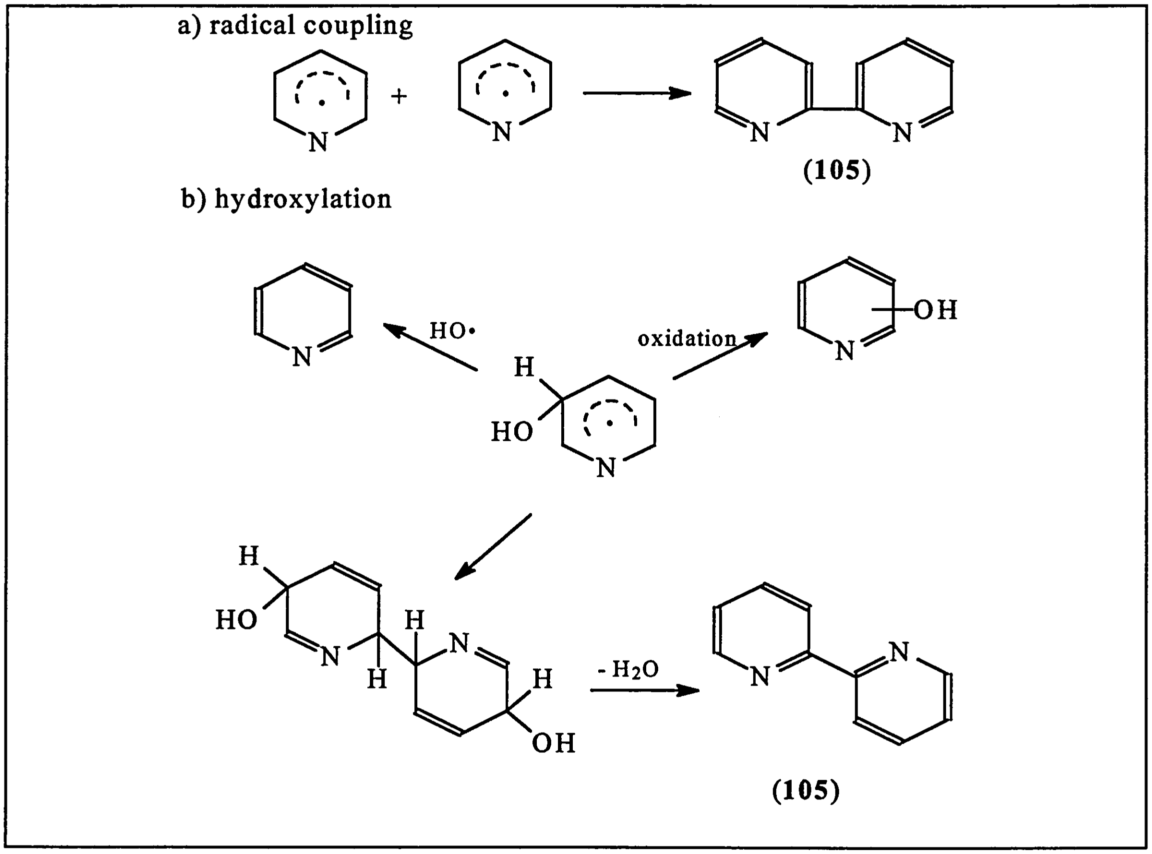
The formation of a pyridine-substituted thiophene (**104**) may be due to the mechanism shown below (Scheme 2.35).

Scheme 2.35.



The second compound, bipyridine (**105**), was derived from the pyridine-acetic acid system. This was confirmed when the reaction was conducted in the absence of the thiophenes resulting in the formation of bipyridines. The formation of bipyridines may be via either radical coupling or hydroxylation[42] (Scheme 2.36).

Scheme 2.36.



In fact, the rate of the reaction of hydroxyl radicals with thiophene seems to be slower than with pyridine. Therefore, the process tends to hydroxylate the large excess of pyridine rather than the thiophene, but the instability of the hydroxypyridines under the reaction conditions leads to the formation of 2,2'-bipyridine (**105**).

The third compound (**106**) that has an apparent molecular ion at *m/z* 182 might be a thiophene-derived compound since it was not observed in the absence of thiophene (blank reaction). It was isolated but structure elucidation has not yet been completed. Interestingly, this component was also observed in the case of 2-methylthiophene as a major product along with (**105**).

Hydroxythiophenes, which were always the main products in the Fenton-catalysed oxidations of thiophenes, were not formed under Gif conditions. A small amount of thiophene-2-aldehyde (**49**) and ring decomposition products (e.g. S_8) were also formed under these conditions.

These results confirm that the hydroxyl radicals in the Fenton oxidation of thiophenes are indeed the main oxidizing species. In the case of Gif conditions, the course in different, and high oxidation state iron complexes ($Fe=O^{IV}$) may be involved rather than hydroxyl radicals. On the other hand hydroxyl radicals may be formed along with the high oxidation state iron complexes and react with pyridine rather than thiophene to give bipyridine as suggested by Perkins [42].

2.3.5. Photocatalytic Oxidation Reactions of 2-Methylthiophene

Thiophenes are light sensitive compounds and easily decompose when exposed to light. As a renewable form, solar energy can be directly used for the mineralisation of hazardous organic chemicals. As indicated in section 1.3.3. a wide range of organic compounds can be destroyed by photochemical processes since the electron transfer process generates very active species in the aqueous media. The combination of light and Fenton's reagent in the oxidation of chlorobenzene with hydrogen peroxide was reported to increase the decomposition rates significantly [43], since UV light increases the rate of formation of hydroxyl radicals. As Fenton-related oxidation of thiophenes is very effective anyway, light-combined Fenton oxidation, which is called "Photo-Fenton Oxidation", has not been studied in this research project. However, as an alternative method, titanium-catalysed photooxidation of 2-methylthiophene has been extensively studied. Titanium-catalysed photooxidation is known as a hydroxyl radical generating system and its application is increasing on the industrial scale. In order to give some contribution to further application of this technology, this new technique has also formed part of this study. Another purpose of this part of the project is to determine the nature of intermediate products which might be similar to those from Fenton-catalysed systems. For these reasons, the photocatalytic oxidation of 2-methylthiophene was studied in aqueous solution and the reaction was conducted in the presence and absence of titanium dioxide under an oxygen atmosphere. Since 2-methylthiophene is not soluble in water, and this affects the oxidation rate, the photocatalysed oxidation was conducted using dichloromethane as co-solvent system or water was employed with vigorous stirring. All of the results were compared for the optimization of conditions.

2.3.5.1. Experimental

Two different experiments were used for the photocatalytic oxidations of 2-methylthiophene; the first oxidation process was carried out in aqueous solution (no dichloromethane) (100 cm^3) while the second requires the presence of dichloromethane /water (50 cm^3/50 cm^3). Each reaction was repeated with and without titanium dioxide and reaction conditions are summarised in Table 2.12.

Table 2.12. Experimental conditions of photocatalytic oxidation of 2-methylthiophene.

2-methylthiophene (mol)	Catalyst	Solvent	Illumination
0.01	-	H_2O	Sunlight
0.01	TiO_2	H_2O	Sunlight
0.01	-	CH_2Cl_2/H_2O	Sunlight
0.01	TiO_2	CH_2Cl_2/H_2O	Sunlight
0.01	-	H_2O	Visible lamp light (> 250 nm)
0.01	TiO_2	H_2O	Visible lamp light (> 250 nm)
0.01	-	CH_2Cl_2/H_2O	Visible lamp light (> 250 nm)
0.01	TiO_2	CH_2Cl_2/H_2O	Visible lamp light (> 250 nm)
0.01	-	H_2O	Low pressure UV lamp (< 250 nm)
0.01	TiO_2	H_2O	Low pressure UV lamp (< 250 nm)
0.01	-	CH_2Cl_2/H_2O	Low pressure UV lamp (< 250 nm)
0.01	TiO_2	CH_2Cl_2/H_2O	Low pressure UV lamp (< 250 nm)

The requirement of a co-solvent system (dichloromethane/water) for the photooxidation of 2-methylthiophene was shown by the preliminary results since no oxidation products were observed in the absence of titanium dioxide when the reaction was conducted in water only. Hsiao *et al.* showed [44] that titanium dioxide-catalysed photooxidation of dichloromethane gave only hydrochloric acid and carbon dioxide over a 4 hour illumination time with 320-400 nm light in a photoreactor. This result indicates that using dichloromethane does not interfere with the oxidation products generated from the photooxidation of 2-methylthiophene. Dissolving 2-methylthiophene in dichloromethane increases the possibility of contact of 2-methylthiophene with the surface of titanium dioxide with vigorous stirring. The photocatalyst used in this study was titanium dioxide powder supplied by Aldrich. The particles are spherical and non-porous, primarily in the anatase structural form with greater than 99.9 % purity. The primary particle size is 325 mesh with a specific BET surface area of 9.8 m^2/g. The 2-methylthiophene and dichloromethane used for the reaction were reagent grade purchased from Aldrich. The reactions were carried out in a quartz reactor. The reactor was cylindrical and ca. 200 cm^3 capacity equipped with a glass stirrer device and was cooled down to 40-45 °C with the help of the water circling outside the reactor. 0.2 gram titanium dioxide and 100 cm^3 double distilled water were added to the reactor vessel. After addition of 2-methylthiophene (1.02 g, 0.01 mol) which was previously dissolved in dichloromethane or water, the suspension was illuminated by an already warmed up low-pressure mercury lamp (254 nm wavelength) and the reaction vessel was sealed. Other photooxidation reactions which require direct sunlight and lamplight were conducted in a three necked pyrex round bottomed flask with magnetic stirrer and a condenser. The temperature was kept at 40-45 °C with a hot plate and the flask was then sealed. After the appropriate time period (from 1 hour to 3 hour), the reaction mixture was extracted with dichloromethane or the dichloromethane phase was separated. After drying over $MgSO_4$, the organic layer was evaporated down to 2 cm^3. In order to compare the resulting products with those from Fenton-catalysed oxidation of 2-methylthiophene, the resulting extract was analysed using the same GC/MS conditions and the same instrument and temperature program 1 as described in section 2.1.

2.3.5.2. Results

All photocatalytic reactions of 2-methylthiophene in the dichloromethane/water system gave three main oxidation products in the absence of titanium dioxide. The reaction products are summarised in Table 2.13 and Scheme 2.36 represents the oxidation products observed. The structures were assigned by comparison with authentic samples or by consideration of mass spectral data.

Scheme 2.36.

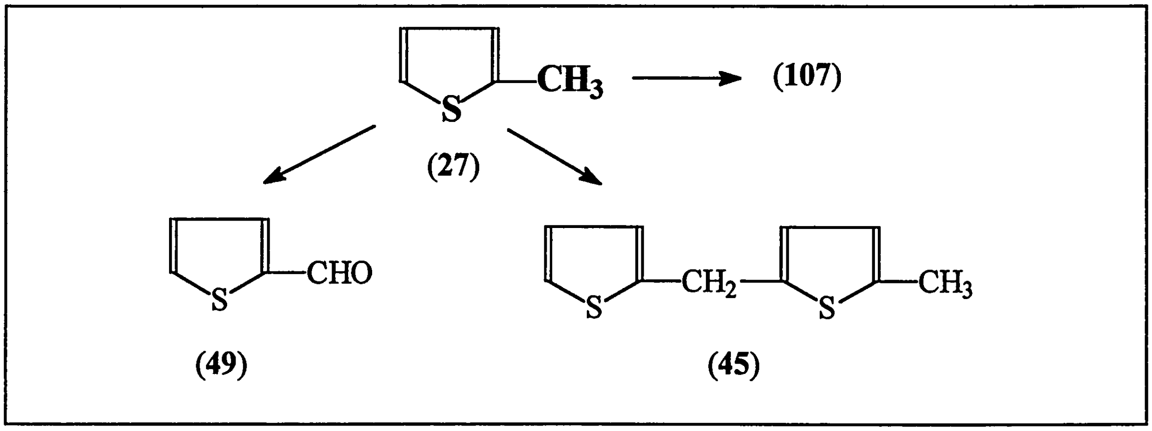


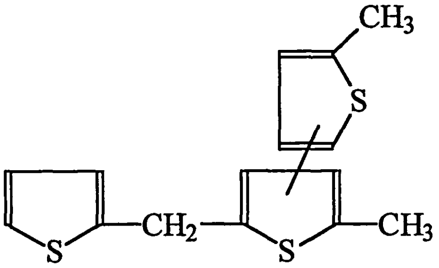
Table 2.13. The products arising from the photocatalysed oxidation of 2-methyl thiophene[1].

Comp. No	t_R(24 hr)	Apparent RMM	Solvent	Proposed structure
45	23.57	194	CH_2Cl_2/H_2O	2-methyl-5-(2-thienylmethyl) thiophene
49	7.83	112	CH_2Cl_2/H_2O	thiophene-2-aldehyde
107*	37.29	290	CH_2Cl_2/H_2O	unknown structure

* Indicates that proposed structure has not been proved by comparison with the authentic substance

[1] In the absence of titanium dioxide

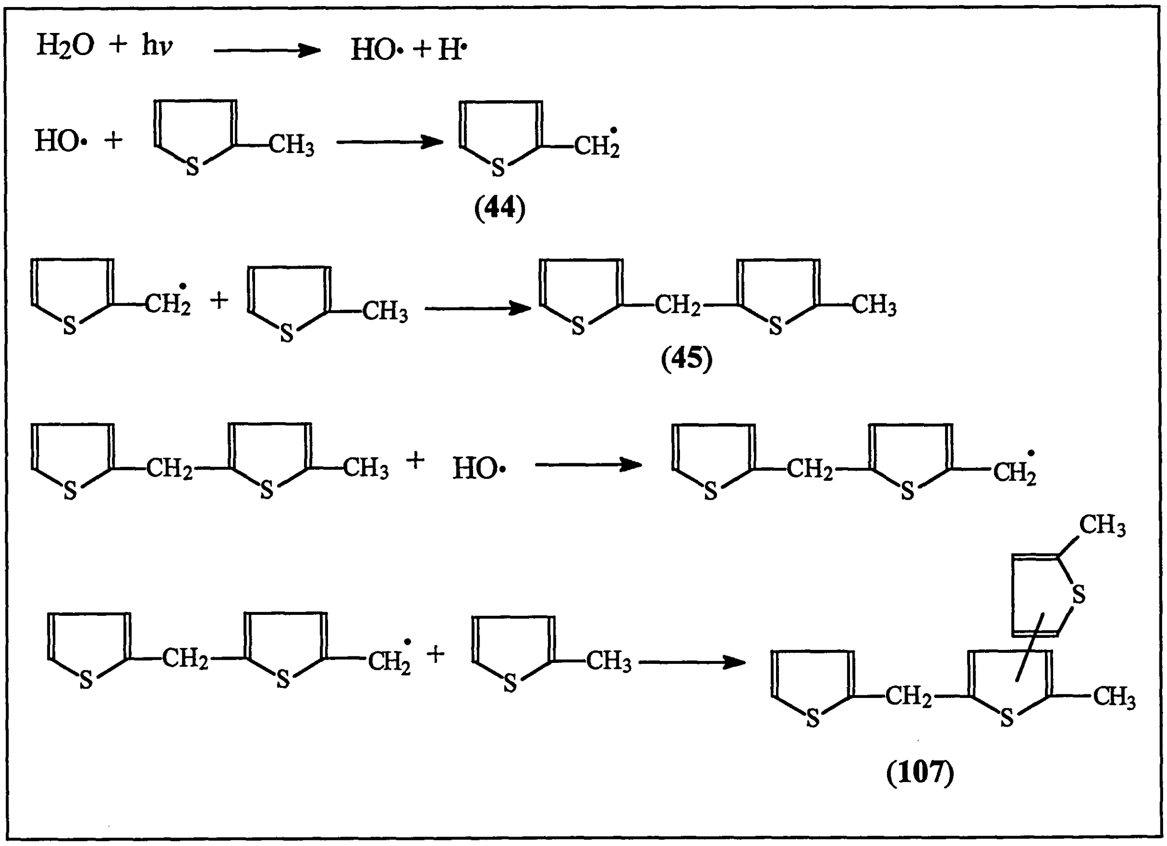
Components (**45**) and (**49**) were confirmed by comparing with authentic samples. The structure of component (**107**) was suggested from the mass spectral fragmentation with an apparent molecular ion at *m/z* 290 and a stable ion at *m/z* 275 (M-15). This compound might be formed due to the addition of another thiophene ring to the component (**45**) since the molecular mass increase is 96. This product was isolated from the reaction mixture as pure brown oil, whose structure has not been completely evaluated but a possible structure (**107**) is suggested.



(107)

The breaking of bonds is a common photochemical reaction usually generating free radicals. Hydroxyl radicals (HO˙) are produced by photolysis of water leading to the formation of further free radical species [45,46]. These free radicals may generate the dimeric compounds (**45**) and (**107**) (Scheme 2.37).

Scheme 2.37.



Longer illumination time significantly increased the formation of component (**107**), resulting in approximately a 1% yield.

Photocatalytic oxidation of 2-methylthiophene in the presence of titanium dioxide gave the same products given above, together with other oxidation products.

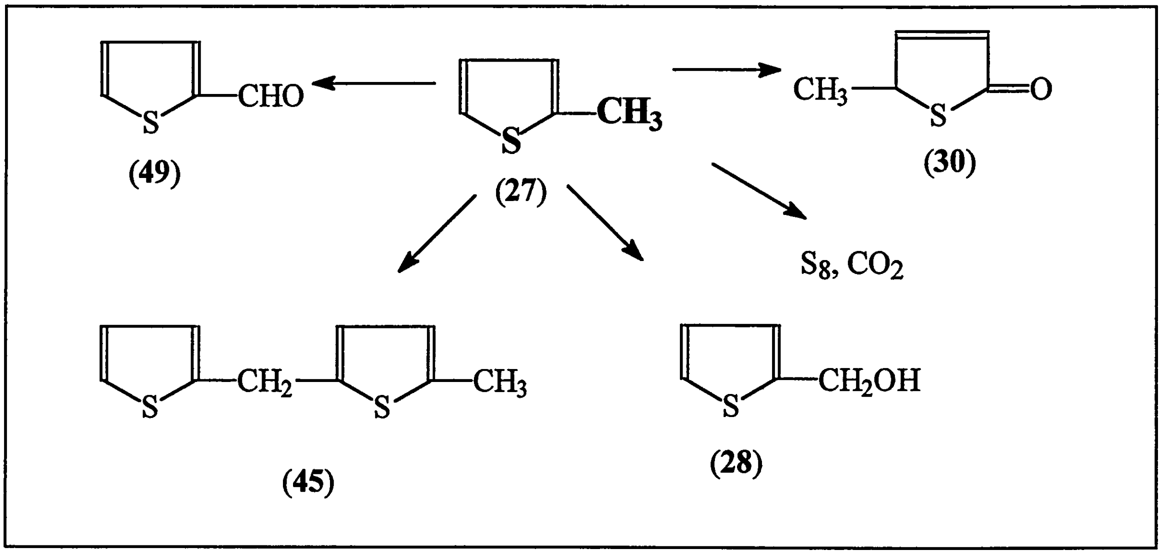
The reaction products are summarised in Table 2.14 and Scheme 2.38 represents the oxidation products observed.

Table 2.14. The products arising from the photocatalysed oxidation of 2-methyl thiophene [1].

Comp. No	t_R(24 hr)	Apparent RMM	Solvent	Proposed structure
28	9.85	112	CH_2Cl_2/H_2O	2-hydroxymethylthiophene
30	10.15	114	CH_2Cl_2/H_2O	5-methyl-(5H)thiophen-2-one
45	23.57	194	CH_2Cl_2/H_2O	2-methyl-5-(2-thienylmethyl) thiophene
49	7.83	112	CH_2Cl_2/H_2O	thiophene-2-aldehyde

[1] In the presence of TiO_2

Scheme 2.38.



All these products were confirmed by comparing them with authentic samples. Similar products to those observed in the absence of titanium dioxide were formed, but using low-pressure UV light shortened the reaction time giving oxidation products even after 1 hour illumination. A second interesting observation from this experiment is the formation of small amounts ring cleavage products, such as S_8 and carbon dioxide. When the concentration of the unreacted 2-methylthiophene was monitored over a 3 hour period, it showed a linear decrease with illumination time. However, titanium dioxide-assisted photocatalytic oxidation is not as effective as Fenton-catalysed oxidations of 2-methylthiophene but may be developed for the treatment of more dilute solutions (e.g. 10^{-5}-10^{-6} mol) as discussed in section 1.3.3.

2.3.6. Summary

The Fenton-catalysed oxidation of thiophene and 2- and 3-methylthiophene in the presence of a complexing agent EDTA and a radical trap TEMPO has generated some interesting findings. When EDTA was used with iron(II), the oxidation of 3-methylthiophene seemed to be slowed down, whereas that of 2-methylthiophene was accelerated. However, as far as the product formation is concerned, no significant difference between the experiments conducted in the absence and presence of EDTA was detected. In particular, the formation of hydroxylated products and dimeric structures still presumably requires the involvement of free radicals.

These hydroxylated products were not formed when TEMPO was present in the reaction mixture, suggesting that the presence of the radical trap interferes with the usual radical-based oxidation process. The formation of oxidation products **(28)**, **(49)**, **(55)** and **(56)** which are thought to be formed from a non-radical reaction mechanism supports this finding.

The Fenton-catalysed oxidation process under Gif conditions also provided some interesting findings, particularly over a 24 hour reaction period. However, hydroxylated thiophenes have not been observed but the formation of the bipyridines and pyridine substituted thiophenes still requires involvement of free radical species.

Although the oxidation rates are much slower, photocatalytic oxidations of 2-methylthiophene gave similar results to the Fenton-catalysed oxidation. The formation of dimeric structures suggests that the products observed might be formed via a radical route similar to that for the iron(II)/hydrogen peroxide system. The photooxidation process is a developing new technique but it seems to be ineffective for oxidative conversion of the concentrated solutions studied in this study. However, further improvements may provide more efficiency for dilute solutions.

2.4. References

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CHAPTER 3.

QUANTITATIVE ANALYSIS OF THE FENTON- RELATED AND FENTON-LIKE OXIDATIONS OF THIOPHENE AND 2- AND 3-METHYLTHIOPHENE

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QUANTITATIVE ANALYSIS OF THE FENTON- RELATED AND FENTON-LIKE OXIDATIONS OF THIOPHENE AND 2- AND 3-METHYLTHIOPHENE

Quantitative analysis was carried out using GC/MS techniques. The initial part of this study required the calibration of the GC/MS system in a linear fashion with regard to the changes in the concentrations of thiophene and 2- and 3-methylthiophene. In order to establish this calibration, graphs were plotted by using appropriate internal standards for each compound. In the preparation of these standards each thiophene, the internal standard and the extraction solvent dichloromethane were supplied by Aldrich. Reactions were carried out in distilled water. Since very little differences were seen in the retention times of 2- and 3-methylthiophenes, 2,5-dimethylthiophene was used as internal standard in the determination of the respective isomeric monomethylthiophene.

3.1. Thiophene: Preparation and Analysis of Standards

The calibration graph was plotted by using quantities of thiophene (ranging from 1.2×10^{-4} to 1.2×10^{-3} mol) and a constant amount of the internal standard (1 mL of stock solution B). Two stock solutions were prepared;

Stock solution A: 1.05 g of thiophene in 100 cm^3 of dichloromethane

Stock solution B: 0.39 g of 2,5-dimethylthiophene in 100 cm^3 of dichloromethane. The standards were then prepared by using set quantities of each stock solution, A and B, and adding them to dichloromethane to give 10 cm^3 aliquots. The volumes of solution A and B are given in Table 3.1.

Table 3.1. The volumes of standard solutions A and B.

Stock A/cm^3	**Stock B/cm^3**
0.1	1.0
0.2	1.0
0.4	1.0
0.6	1.0
0.8	1.0
1.0	1.0

Each standard was prepared in duplicate and shaken with 2x5 cm^3 of water. Since the original Fenton-catalysed oxidation reaction samples require an extraction into dichloromethane and then drying, these processes inevitably cause the loss of thiophene in variable amount. Therefore, the above standards were also shaken with water , and the dichloromethane layer was dried using magnesium sulphate and each extract were analysed by GC/MS.

GC/MS Analysis

The conditions for GC/MS analysis required some instrumental modifications due to low retention time (t_R = 1.43), it was not possible to obtain an appropriate peak area for the thiophenes. Instead of SE-54, a more polar column, carbowax, made it possible to obtain a GC peak for thiophene with longer retention time (t_R = 2.03). Additionally, a new ramp program was used, allowing the column to cool down to 30° C and holding it at this temperature for 5 minutes which gave a better GC peak. The new temperature program was adopted, involving a ramp of 30° C (5 minutes) to 270° C (ca. 35° C/min).

Peak areas of standard mixture of solutions A and B were calculated and a linear ratio values obtained. These values were then plotted against the concentration of thiophene.

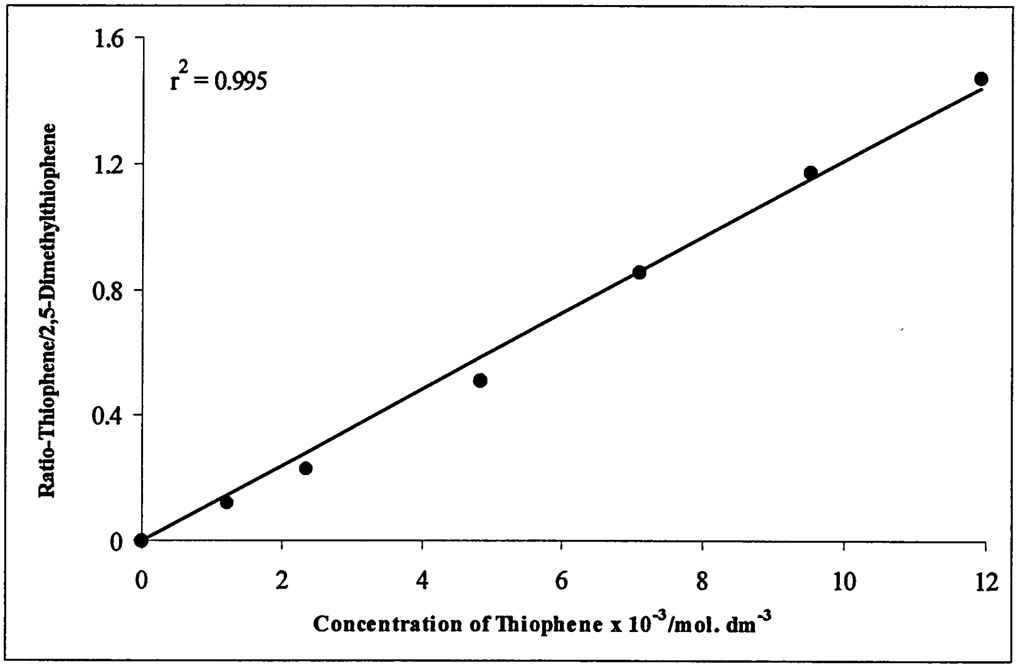
Results

Table 3.2. The ratios obtained from the standard solution mixture of A and B for different thiophene concentrations.

Concentration of thiophene x 10^{-3}/mol dm^{-3} (A)	**Ratio thiophene (A)/2,5-dimethylthiophene (B)**	**% RSD**
1.21	0.120	5.0
2.33	0.231	9.2
4.83	0.512	6.3
7.10	0.851	5.1
9.52	1.170	3.2
11.91	1.473	7.5

The values are represented graphically below and the graph is found to be a straight line with a correlation coefficient of 0.995.

Figure 3.1. Standard calibration graph for thiophene.



This graph proves that the GC/MS system does respond linearly to the changes in the concentration of thiophene.

3.2. 2-Methylthiophene: Preparation and Analysis of Standards

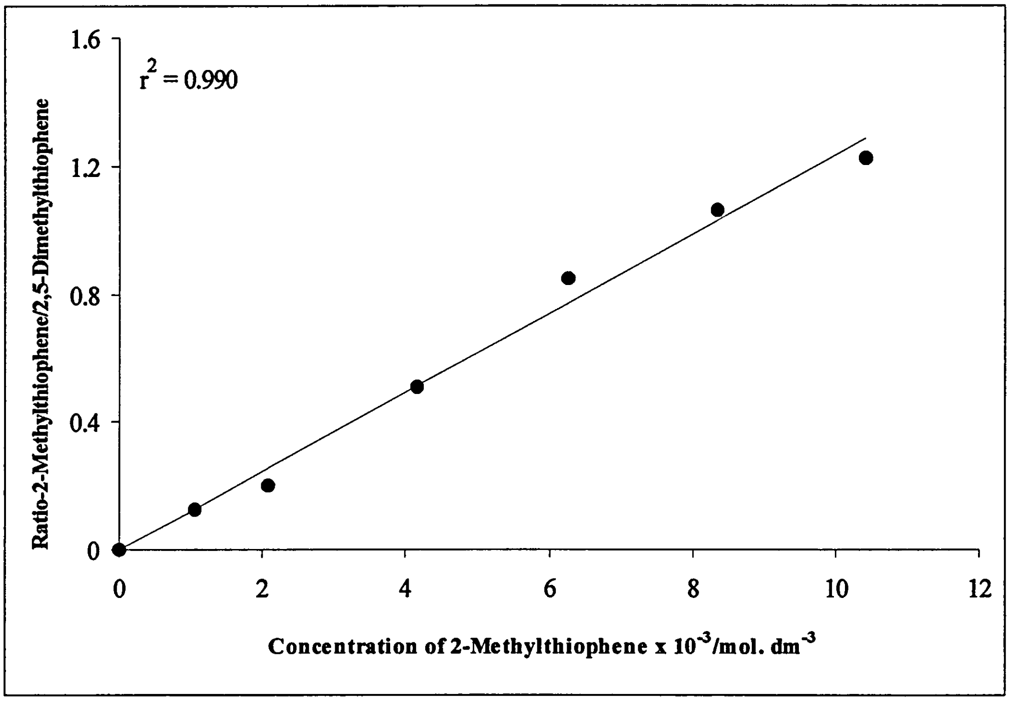
The preparation and analysis of standards for 2-methylthiophene (1.01 g in 100 cm^3 dichloromethane) was carried out in exactly the same way as for those in section 3.1. above, using 2,5-dimethylthiophene as internal standard (stock solution B). GC conditions used for the analysis of standards in section 3.1. were also adopted.

Results

Table 3.3. The ratios obtained from the standard solution mixture of A and B for different 2-methylthiophene concentrations.

Concentration of 2-methyl thiophene x 10^{-3}/mol dm^{-3} (A)	**Ratio 2-methylthiophene (A)/ 2,5-dimethylthiophene (B)**	**% RSD**
1.04	0.125	2.3
2.08	0.202	4.2
4.16	0.511	2.1
6.25	0.850	5.6
8.33	1.060	1.4
10.42	1.221	1.2

Figure 3.2. Standard calibration graph for 2-methylthiophene.



The values are represented graphically and the graph is found to be a straight line with a correlation coefficient of 0.990. Figure 3.2 shows standard calibration graph of 2-methylthiophene and GC/MS system does respond linearly to changes in concentration of 2-methylthiophene.

3.3. 3-Methylthiophene: Preparation and Analysis of Standards

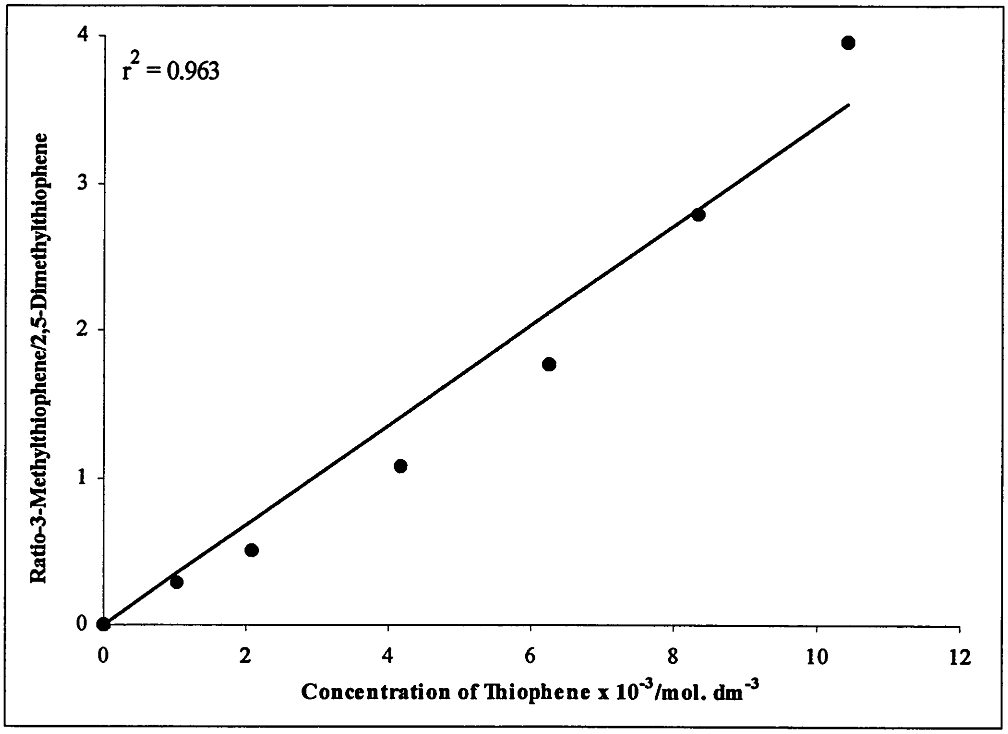
The preparation and analysis of standards for 3-methylthiophene was carried out in exactly the same way as for those in section 3.1. above, using 2,5-dimethylthiophene as internal standard (stock solution B). GC conditions used for the analysis of standards in section 3.1. were also adopted.

Table 3.4. The ratios obtained from the standard solution mixture of A and B for different 3-methylthiophene concentrations.

Concentration of 3-methyl thiophene x 10^{-3}/mol dm^{-3} (A)	Ratio 3-methylthiophene (A)/ 2,5-dimethylthiophene (B)	% RSD
1.04	0.292	2.7
2.08	0.502	3.2
4.16	1.070	6.1
6.25	1.762	4.5
8.33	2.788	3.8
10.42	3.962	1.4

The values are represented graphically below and the graph is found to be a straight line with a correlation coefficient of 0.963.

Figure 3.3. Standard calibration graph for 3-methylthiophene.



3.4. Catalysed Oxidation Reactions of Thiophene and 2- and 3-Methylthiophene

The oxidation reactions were carried out exactly as outlined in section 2.1. Sampling for quantitative determination was made at regular intervals during the oxidation reaction. Sample preparation for the quantitative analysis of each of the reaction mixtures involved taking 1 cm^3 of the reaction mixture after a set time, spiking it with 1 cm^3 of the internal standard stock solution B and then making up to 10 cm^3 aliquots with water. The aliquot (10 cm^3) was then extracted with dichloromethane and the resulting extracts were dried using magnesium sulphate. Each sample was then analysed using GC/MS and this procedure was repeated with three replicates of each sample to avoid sampling variance, since, in spite of vigorous stirring, the reaction mixture may not be homogenous and repeating the sampling would help to obtain more reliable results in the determination of the concentration of unreacted thiophenes. Thus, concentrations of unreacted thiophenes given below are the means of these results and relative standard deviations. GC/MS conditions used for the analysis of standards and samples in section 3.1 above were adopted.

3.4.1. Results

The results of metal catalysed oxidations of thiophene and 2- and 3-methylthiophenes considered here are given in two main sections, Fenton-related and Fenton-like oxidations of thiophenes. Each of the Fenton-related and Fenton-like oxidation systems was investigated over two different time periods; 1 hour and 24 hour and reactions were carried out in water. The results are presented in Tables. which include the ratio values observed between the residual thiophene and the appropriate internal standard used. The associated concentration values, indicating the amount of each of the thiophenes residual after the set time period, were then determined from the appropriate calibration graph. These values are also expressed as a percentage of the initial concentration which makes the results more understandable. Initially, data were acquired after 1 hour and 24 hour after the reaction started. The oxidation reactions of thiophenes were then monitored for first 3 hour period after the reaction started and the results obtained from each of the catalyst systems are given in corresponding tables and graphs. The residual thiophene values were then plotted against reaction time periods.

3.4.1.1. Fenton-related and Fenton-like Oxidations of Thiophene

Table 3.5 lists each of the different Fenton-related and Fenton-like catalyst systems for the oxidation of thiophene.

When the oxidation reaction of thiophene using Fenton-related reagents was monitored over the first 3 hours after the reaction started (1 cm^3 sample was taken out every 15 minutes in the first 1 hour, and then sampling was carried on at hourly intervals), complete oxidation was observed at the end of first 30 minutes period. The residual thiophene concentrations are given in Table 3.6 and plotted against time in Figure 3.4.

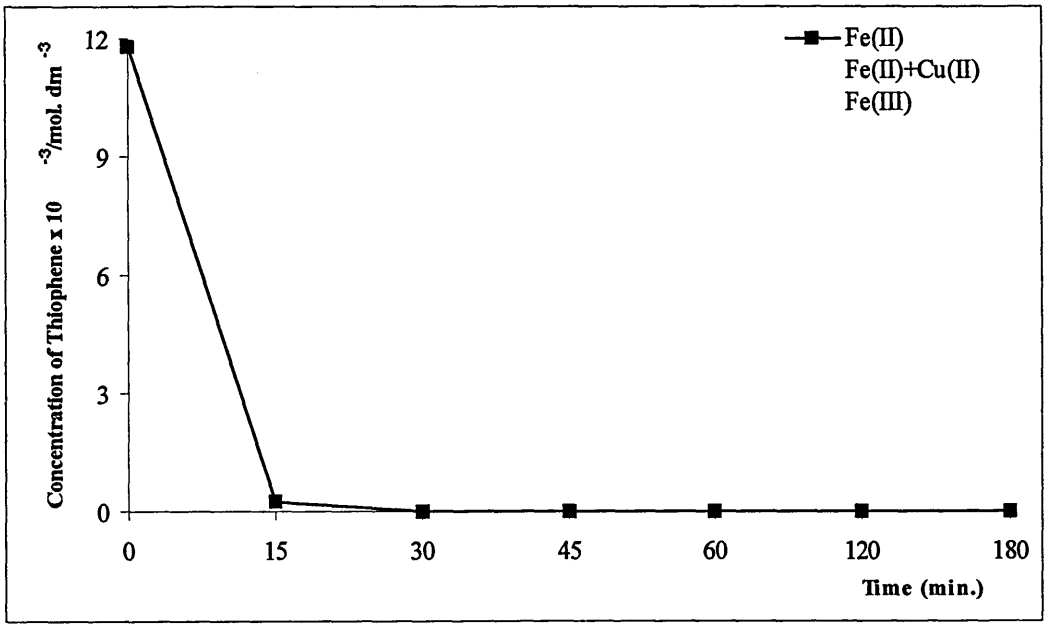
Table 3.5. Residual concentrations of thiophene in the Fenton-related and Fenton-like catalyst systems.

Catalyst	Ratio Values	%-RSD	Concentration of thiophene x 10^{-3}/mol dm^{-3}	Residual Thiophene (%)
Fe^{II}/H_2O_2				
1 hour	-	-	< 0.1	< 1.0
24 hour	-	-	< 0.1	< 1.0
Fe^{III}/H_2O_2				
1 hour	-	-	< 0.1	< 1.0
24 hour	-	-	< 0.1	< 1.0
$Fe^{II}/Cu^{II}/H_2O_2$				
1 hour	-	-	< 0.1	< 1.0
24 hour	-	-	< 0.1	< 1.0
V^{IV}/H_2O_2				
1 hour	0.575	2.4	4.46	37.5
24 hour	0.337	6.7	2.67	22.5
Cu^{I}/H_2O_2				
1 hour	1.443	2.1	11.31	95.0
24 hour	0.286	3.5	2.17	18.3
Cu^{II}/H_2O_2				
1 hour	1.421	4.4	11.51	96.7
24 hour	0.762	5.1	5.85	49.2
Ti^{III}/H_2O_2				
1 hour	0.49	3.6	4.26	35.8
24 hour	0.46	4.2	4.07	34.2

Table 3.6. Residual thiophene concentrations with Fenton-related reagents; Fe(II), Fe(III), and Fe(II) + Cu(II)

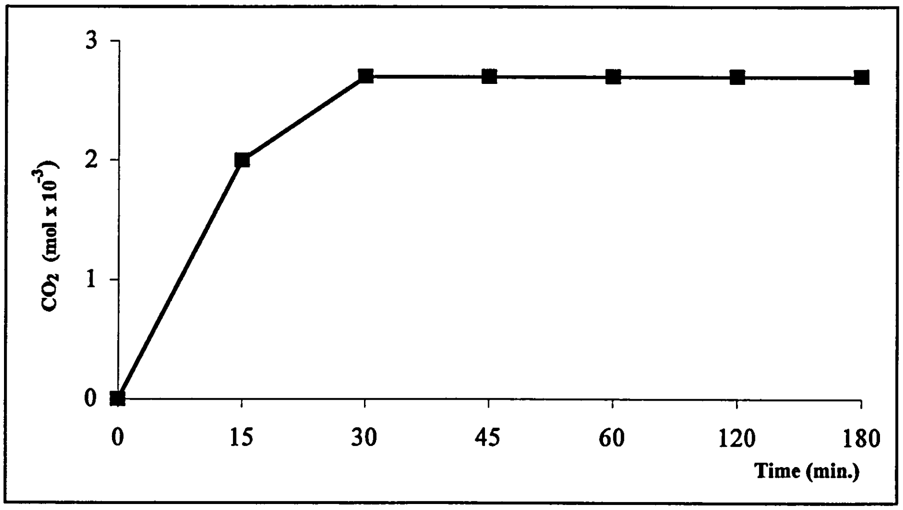
Concentration of thiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual Thiophene (%)
11.80	0	4.3	100.0
0.24	15	1.7	2.0
-	30	-	0.0

Figure 3.4. Residual thiophene concentrations with Fenton-related reagents; Fe(II), Fe(III), and Fe(II) + Cu(II)



The graph in Figure 3.4 shows a very sharp initial decrease in the concentration of thiophene over the first 15 minutes and thereafter unreacted thiophene was not observed, indicating that all of the thiophene has been oxidised by hydrogen peroxide in the presence of Fenton's reagent under these conditions. Essentially the same results were observed in the case of the Fenton-related iron(III) and iron(II)+copper(II) catalyst systems. The oxidation reaction appear to be completely destructive, since only traces of minor oxidation products were observed when the reaction mixture was analysed (after extracting into dichloromethane) using the GC/MS technique. The oxidation with iron(II) and iron(III) resulted in the formation of 2-hydroxythiophene (**13**) in a yield of less than 1%, and so presumably other oxidation products were formed but had undergone further destructive oxidation. Interestingly, addition of copper(II) ions significantly increased the formation of 2-hydroxythiophene from 1% to 9%. Complete oxidative destruction of the ring system was indicated by the formation of carbon dioxide which was collected into a dilute barium hydroxide solution (3.15 g/100 cm^3) over a 3 hour period, in a sealed system. The precipitated barium carbonate was filtered off and dried, enabling the amount of carbon dioxide to be calculated. It was shown that 0.0027 mol carbon dioxide formed from 0.01 mol thiophene. The formation of carbon dioxide was also monitored over a 3 hour period by repeating this procedure every 30 minutes after reaction started and the results are represented graphically in Figure 3.5.

Figure 3.5. Amount of carbon dioxide generated from the oxidation of thiophene in the presence of Fenton's reagent.



The Fenton-like oxidation reactions of thiophene using vanadium(IV), copper(I), copper(II) and titanium(III) catalyst systems were also individually monitored for three hour reaction periods and the results are given in Table 3.7, 3.8, 3.9 and 3.10 respectively.

Table 3.7. Residual thiophene concentrations with the V(IV)/H_2O_2 system.

Concentration of thiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual Thiophene (%)
11.80	0	4.2	100.0
6.65	15	2.3	55.8
6.65	30	3.7	55.8
6.60	45	2.6	55.0
4.46	60	2.4	37.5
4.40	120	5.2	37.4
4.26	180	4.4	35.8

Table 3.8. Residual thiophene concentrations with the Cu(I)/H_2O_2 system.

Concentration of thiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual Thiophene (%)
11.80	0	4.2	100.0
11.86	15	3.6	100.0
11.90	30	2.3	100.0
11.31	45	4.6	95.0
11.37	60	3.1	95.0
11.28	120	3.0	95.0
7.74	180	5.7	65.8

Table 3.9. Residual thiophene concentrations with the Cu(II)/H_2O_2 system.

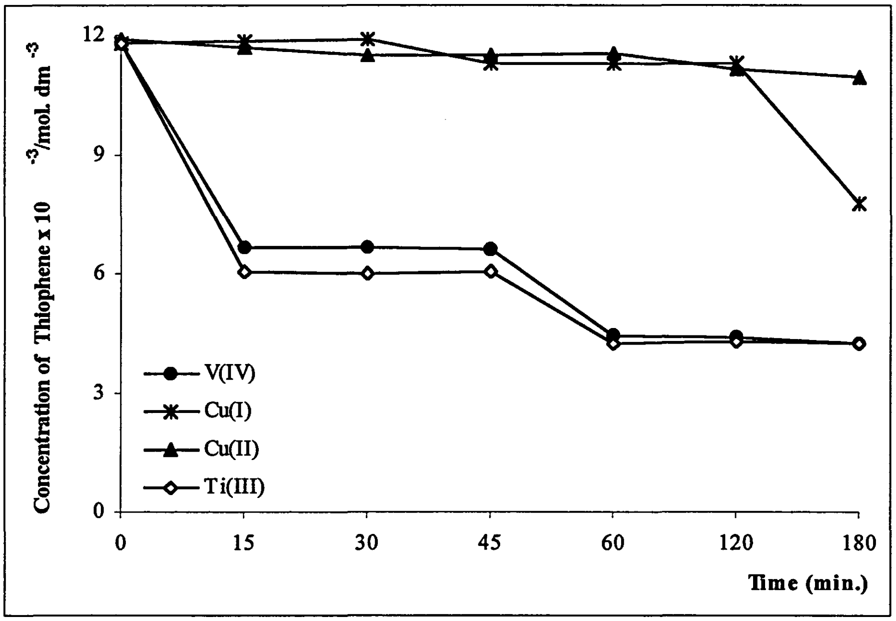
Concentration of thiophene x 10^{-3}/mol dm^{-3}	**Time (minutes)**	**% RSD**	**Residual Thiophene (%)**
11.91	0	3.3	100.0
11.12	15	5.4	98.4
11.52	30	2.8	96.7
11.50	45	3.7	96.7
11.54	60	1.9	96.7
11.12	120	2.5	93.4
10.92	180	3.9	91.7

Table 3.10. Residual thiophene concentrations with the Ti(III)/H_2O_2 system.

Concentration of thiophene x 10^{-3}/mol dm^{-3}	**Time (minutes)**	**% RSD**	**Residual Thiophene (%)**
11.82	0	6.6	100.0
6.05	15	4.2	50.8
6.00	30	3.5	50.6
6.05	45	2.3	50.8
4.26	60	4.1	35.8
4.28	120	3.0	35.8
4.26	180	1.6	35.8

The results obtained from Tables (3.7-3.10) are represented graphically in Figure 3.6 below. All systems are shown in the same graph with different patterns.

Figure 3.6. Residual thiophene concentrations with Fenton-like reagents; V(IV), Cu(I), Cu(II) and Ti(III)



It is obvious that Fenton-like oxidations of thiophene are not as effective as with iron-containing systems. After a three hour oxidation period, both vanadium(IV) and titanium(III) systems oxidized most of thiophene, residual thiophene is only 35.8 % while this decreased down to 22.5 % with vanadium(IV) after a 24 hour reaction period. The titanium(III) system did not show any significant decrease (residual thiophene 34.2 %) after 24 hour.

However, an interesting observation was achieved with copper(I) and copper(II) systems. Both of them oxidise only small amounts of thiophene over a 3 hour reaction period, but, when the reactions were left to stand for 24 hour, the residual thiophene had decreased to 18.3 % for Cu(I) and 49.2 % for Cu(II) systems. These oxidation reactions proceeded slower than other systems, but resulted in the formation of larger amounts of 2-hydroxythiophene. More interestingly, when the oxidation reaction was carried out with the excess hydrogen peroxide (0.2 mol; 24.8 cm^3, 27 % H_2O_2) over 24 hour, the resulting 2-hydroxythiophene was obtained in a preparatively useful 59 % overall yield [1]. A single-step procedure for the specific oxidation of thiophene to 2-hydroxythiophene and its thiolactone tautomers under aqueous conditions was subsequently developed. Several other routes to the 2-hydroxythiophene system have been described, but all of them involve several steps and some resulted in significantly lower yields. According to the literature, 2-hydroxythiophene was isolated in 22 % overall yield from the oxidation, using oxygen gas, of 2-thienylmagnesium bromide [2], in 28-70 % yield by the oxidation of 2-thienylboronic acid using hydrogen peroxide [3] and in 10 % yield from the reaction of 2-thienyllithium with 1,2,3,4-tetrahydro-1-naphthyl hydroperoxide [4]. It has also been prepared by heating 2-butoxythiophene with toluene-*p*-sulphonic acid at 150 °C [5], and by the hydrolysis of 2-thienylisopropyl carbonate, obtained together with the related 3-thienyl isomers, via oxygenation of thiophene with diisopropyl peroxydicarbonate in the presence of copper(II) chloride in acetonitrile [6].

The formation of 2-hydroxythiophene in the oxidation of thiophene using the above aqueous peroxide-copper(II) system strongly implies the involvement of hydroxyl radicals under these conditions, arising from a Fenton-like system. 2-Hydroxythiophene was also formed as the principal product in the oxidation of thiophene under aqueous conditions using either iron(II)/ or iron(III)/hydrogen peroxide reagents, although overall yields were lower (9.0 %) and traces of other products, e.g. ring cleavage products, were detected, compared to the outcome of the copper(II)/hydrogen peroxide oxidation, which is remarkably clean and in high yield.

3.4.1.2. Fenton-related and Fenton-like Oxidations of 2-Methylthiophene

Quantitative analysis was also carried out on the Fenton-related and Fenton-like oxidations of 2-methylthiophene using the experimental procedure as outlined in sections 2.1 and 3.4.1.

The ratio values observed between 2-methylthiophene and the internal standard were used for the determination of residual 2-methylthiophene concentration in each reaction by using the appropriate calibration graph. Table 3.11 below lists each of the Fenton-related and Fenton-like catalyst systems for the oxidation of 2-methylthiophene for 1 hour and 24 hour reaction periods. All results were obtained from the oxidation of 0.01 mol 2-methylthiophene using 0.02 mol hydrogen peroxide and the reactions were carried out in water only (no co-solvent was used).

From Table 3.11, it may be seen that iron-containing catalyst systems possess great oxidation capacity for 2-methylthiophene. In particular, the Fe(III)/H_2O_2 system has achieved 100 % oxidation of 2-methylthiophene to the range of oxidation products outlined in section 2.2.1.2 (smaller hydrogen peroxide concentration; 6.15 cm^3, 27 % H_2O_2, 0.02 mol). In the presence of an excess of hydrogen peroxide, all 2-methylthiophene disappeared in the first half hour, giving only minor amount of oxidation products (less than 1.0 %). A combination of copper(II) ions with Fe(II) ions seemed to improve the oxidation reaction, and the residual 2-methylthiophene decreased from 49.7 to 40.1 % in a one hour reaction period.

Table 3.11. Residual concentrations of 2-methylthiophene in the Fenton-related and Fenton-like catalyst systems.

Catalyst	Ratio Values	% RSD	Concentration of 2-methyl thiophene x 10^{-3}/mol dm^{-3}	Residual 2-methylthiophene (%)
Fe^{II}/H_2O_2				
1 hour	0.670	2.3	5.17	49.7
24 hour	-	-	-	0.0
Fe^{III}/H_2O_2				
1 hour	-	-	-	0.0
24 hour	-	-	-	0.0
$Fe^{II}/Cu^{II}/H_2O_2$				
1 hour	0.583	4.7	4.18	40.1
24 hour	-	-	-	0.0
V^{IV}/H_2O_2				
1 hour	0.575	2.4	4.46	37.5
24 hour	0.337	6.7	2.67	22.5
Cu^{I}/H_2O_2				
1 hour	0.993	5.0	7.82	75.0
24 hour	0.304	2.9	2.71	26.0
Cu^{II}/H_2O_2				
1 hour	0.722	4.7	5.83	56.0
24 hour	2.163	2.5	2.18	21.0
Ti^{III}/H_2O_2				
1 hour	1.160	4.4	9.17	88.0
24 hour	0.920	1.6	6.67	63.9

When the reaction was left for over 24 hour, all three Fenton-related (Fe^{II}/H_2O_2, Fe^{III}/H_2O_2, and $Fe^{II}/Cu^{II}/H_2O_2$) systems have achieved 100 % conversion, resulting in the formation of the range of oxidation products outlined in section 2.2.1.2., mainly 5-

methyl-2-hydroxythiophene (as its thione tautomers) in *ca.* 10 % yield. In addition to this, other significant products, dihydroxythiophenes and the dimeric compound 2-methyl-5-(2-thienylmethyl)thiophene were formed in less than 10 % yield. The oxidation reaction of 2-methylthiophene using Fenton-related reagents (0.01 mol 2-methylthiophene and 0.02 mol hydrogen peroxide) was monitored over the first three hours after the reaction was started. The same sampling technique was applied as detailed in section 3.4.2.1, the residual thiophene concentrations are given in Tables 3.12, 3.13 and 3.14 for Fe^{II}/H_2O_2, $Fe^{II}/Cu^{II}/H_2O_2$ and Fe^{III}/H_2O_2 respectively.

Table 3.12. Residual 2-methylthiophene concentrations with the $Fe(II)/H_2O_2$ system.

Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.42	0	5.1	100.0
9.72	15	2.4	93.3
8.00	30	4.1	76.8
5.91	45	4.0	56.7
5.17	60	2.3	49.7
1.46	120	8.5	14.1
-	180	-	0.0

Table 3.13. Residual 2-methylthiophene concentrations with $Fe(II)/Cu(II)/H_2O_2$ system.

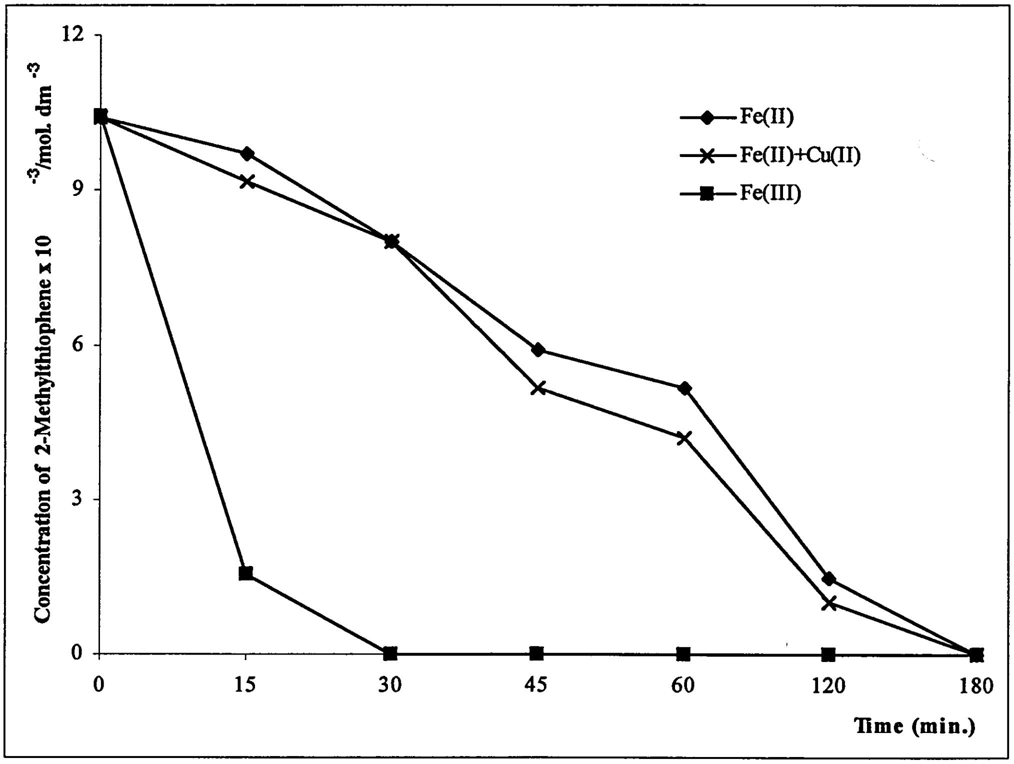
Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.40	0	1.2	100.0
9.16	15	6.6	89.8
8.00	30	7.1	76.8
5.17	45	3.4	49.7
4.18	60	4.7	40.1
1.01	120	9.3	9.6
-	180	-	0.0

Table 3.14. Residual 2-methylthiophene concentrations with the Fe(III)/H_2O_2 system.

Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.46	0	4.4	100.0
1.56	15	2.8	15.0
-	30	-	0.0

The results from tables 12, 13 and 14 were represented graphically in Figure 7 below.

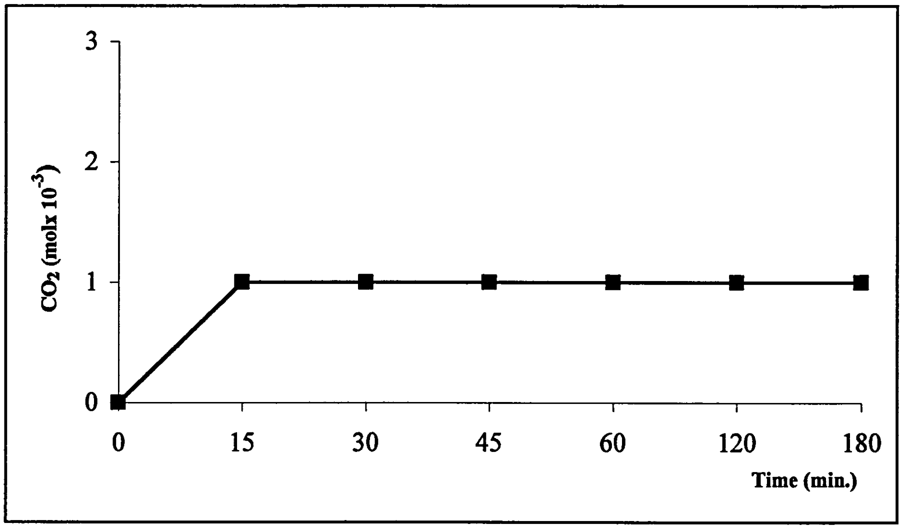
Figure 3.7. Residual 2-methylthiophene concentrations with Fenton-related reagents; Fe(II), Fe(III), and Fe(II) + Cu(II)



Apparently, the iron(III)-catalysed oxidation reaction converts all of the 2-methylthiophene into oxidation products over the first 30 minutes of the reaction, whereas it takes almost 3 hours with the iron(II) and iron(II)/copper(II) catalyst systems. All three catalyst systems give rise to the same range of oxidation products.

The formation of carbon dioxide was monitored for 3 hours by repeating the procedure described in section 3.4.2.1. for Fe(III)/H_2O_2 system resulting in the formation of 0.0018 mol carbon dioxide from 0.01 mol 2-methylthiophene. The results are presented graphically in Figure 3.8.

Figure 3.8. Amount of carbon dioxide generated from the oxidation of 2-methyl thiophene in the presence of Fenton's reagent.



The shape of the graph in Figure 3.8 is very similar to that of Figure 3.5. Each graph showes a sharp increase in the amount of carbon dioxide over the first 30 minutes but thereafter it remains unchanged for the rest of the reaction period. It is assumed, therefore, that the oxidation of 2-methylthiophene has reached completion in 30 minutes, giving a range of oxidation products and to some extent also having undergone a major ring cleavage. The Fenton-like oxidation reactions of 2-methylthiophene using vanadium(IV), copper(I), copper(II) and titanium(III) catalyst systems were also monitored individually over a 3 hour reaction period and the results are given in Tables (3.15, 3.16, 3.17 and 3.18) respectively.

Table 3.15. Residual 2-methylthiophene concentrations with the V(IV)/H_2O_2 system

Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.39	0	1.2	100.0
5.42	15	2.6	52.0
5.42	30	3.0	52.0
5.00	45	4.4	48.0
3.45	60	3.4	33.9
3.41	120	5.3	32.7
3.13	180	4.2	30.0

Table 3.16. Residual 2-methylthiophene concentrations with the Cu(I)/H_2O_2 system

Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.44	0	1.3	100.0
8.26	15	6.6	79.5
7.82	30	3.1	75.0
7.81	45	2.7	75.0
7.82	60	5.0	75.0
5.62	120	8.6	53.9
4.79	180	7.4	46.0

Table 3.17. Residual 2-methylthiophene concentrations with the Cu(II)/H_2O_2 system

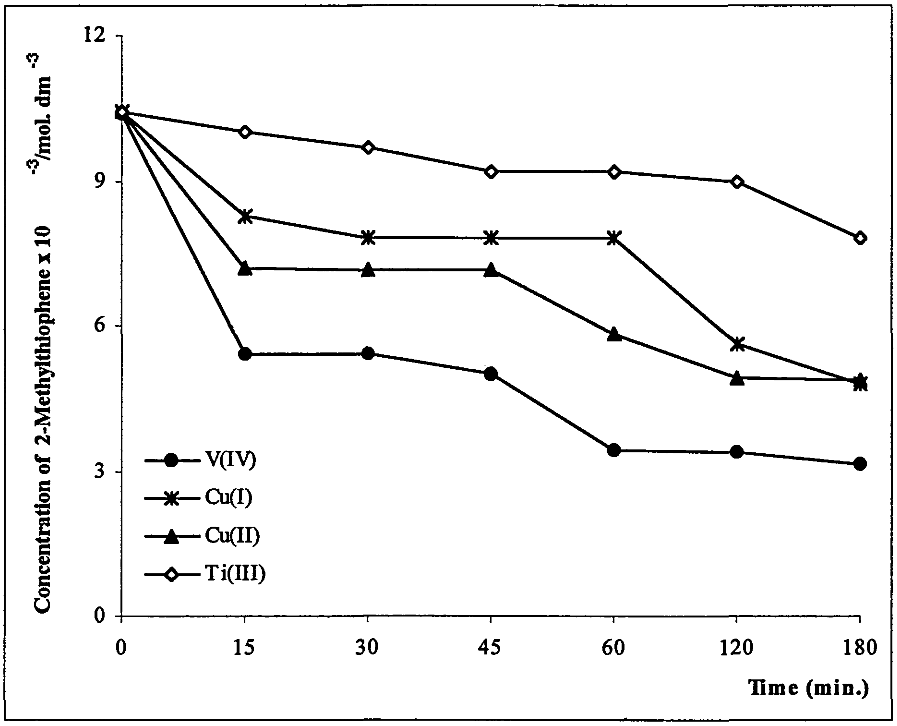
Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.42	0	4.2	100.0
7.18	15	3.4	68.9
7.16	30	7.5	68.7
7.15	45	2.7	68.6
5.83	60	4.7	56.0
4.91	120	1.9	47.1
4.90	180	2.2	47.1

Table 3.18. Residual 2-methylthiophene concentrations with the Ti(III)/H_2O_2 system

Concentration of 2-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 2-methylthiophene (%)
10.42	0	5.5	100.0
10.00	15	3.9	96.9
9.69	30	5.8	93.0
9.17	45	2.6	88.0
9.17	60	1.5	88.0
8.96	120	4.4	86.0
7.82	180	4.6	75.0

The results given in Tables (3.15-3.18) are presented graphically in Figure 3.9 and all systems are shown in the same graph with different patterns.

Figure 3.9. Residual 2-methylthiophene concentrations with Fenton-like reagents; V(IV), Cu(I), Cu(II) and Ti(III).



Again, the Fenton-like oxidations of 2-methylthiophene are not as effective as the iron/hydrogen peroxide systems. Although the oxidative conversion increased on leaving the reaction for 24 hours, the concentration of 2-methylthiophene falling from 5.83x10^{-3} to 2.18x10^{-3} mol dm^{-3} for Cu(II)/H_2O_2 system, some of the 2-methylthiophene has still remained unchanged. All Fenton-like oxidations of 2-methylthiophene resulted in the formation of the same range of oxidation products as observed in the Fenton-related oxidations. If the three hour reaction period is taken into consideration, the vanadium(IV)/H_2O_2 system has achieved a greater degree of oxidation than Fenton-related oxidation systems since the residual 2-methylthiophene fell to 52 % in the first 15 minutes, compared to the iron(II)/H_2O_2 system in which only 6.7 % of initial 2-methylthiophene is oxidised in the same time period.

The oxidation products formed are, again, very similar to those formed in the Fenton-catalysed oxidation of 2-methylthiophene. The evidence for radical chemistry occurring when vanadium(IV), copper(I), copper(II) and titanium(III) are present as the catalyst is provided by the formation of dimeric structures and hydroxythiophene components. Significantly, copper(II) ions showed an increase in the extent of formation of 5-methyl-2-hydroxythiophene (from 10 to 13-15 %) and 2-methyl-5-(2-thienylmethyl) thiophene compared to other systems.

3.4.1.3. Fenton-related and Fenton-like Oxidations of 3-Methylthiophene

Quantitative analysis is also carried out with the Fenton-related and Fenton-like oxidations of 3-methylthiophene using the experimental procedure outlined in sections 2.1 and 3.4.1 in this Chapter. The results are detailed in tables below, where the ratio values were used for the determination of the residual 3-methylthiophene concentration by use of the appropriate calibration graph shown in Figure 3.3. Table 3.19 below lists each of the different Fenton-related and Fenton-like catalyst systems for the oxidation of 3-methylthiophene for 1 hour and 24 hour reaction periods.

All results were obtained from the oxidation of 0.01 mol 3-methylthiophene using 0.02 mol hydrogen peroxide. The reaction was carried out in water only (no co-solvent was used). From Table 3.19, it can be seen that the oxidation of 3-methylthiophene is slower and less effective than the 2-methylthiophene oxidation.

Table 3.19. 3-methylthiophene

Catalyst	Ratio Values	% RSD	Concentration of 3-methyl thiophene x 10^{-3}/mol dm^{-3}	Residual 3-methylthiophene (%)
Fe^{II}/H_2O_2				
1 hour	0.512	2.6	2.14	20.6
24 hour	-	-	-	0.0
Fe^{III}/H_2O_2				
1 hour	1.770	4.8	6.30	60.5
24 hour	0.714	6.3	2.64	25.3
$Fe^{II}/Cu^{II}/H_2O_2$				
1 hour	1.170	4.2	4.29	41.2
24 hour	0.520	1.6	2.18	20.9
V^{IV}/H_2O_2				
1 hour	2.788	4.0	8.32	79.8
24 hour	1.196	2.9	4.41	42.3
Cu^{I}/H_2O_2				
1 hour	3.201	5.5	9.95	95.5
24 hour	2.283	2.4	7.94	76.2
Cu^{II}/H_2O_2				
1 hour	3.225	8.1	9.57	91.9
24 hour	1.680	6.7	6.17	59.2
Ti^{III}/H_2O_2				
1 hour	3.367	5.9	9.83	94.3
24 hour	2.275	2.0	7.30	70.1

Only iron(II)/H_2O_2 (Fenton's reagent) has achieved 100 % oxidation over the 24 hour reaction period, and all other catalyst systems did not show great oxidation capacity, even iron(III)/H_2O_2 was able to oxidise *ca.* 39.5 % of 3-methylthiophene with the residual 3-methylthiophene at 60.5 % for 1 hour and 75 % for 24 hours. Interestingly the Fe(II)/Cu(II)/H_2O_2 system showed a lower oxidation capacity than the iron(II)/H_2O_2 system. Somehow addition of copper(II) ions reduces the rate of oxidation of 3-methylthiophene over the first hour, but the reaction reaches ca. 79.1 % conversion rate after 24 hours.

The Fenton-like oxidation of 3-methylthiophene using copper(I), copper(II) and Ti(III) have achieved only 5-10 % oxidation of 3-methylthiophene over a 1 hour reaction period, but leaving the reactions for another 23 hours has improved the oxidative conversion, with residual level of 3-methylthiophene of 59.2-76.2 %. However, these systems are less effective than the Fenton-related catalyst systems. The vanadium(IV)-catalysed oxidation reaction oxidises ca. 57.7 % of 3-methylthiophene after 24 hours.

In the Fe(II)/H_2O_2 system, two major oxidation products, 3-methyl-2-hydroxythiophene and 4-methyl-2-hydroxythiophene (components **58** and **59** respectively) were isolated from the reaction mixture of 3-methylthiophene in 14.0 and 6.8 % yields respectively. Although only 40.8 % of 3-methylthiophene was oxidised by the copper(II)/H_2O_2 system, the oxidation resulted in the formation of components (**58**) and (**59**) in 11.5 and 8.5 % yields, respectively. The oxidation reactions of 3-methylthiophene using Fenton-related and Fenton-like reagents (0.01 mol 3-methylthiophene and 0.02 mol hydrogen peroxide) were also monitored over the first three hours after the reactions were initiated. The same sampling technique was applied as described above. The results are given in tables 3.20, 3.21 and 3.22 for the Fe(II)/H_2O_2, Fe(II)/Cu(II)/H_2O_2 and Fe(III)/H_2O_2 systems, respectively.

Table 3.20. Residual 3-methylthiophene concentrations with the Fe(II)/H_2O_2 system

Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.43	0	2.0	100.0
5.91	15	1.9	56.7
5.29	30	1.4	50.8
4.40	45	3.8	42.3
2.14	60	1.5	20.6
3.27	120	6.5	31.4
1.89	180	4.6	18.1

Table 3.21. Residual 3-methylthiophene concentrations with the Fe(II)/Cu(II)/H_2O_2 system

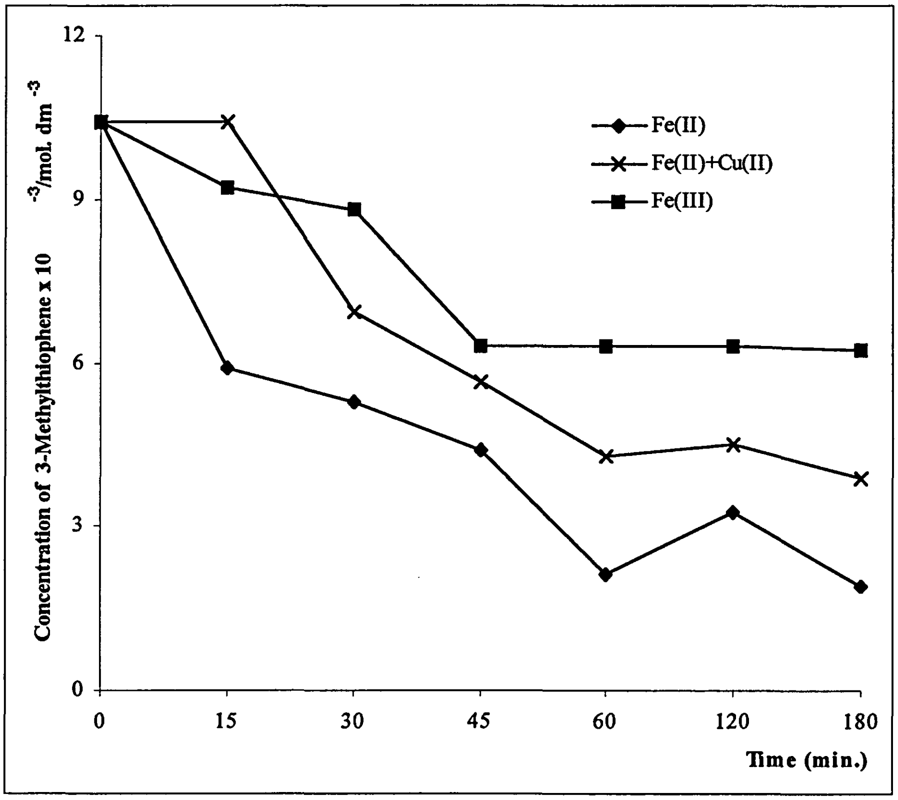
Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.42	0	6.8	100.0
10.42	15	3.1	100.0
6.93	30	5.3	66.5
5.66	45	2.7	54.4
4.29	60	3.9	41.2
4.53	120	1.1	43.5
3.89	180	4.5	37.4

Table 3.22. Residual 3-methylthiophene concentrations with the Fe(III)/H_2O_2 system

Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.43	0	2.2	100.0
9.20	15	2.6	88.3
8.82	30	6.5	84.6
6.30	45	4.0	60.5
6.30	60	3.5	60.5
6.30	120	5.1	60.5
6.25	180	4.9	60.3

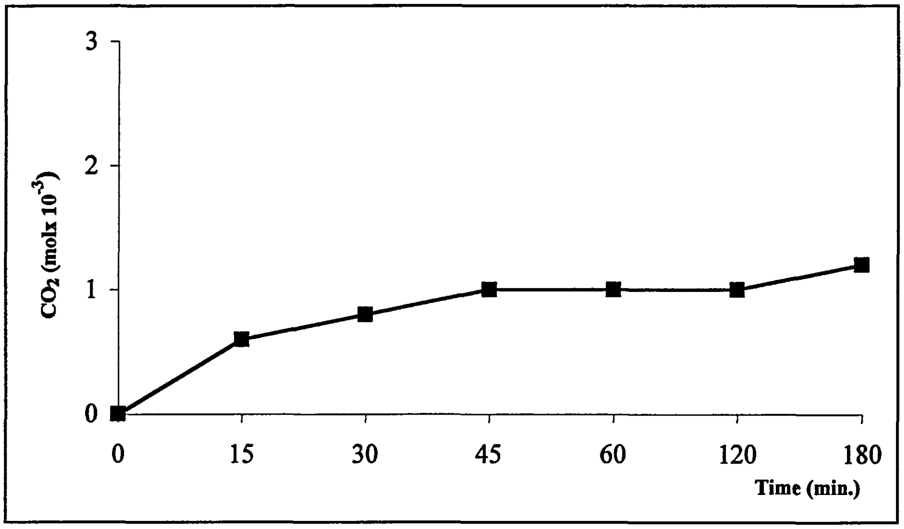
The results from Tables (3.20-3.22) were represented graphically in Figure 10.

Figure 3.10. Residual 3-methylthiophene concentrations with Fenton-related reagents; Fe(II), Fe(III), and Fe(II) + Cu(II)



From Table 3.20 and Figure 3.10, it can be seen that half of the 3-methylthiophene was oxidised over the first 30 minutes by using iron(II)/H_2O_2 system which is the most effective one. The residual 3-methylthiophene concentration decreased from 5.29×10^{-3} mol dm^{-3} to 1.89×10^{-3} mol dm^{-3} over the residual 2.5 hour and it was assumed that the reaction would havegone to completion in a 3-4 hour reaction period. The formation of carbon dioxide was also monitored over for the 3 hour Fe(II)/H_2O_2 system by repeating the procedure described in section 3.4.2.1., resulting in the formation of 0.0012 mol CO_2 from 0.01 mol 3-methylthiophene. Figure 3.11 shows the formation of carbon dioxide with reaction time.

Figure 3.11. Amount of carbon dioxide generated from the oxidation of 3-methyl thiophene in the presence of Fenton's reagent.



Carbon dioxide concentration increased steadily in the first 30 minutes and then showed a linear increase over the rest of the reaction period; 0.0012 mol carbon dioxide was generated after a 3 hour reaction time. Again, it was assumed that carbon dioxide was formed from the ring cleavage of 3-methylthiophene.

The Fenton-like oxidation reactions of 3-methylthiophene using vanadium(IV), copper(I), copper(II) and titanium(III) catalyst systems were also monitored individually over 3 hours. The results are given in tables (3.23, 3.24, 3.25 and 3.26) below.

Table 3.23. Residual 3-methylthiophene concentrations with the V(IV)/H_2O_2 system

Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.42	0	2.7	100.0
8.83	15	3.1	84.7
8.83	30	4.9	84.7
8.83	45	5.0	84.7
8.32	60	1.3	79.8
5.66	120	4.6	54.4
5.66	180	1.9	54.4

Table 3.24. Residual 3-methylthiophene concentrations with the Cu(I)/H_2O_2 system

Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.42	0	2.8	100.0
10.42	15	5.1	100.0
9.95	30	4.4	95.5
9.95	45	3.7	95.5
9.95	60	3.0	95.5
9.95	120	2.8	95.5
9.90	180	6.0	95.0

Table 3.25. Residual 3-methylthiophene concentrations with the Cu(II)/H_2O_2 system

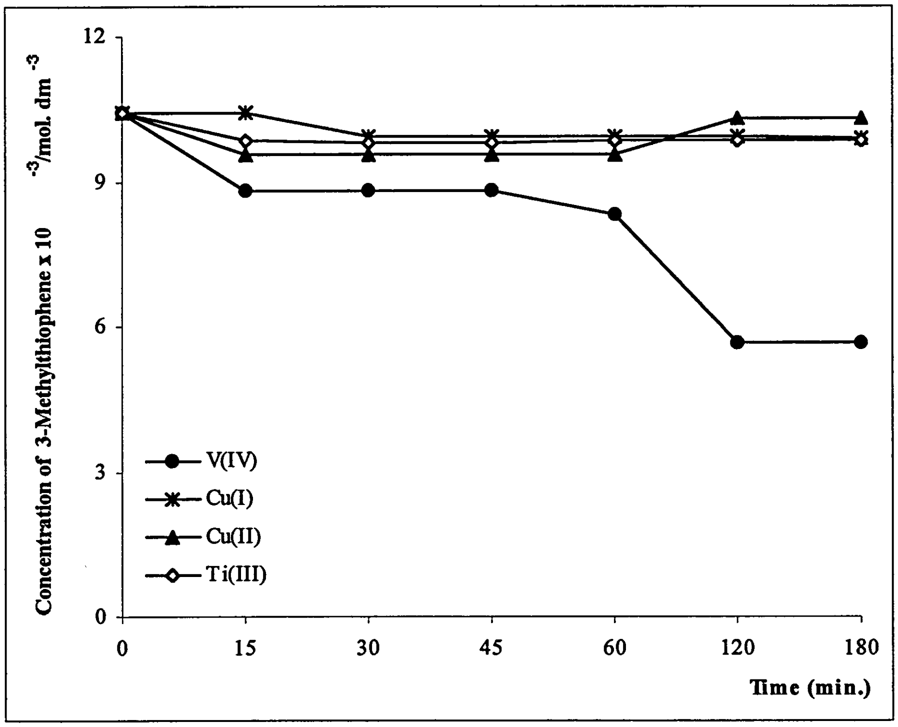
Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.42	0	1.9	100.0
9.57	15	2.0	91.9
9.57	30	2.2	91.9
9.57	45	2.4	91.9
9.57	60	1.7	91.9
10.29	120	4.5	98.8
10.29	180	4.2	98.8

Table 3.26. Residual 3-methylthiophene concentrations with the Ti(III)/H_2O_2 system

Concentration of 3-methylthiophene x 10^{-3}/mol dm^{-3}	Time (minutes)	% RSD	Residual 3-methylthiophene (%)
10.42	0	2.1	100.0
9.84	15	3.0	94.3
9.82	30	2.8	94.2
9.82	45	2.6	94.2
9.83	60	2.5	94.3
9.83	120	2.0	94.3
9.83	180	2.2	94.3

The results shown in Tables (3.22-3.26) are also represented graphically in Figure 3.12 for all Fenton-like oxidation reactions of 3-methylthiophene.

Figure 3.12. Residual 3-methylthiophene concentrations with Fenton-like reagents; V(IV), Cu(I), Cu(II) and Ti(III).



As discussed earlier, the Fenton-like oxidation of 3-methylthiophene involving copper(I), copper(II) and titanium(III) catalyst systems did not achieve significant conversion. Only the vanadium(IV) catalyst system has converted approximately 50 % of 3-methylthiophene over a 3 hour reaction period,. although this lower degree of oxidation showed some similarity to those obtained from the Fenton-related oxidations of 3-methylthiophene.

3.4.2. Summary

The oxidation reactions of thiophene and 2- and 3-methylthiophene involving the use of Fenton-related and Fenton-like catalyst systems showed some differences from each other. Apparently, under the oxidising conditions used, unsubstituted thiophene is the most easily oxidised using all iron-based Fenton-related systems (Table 3.5 and 3.6). In the first 15 minutes of the reaction, 2-hydroxythiophene was formed as a major oxidation product. It is obvious that the oxidation state of the iron (Fe(II) or Fe(III)) does not have any effect on the course of the reaction, both reaction pathways appearing to give hydroxylated products under these conditions. However, it is interesting that the quantitative amount of 2-hydroxythiophene was increased (from 1.0 % to 9.0 %) by the addition of copper(II) ions.

In the case of 2-and 3-methylthiophene, however, Fe(III)/H_2O_2 is the most effective system for the oxidation of 2-methylthiophene over a 1 hour reaction period, while only the Fe(II)/H_2O_2 system oxidised 99 % of the initial concentration of 3-methylthiophene (Table 3.19) over a 24 hour reaction period. The oxidation of 3-methylthiophene was found to be less efficient, as discussed in section 2.2.1.3, for all of the oxidising systems, even over a 24 hour reaction period. From the oxidations of 2- and 3-methylthiophene, it can be concluded that the Fe(II)/H_2O_2 mixture is still the most effective catalyst system and there is no improvement in the use of the new catalyst systems (e.g. Fe(II)/Cu(II)/H_2O_2.

The Fenton-like oxidations of thiophene, 2- and 3-methylthiophene were always less effective than Fenton-related systems. Although both gave a similar range of products via the formation of hydroxyl radicals, there were differences in individual yields, such as with Cu(II)/ H_2O_2 system. The formation of 2-hydroxythiophenes and dithienylmethanes was significantly increased by the use of the Cu(II)/ H_2O_2 oxidation system and seems to promote the extent of the formation of hydroxyl radicals.

In order to make a contribution to the debate associated with the oxidising species responsible for the destruction of each of the thiophenes, the quantitative analysis was also carried out with the Fenton-catalysed oxidations of appropriate thiophene in the presence of the complexing agent EDTA and the radical trap TEMPO. The results showed that the presence of EDTA resulted in a significant increase in rate in the case of the 2-methylthiophene-Fe(II)-H_2O_2-EDTA system. Similarly, the rate of oxidation of 3-methylthiophene, was also increased using the Fe(II)-H_2O_2-EDTA system, the residual 3-methylthiophene being reduced from 49.7 % to 8.9 %. However, the oxidation of thiophene was not affected by the addition of EDTA to the catalyst system. Apparently, there are some similarities between the oxidation products formed in the Fenton-catalysed reactions of the thiophenes in the presence and absence of EDTA. The involvement of radical chemistry is still evident as indicated by the formation of the 2-hydroxythiophenes and dimeric structures as main oxidation products. The Fenton-catalysed oxidation of thiophene, 2- and 3-methylthiophene was obstructed by the presence of the radical trap, TEMPO in that 94 % of 2-methylthiophene was left unreacted. The oxidation products discussed in chapter 2 have not been observed in the presence of TEMPO.

The formation of an extensive amount of carbon dioxide indicates that the catalytic oxidations of the thiophenes leads to mainly oxidative decomposition.

3.5. References

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CHAPTER 4

SYNTHESIS OF STANDARD COMPOUNDS

CHAPTER 4

SYNTHESIS OF STANDARD COMPOUNDS

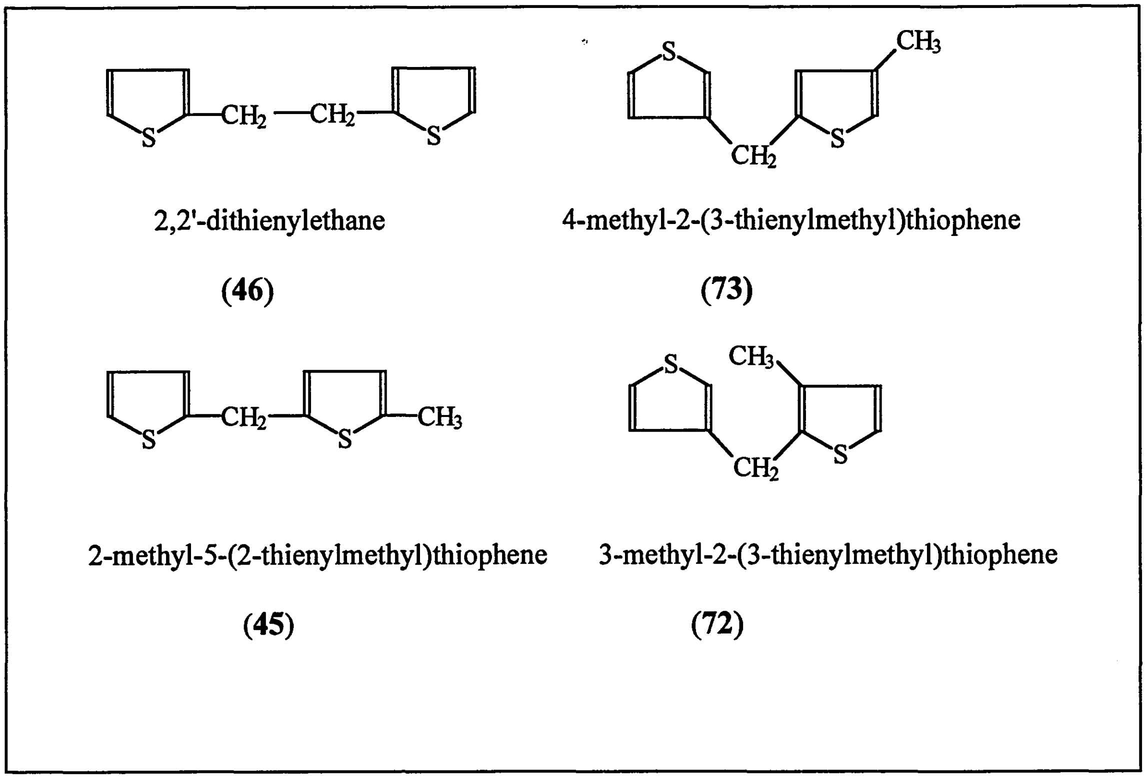
The Fenton-catalysed oxidations of thiophene and 2- and 3-methylthiophene resulted in complex mixtures of products in each case and the identification of these intermediate products would provide useful information about the reaction pathway. Some of the components of the mixtures were identified by comparison with commercially available products or synthetic standards. However, most of them were not commercially available or they have not been synthesized before. Therefore, the preparation of some components was required, since one of the main targets of this research project was to characterise these compounds, and that will be discussed in this chapter.

The compounds discussed in this chapter were required for comparison with products from the oxidation reactions studied. They were either prepared by literature methods or new syntheses were developed.

4.1. Synthesis of a Range of Standard Reference Dimeric Structures

The Fenton-catalysed oxidations of 2- and 3-methylthiophene gave oxidation products each of which has a molecular ion at *m/z* 194 and the possible products are shown in Figure 4.1.

Figure 4.1. Possible structures for *m/z* 194.



2,2'-dithienylethane

(46)

4-methyl-2-(3-thienylmethyl)thiophene

(73)

2-methyl-5-(2-thienylmethyl)thiophene

(45)

3-methyl-2-(3-thienylmethyl)thiophene

(72)

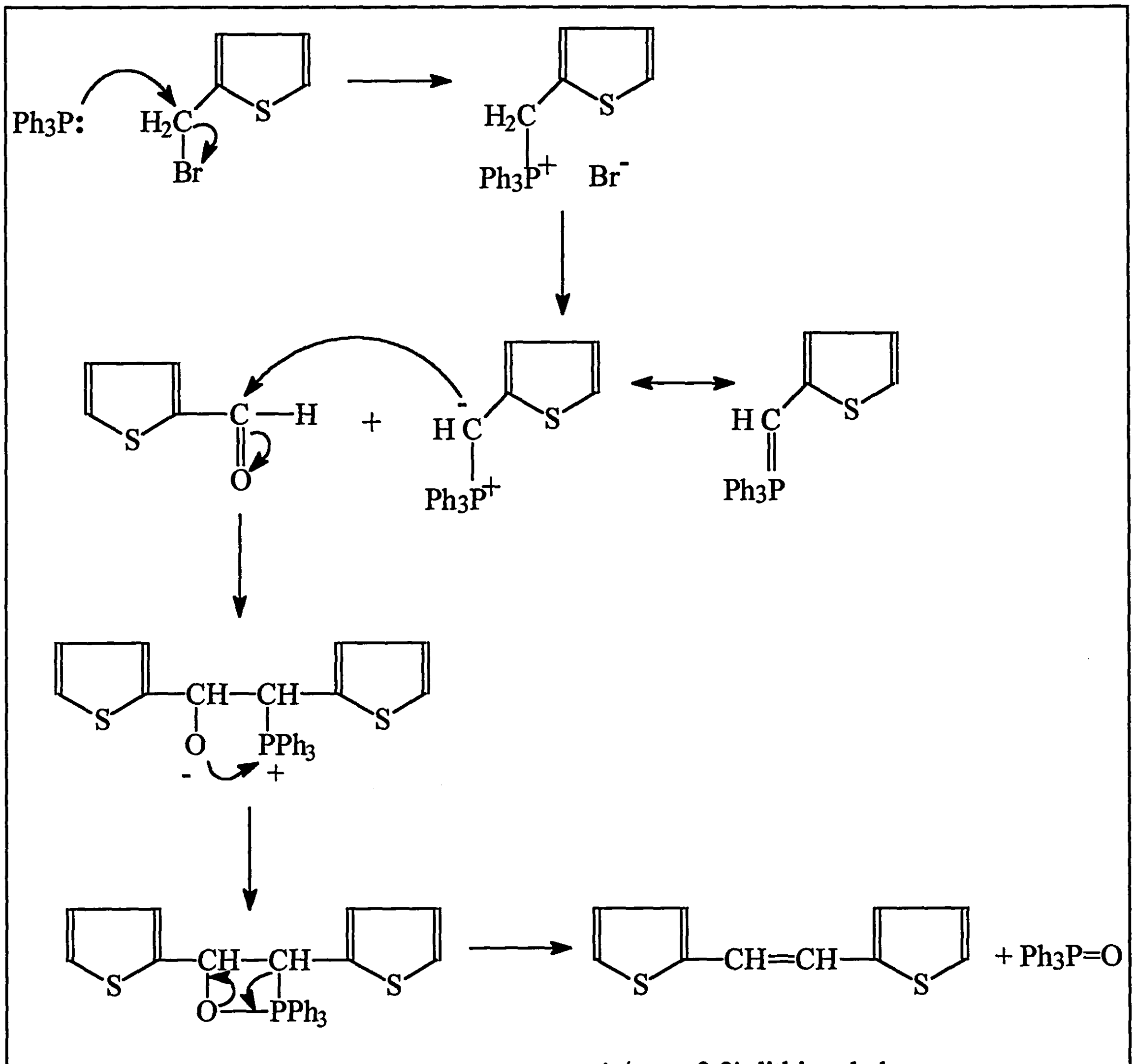
2,2'-Dithienylethane and 2-methyl-5-(2-thienylmethyl)thiophene are possible oxidation products formed from the oxidation of 2-methylthiophene under certain conditions and the other two are from 3-methylthiophene.

4.1.1. Preparation of 2,2'-Dithienylethane (46)

2,2'-Dithienylethane was prepared via the hydrogenation of the appropriate unsaturated compound 2,2'-dithienylethene (**108**). Although the dithienylethane has been prepared before [1], it is not commercially available. Therefore, the preparation of this compound required a comparison with the product formed in the Fenton-catalysed oxidation of 2-methylthiophene.

2,2'-Dithienylethene was prepared by the Wittig reaction [2] in which the alkyl halide, 2-chloromethylthiophene, was allowed to react with triphenylphosphine to give the phosphonium salt which was treated with a strong base, sodium methoxide, to give an ylide which reacted rapidly with 2-thiophene aldehyde to form **(108)**, as a mixture of *cis* and *trans* isomers, and triphenylphosphine oxide (Scheme 4.1).

Scheme 4.1.

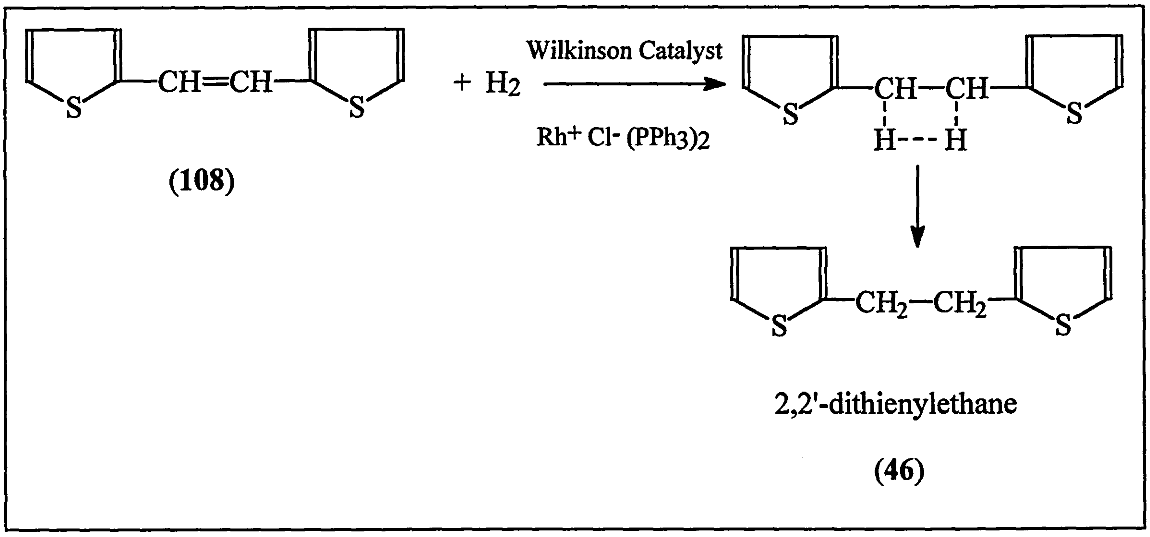


cis/trans 2,2'-dithienylethene

(108)

The alkene mixture was reduced in the presence of Wilkinson catalyst, and this hydrogenation resulted in the formation of 2,2'-dithienylethane (**46**) in quantitative yield (Scheme 4.2).

Scheme 4.2.



4.1.1.1. Experimental

4.1.1.1.1. Synthesis of *cis/trans* 2,2'-Dithienylethene (108)

Thiophene-2-aldehyde (0.12 g, 0.001 mol) and 2-thienylmethyltriphenylphosphonium bromide (0.44 g, 0.001 mol) were added to dry methanol (3 cm^3). Sodium methoxide (5 cm^3, 0.2 M)) in dry methanol was added dropwise from a pressure equalizing funnel while stirring under a nitrogen atmosphere. After 30 minutes, 5 cm^3 water was added to the reaction mixture which was then extracted with diethyl ether (4x20 cm^3). The combined organic extracts were dried with magnesium sulphate and the excess solvent was removed under reduced pressure to give 0.48 g of a white-light yellow crystalline solid. Two spots which immediately reacted with the indicator, potassium permanganate, were identified by thin layer chromatography (TLC) analysis using dichloromethane/methanol, 4:1 as developer. These were indicative of the presence of easily oxidisable groups in the compounds of interest, i.e. the double bonds.

No attempts were made to purify the mixture since the reaction product analysed using GC/MS techniques showed two clear peaks and they were carried on the next step of the reaction.

GC/MS Analysis

The same instrument and temperature program 1 outlined in section 2.1 in Chapter 2 were used for the analysis of the reaction products. Two major peaks were observed in the GC trace at retention time (t_R) 28.85 and 29.59 minutes respectively, both exhibiting an apparent ion at *m/z* 192.

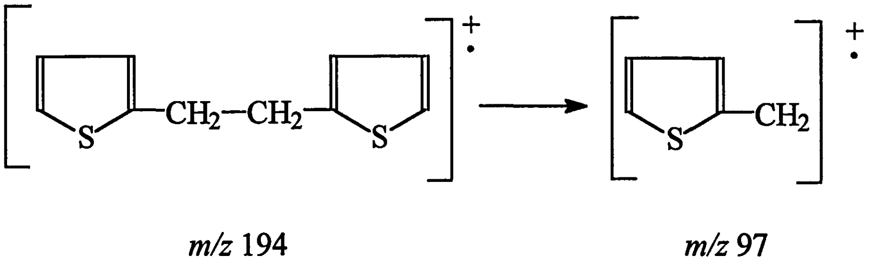
4.1.1.1.2. Synthesis of 2,2'-Dithienylethane (46)

A mixture of *cis/trans* 2,2'-dithienylethene (0.19 g, 0.001 mol) was dissolved in methanol (10 cm^3) and a catalytic amount of Wilkinson reagent was added. The reaction was stirred under a positive pressure of hydrogen and monitored by TLC. A few hours later, the reaction mixture was investigated by TLC and the spots corresponding to the *cis/trans* 2,2'-dithienylethene had disappeared, indicating the completion of the reaction. The catalyst was filtered and excess methanol was removed. The resulting brown oil was analysed using GC/MS.

No attempt was made to purify 2,2'-dithienylethane as only retention time and mass spectral data were required for the comparison purpose. Therefore, GC/MS analysis was carried out with the crude product.

GC/MS Analysis

The same instrument and temperature program 1 outlined in section 2.1 were used for the analysis of the reaction products. A major peak was observed at a t_R=25.32 minutes and this compound exhibited an apparent molecular ion at *m/z* 194. Although the retention time was similar to that of the product observed in the Fenton-catalysed oxidation of 2-methylthiophene, the mass spectral fragmentation was completely different. For 2,2'-dithienylethane, the following fragmentation pathway was observed, where the fragment ion at *m/z* 97 is found to be the base peak.



However, the oxidation product of 2-methylthiophene exhibits an apparent molecular ion at *m/z* 194 and a base peak at *m/z* 179 from loss of the methyl group ($-CH_3$) indicating that the dimer still possesses a methyl group. This phenomenon led to the synthesis of dithienylmethane system.

4.1.2. Preparation of Dithienylmethanes

A variety of dithienylmethane structures was thought to have been observed during the investigation of the oxidation of 2- and 3-methylthiophenes. The possible structures (components **45**, **72** and **73**) were given in Figure 4.1.

All of these structures could have been formed via the oxidative radical reactions involving 2- and 3-methylthiophene as discussed earlier in Chapter 2. These dimeric structures do not appear to have been characterized previously and nothing was found in the literature related to their synthesis. Hence, new synthetic methods were developed for their preparation.

4.1.2.1. Preparation of 2-Methyl-5-(2-thienyl)thiophene (45)

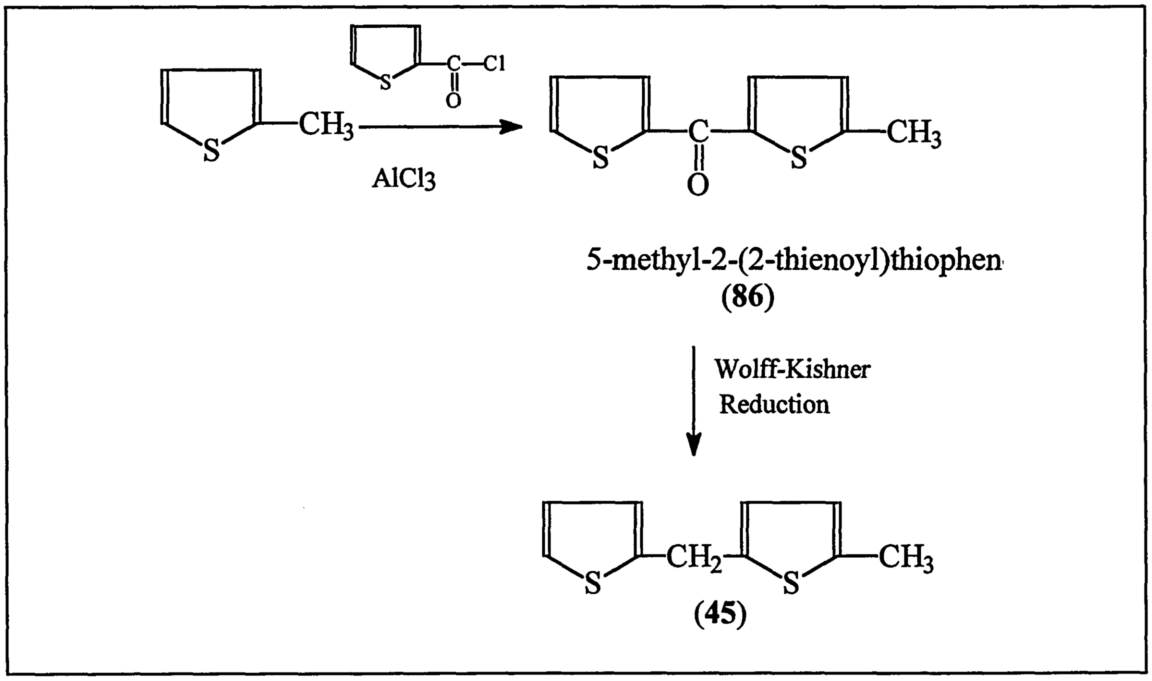
Since 2-methyl-5-(2-thienyl)thiophene (**45**) has not been prepared before, two new synthetic methods were developed in this study.

4.1.2.1.1. Method 1

Friedel-craft acylation of 2-methylthiophene with 2-thienylcarbonyl chloride proceeded smoothly to give the expected ketone. Clemmensen reduction (Zn, Hg, HCl) of this gave the desired dithienyl methane (**45**), but only as a minor component in a disappointingly complex mixture of products. However, Wolff-Kishner reduction [3] (hydrazine hydrate, NaOH, diethylene glycol) gave the desired compound in good yield (Scheme 4.3).

It was isolated by column chromatography and fully characterized.

Scheme 4.3.



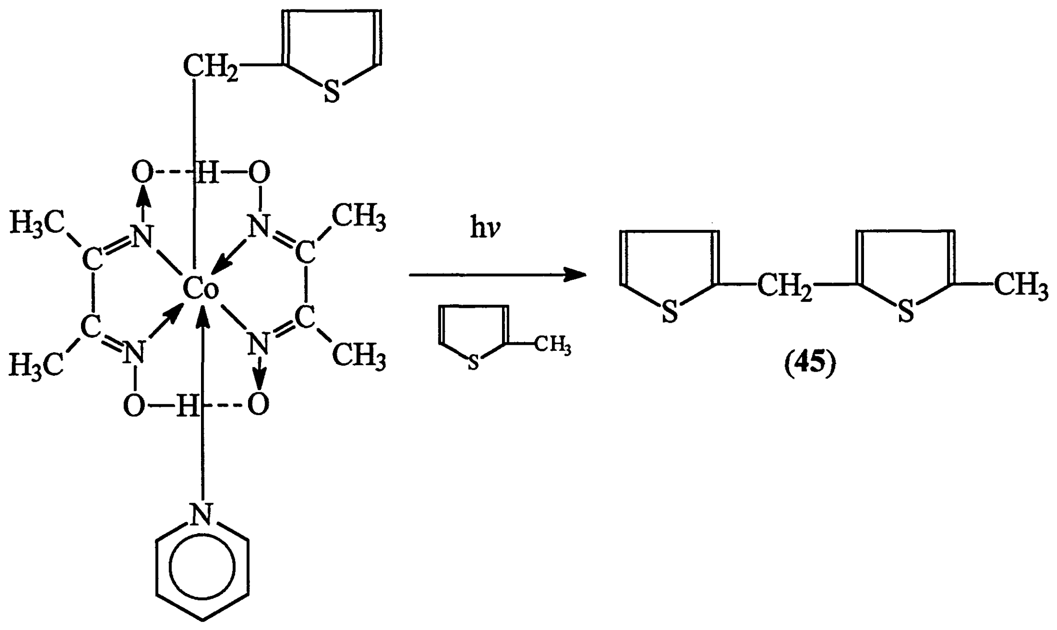
5-methyl-2-(2-thienoyl)thiophen
(86)

(45)

4.1.2.1.2. Method 2

In this approach, the synthesis of the appropriate thienylmethylcobaloxime complex was carried out. Such cobaloxime complexes are known to undergo photolysis by visible light to form alkyl radicals which can subsequently be trapped [4]. Therefore, it was anticipated that a thienylmethyl radical might be formed from the photolysis of thienylmethylcarboxime complex and subsequently trapped by a protonated methylthiophene, present in the reaction mixture, to give the desired dithienylmethane, This is illustrated below in Scheme 4.4.

Scheme 4.4.

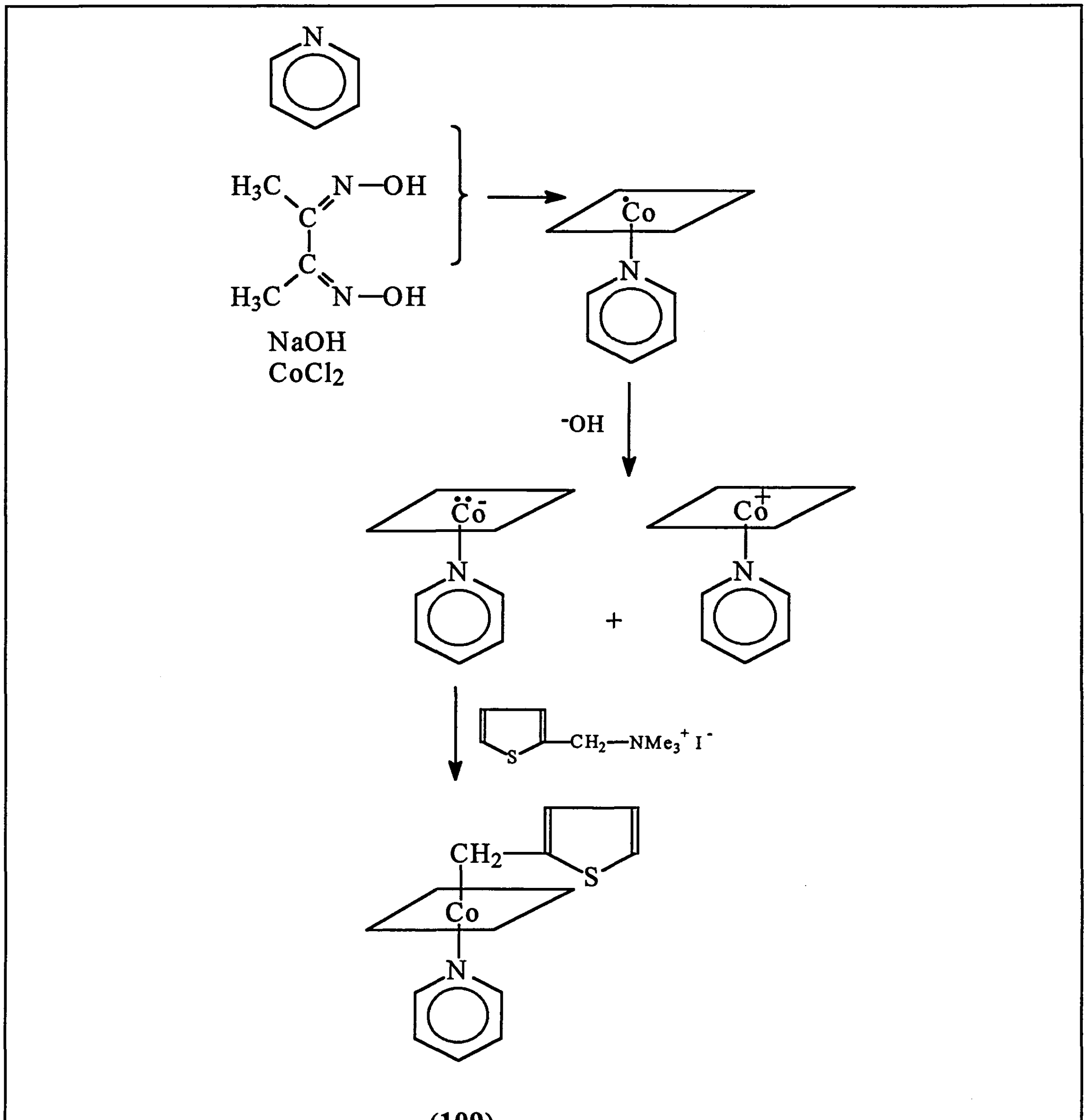


(45)

thienylmethyl cobaloxime complex
(109)

The thienylmethyl cobaloxime complex is prepared from the combination of dimethylglyoxime, cobalt(II) chloride and pyridine together in the presence of a base, such as sodium hydroxide. The cobalt(III) species **(109)** was prepared by addition of the previously prepared 2-thienylmethyltrimethylammonium iodide salt to an intermediate Co(I) cobaloxime complex as indicated in Scheme 4.5 (the full structure of cobaloxime is given in Scheme 4.4). The complex **(109)** was then subjected to photolysis in the presence of excess 2-methylthiophene. Subsequent GC/MS analysis showed the presence of trace amounts of the dithienylmethane **(45)**.

Scheme 4.5.

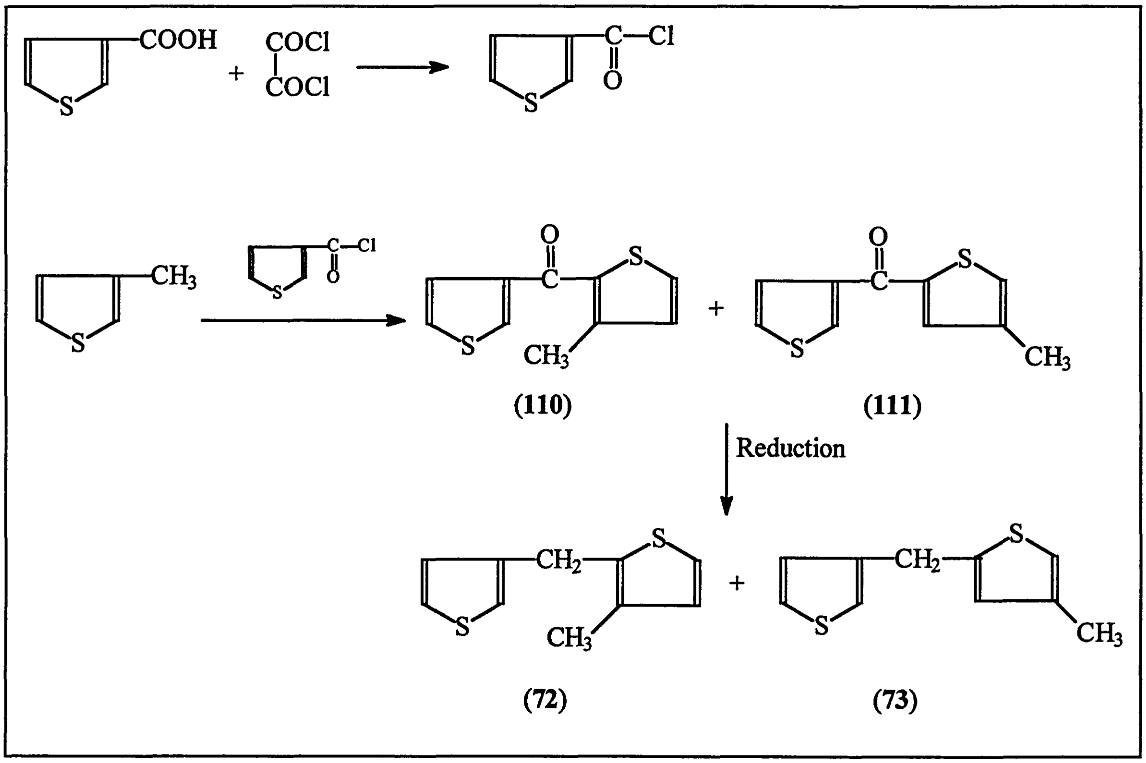


(109)

4.1.2.2. Preparation of 3-Methyl-2-(3-thienylmethyl)thiophene (72) and 4-Methyl-2-(3-thienylmethyl) thiophene (73)

It was thought that one of these two possible compounds would have been formed in the Fenton-catalysed oxidation of 3-methylthiophene. They were prepared by using a similar method to that discussed in section 4.1.2.1.1.1. (method 1) involving the Friedel-Craft acylation of 3-methylthiophene with 3-thienylcarbonyl chloride followed by Wolff-Kishner reduction. This reaction gave the expected products (72) and (73) (Scheme 4.6).

Scheme 4.6.



These could not be separated by flash chromatography, but GC/MS analysis revealed the presence of the two isomers, having virtually identical retention times and mass spectral fragmentation patterns. An unequivocal distinction between the alternative structures was impossible, and therefore, it is not clear which the isomer was formed in the Fenton-catalysed oxidation of 3-methylthiophene.

4.1.2.3. Experimental

4.1.2.3.1. Synthesis of 2-Methyl-5-(2-thienylmethyl) thiophene (45)-Method 1

a) Synthesis of 2-(2-thienoyl)-5-methylthiophene (86)

Under ice cooling, anhydrous aluminum chloride (10 g, 0.07 mol)) was added to dichloromethane (50 cm^3) and treated with 2-thienylcarbonyl chloride (7.53 g, 0.1 mol). 2-Methylthiophene (4.85 g, 0.05 mol) in dichloromethane (20 cm^3) was added slowly to the reaction mixture and stirred for 2 hour at room temperature. Aqueous hydrochloric acid (2.0 M, 50 cm^3) was then added dropwise, and the organic layer was separated, dried over anhydrous magnesium sulphate, and evaporated. The crude residue was purified by flash column chromatography to give 2-(2-thienoyl)-5-methylthiophene.

GC/MS Analysis

Using the same instrument and temperature program 1 described in section 2.1, a major peak was observed at t_R = 31.82 and this compound exhibited an apparent molecular ion at *m/z* 208. Its full characterization is as follows;

2-(2-thienoyl)-5-methylthiophene: colorless crystals, m.p. 48 °C, δ ^1H ($CDCl_3$): 2.6 (s, CH_3); 6.85 (m, 1H); 7.16 (dd, 1H, J = 5, 4 Hz); 7.66 (dd, 1H, J = 5, 1 Hz); 7.72 (dd, 1H, J = 4, Hz) 7.85(dd, H, J=4, 1 Hz) ppm. Found *m/z* 208.0183 (M^+ 85 %) $C_{10}H_8OS_2$ requires *m/z* 208.00166 (M^+).

b) Wolff-Kishner reduction of 2-(2-thienoyl)-5-methylthiophene

The above ketone (1.04 g, 0.005 mol), hydrazine hydrate (1 cm^3, 0.015 mol) sodium hydroxide (1 g, 0.025 mol) and diethylene glycol (12 cm^3, 0.025 mol) were heated together with stirring under reflux for 2 hour. The reflux condenser was then replaced by a distillation adapter and condenser, and the temperature was then slowly raised to 195-200 °C and held for 6 hours, during which time a mixture of hydrazine and water distilled over. The residue was then cooled, diluted with water (20 cm^3), the acidity was adjusted to pH = 1.0-2.0 with concentrated hydrochloric acid, and the product was extracted in into dichloromethane. The organic phase was washed with water and saturated sodium chloride solution, dried over anhydrous magnesium sulphate, and evaporated. The crude residue was purified by flash column chromatography on silica using petroleum-dichloromethane (9:1) as eluent giving 2-methyl-5-(2-thienylmethyl)thiophene in 40 % yield.

GC/MS analysis

Using the same instrument and temperature program 1 described in section 2.1, a major peak was observed at $t_R = 23.92$ exhibiting an apparent molecular ion at *m/z* 194.

The mass spectral fragmentation of this compound was shown in Figure 2.10 in Chapter 2. Its full characterization is as follows;

2-methyl-5-(2-thienylmethyl)thiophene: brown oil; δ ^{1}H ($CDCl_3$): 2.7 (s, 3H); 4.5 (s, 2H), 6.68 (d, 1H, J = 3.25 Hz); 6.77 (d, 1H, J = 3.25 Hz); 6.98 (dd, 1H, J = 3.5, 1.05

Hz); 7.04 (dd, 1H, J = 3.5, 5.05 Hz) and 7.25 (dd, 1H, J = 5.05, 1.05 Hz) ppm. Found *m/z* 194.0026 (M^+, 80.4 %), $C_{10}H_{10}S_2$ requires *m/z* 194.0020 (M^+).

4.1.2.3.2. Synthesis of 2-Methyl-5-(2-thienylmethyl)thiophene (45)-Method 2

a) Synthesis of 2-thienylmethyl Co $(dmgH)_2$ pyridine (**109**) [4,5]

Under a nitrogen atmosphere, dimethylglyoxime (2.32 g, 0.02 mol) and cobalt(II)chloride hexahydrate (2.37 g, 0.01 mol) was added to the degassed methanol (40 cm^3) and stirred. Pyridine (0.8 cm^3, 0.01 mol) was then added to the flask via a syringe followed by a sodium hydroxide solution (1.6 g, 0.04 mol, 5 cm^3 water). After the blue/black color of the cobalt(I) species was developed, 2-thienylmethyltrimethylammonium iodide (3 g, 0.01 mol) [prepared from 2-dimethylaminomethylthiophene and iodomethane (1:4) mixture under a nitrogen atmosphere; white salt] in methanol (5 cm^3) was then injected into the reaction mixture and immediately the orange/brown color of the cobalt(III) cobaloxime was formed.

Upon work up, excess (water 950 cm^3) was added to the reaction mixture and extraction was carried out using dichloromethane (3x100 cm^3). The extracts were combined and dried using magnesium sulphate. The excess dichloromethane was removed under reduced pressure to give 1.58 g red-brown solid cobaloxime.

^1H NMRresults are given below;

*2-thienylmethyl Co (dmgH)$_2$ pyridine (**109**)*; dark red brown solid; δ ^{1}H ($CDCl_3$): 2.08 (s, CH_3); 3.06 (s, CH2), 6.78 (d, 2H); 7.13 (d, 1H); 7.35 (m, 2H); 7.75 (m, 1H); 8.57 (d, 2H); 13.42 (s, 1H); ppm.

b) The photolysis of 2-thienylmethyl Co (dmgH)$_2$ pyridine

The cobaloxime complex (0.17 g, 0.00037 mol), 2-thienylmethyl Co (dmgH)$_2$ pyridine, that had previously been prepared was added to ethanol (10 cm^3) together with 2-methylthiophene (0.03 g, 0.00037 mol). Under a nitrogen atmosphere, the system was stirred and irradiated with a 500 Watt light supply for 4 hours. After this time, the mixture was allowed to cool and then analysed using GC/MS technique.

GC/MS Analysis

Using the same instrument and temperature program 1 described in section 2.1 in Chapter 2, a major peak was observed at t_R = 24.28 exhibiting an apparent molecular ion at *m/z* 194. Both retention time and mass spectral fragmentation of this compound were the same as for the compound prepared in section 4.1.2.3.1-a. Therefore, it is concluded that the desired compound, 2-methyl-5-(2-thienylmethyl)thiophene is formed via the photolysis of the cobaloxime complex in the presence of 2-methylthiophene. Its full characterization has already been given in section 4.1.2.3.1-b.

4.1.2.3.3. Synthesis of 3-Methyl-2-(3-thienylmethyl)thiophene (72) and 4-Methyl-2-(3-thienylmethyl)thiophene (73)-Method-1

a) Synthesis of 3-methyl-2-(3-thienoyl)thiophene (110) and 4-methyl-2-(3-thienoyl) thiophene (111)

Thiophene-3-carboxylic acid (1 g, 0.008 mol) and predistilled oxalyl chloride (1.5 g, 0.01 mol) were mixed under a nitrogen atmosphere in 20 cm^3 dry tetrahydrofuran (THF) and left overnight. This gave the desired 3-thienylcarbonyl chloride in quantitative yield and it was subsequently used for the synthesis of the corresponding ketones. Friedel-Craft acylation of 3-thienylcarbonyl chloride (7.53 g, 0.1 mol) and 3-methylthiophene (4.85 g, 0.05 mol) gave a mixture of isomeric ketones using the same experimental conditions as given in 4.1.2.3.-a.

GC/MS Analysis

The GC/MS analysis, which was carried out using the same instrument and temperature program as outlined in section 2.1. in, showed that two isomeric ketones **(110)** and **(111)** had been formed in a relative amount of 5:3 from the above reaction with retention times of t_R = 30.05 and 31.52 respectively. Both gave the same mass spectral fragmentation. Although a mixture of these ketones could be isolated from the reaction mixture, all attempts failed with regard to their separation.Chemical characterization of this mixture is as follows;

3-methyl-2-(3-thienoyl)thiophene (110) and 4-methyl-2-(3-thienoyl) thiophene (111): colorless crystals, m.p. 45 °C, δ ^{1}H ($CDCl_3$): 2.60 (s, CH_3); 6.83 (m, 1H), 7.15 (m, 1H); 7.70 (m, 2H) and 7.85 (m, 1H) ppm. Found *m/z* 208.00124 (M^+, 55 %), $C_{10}H_8OS_2$ requires *m/z* 208.00166 (M^+).

b) Wolff-Kishner reduction of **(110)** and **(111)**

The same Wolff-Kishner reduction method described in section 4.1.2.3.1-b was repeated here and gave a dithienylmethane mixture that could not be separated. The combined yield was 37 %.

GC/MS Analysis

Using the same instrument and temperature program 1 identified the components of interest, with t_R = 24.38 and 24.82 retention times in a relative amount of 4:3, both exhibiting molecular ions at *m/z* 194 and identical mass spectral fragmentation making impossible an unequivocal distinction between two isomers. Chemical characterization of this mixture is as follows;

*3-methyl-2-(3-thienylmethyl)thiophene (72) and 4-methyl-2-(3-thienylmethyl)thiophene (73):*isolated as yellow oil (37 %), δ ^{1}H ($CDCl_3$): 2.45 (s, 3H); 4.30 (s, 2H), 6.58 (m, 1H); 6.66 (m, 1H) and 6.85-7.00 (m, 2H) and 7.15 (m, 1H) ppm. Found *m/z* 194.0034 (M^+, 70 %), $C_{10}H_{10}S_2$ requires *m/z* 194.0020 (M^+).

4.2 Synthesis of Hydroxylated Methylthiophenes

The (3H)- and (5H)-thiophen-2-one tautomers of 2-hydroxy-5-methylthiophene, 2-hydroxy-3-methylthiophene and 2-hydroxy-4-methylthiophene are the principal products from 2- and 3-methylthiophene. These products were not formed when the reaction was conducted in the presence of the radical trap TEMPO indicating the involvement of a radical reaction pathway. Hydroxylated 2- and 3-methylthiophenes were prepared using a literature method suggested by Hörnfeldt *et al.* [6] via hydrogen peroxide oxidation of the corresponding thiopheneboronic acid [6,7]. An extensive study has been carried out for the preparation of 2-hydroxythiophenes by this group. This method was first used by Amley and Chellenger [8] and Hawthorne [9] for the preparation of phenol. The compounds **(29)**, **(30)**, **(58)** and **(59)** were prepared to use as reference compounds of the oxidation products of 2- and 3-methylthiophene (Figure 4.2).

Figure 4.2. Hydroxylated methylthiophenes

5-methyl-(3H)-thiophen-2-one
(29)

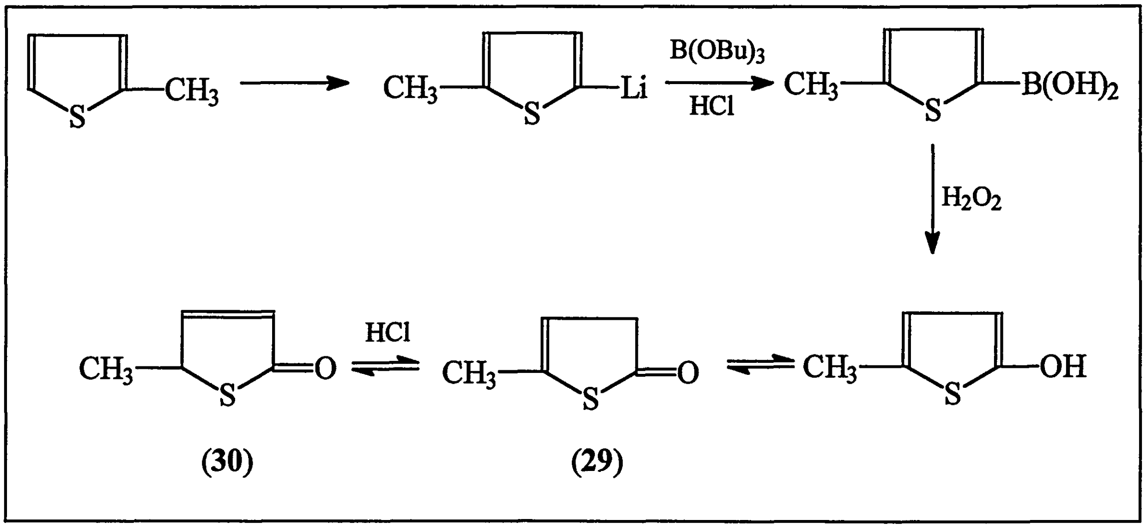
5-methyl-(5H)-thiophen-2-one
(30)

3-methyl-(5H)-thiophen-2-one
(58)

4-methyl-(5H)-thiophen-2-one
(59)

The boronic acids were obtained from the reactions of the thienyllithium derivatives with n-tributylborate and oxidation of these compounds by hydrogen peroxide gave hydroxy methylthiophenes. The reaction pathway for the preparation of 5-methyl-2-hydroxythiophene (or its tautomers) is shown in Scheme 4.7.

Scheme 4.7.



4.2.1. Experimental

4.2.1.1. Synthesis of 5-methyl-(3H)-thiophen-2-one (29)

n-Butyllithium (31.2 cm^3, 1.6 M in hexane) in hexane was added dropwise to thiophene (4.9 g, 0.04 mol) in dry ether (50 cm^3) under nitrogen at room temperature at such a rate as to maintain gentle reflux. The resulting thienyllithium compound was refluxed for a further twenty minutes and then cooled to -70 °C and treated with n-tributylborate (19.0 cm^3, 0.05 mol) in dry ether (40 cm^3) all at once. After stirring at -70 °C for 4 hours, the reaction mixture was allowed to warm up to 0 °C and shaken with hydrochloric acid (100 cm^3, 1M). The layers were separated, the aqueous phase was extracted with ether and the combined ethereal phases were extracted with sodium hydroxide solution (100 cm^3, 1M). After acidification of the alkaline solution with cold hydrochloric acid, the precipitated acid was filtered off and immediately dissolved in ether. Hydrogen peroxide (25 cm^3, 10 %) was added dropwise to the ethereal boronic acid under nitrogen. After the completion of the addition, the mixture was refluxed for 1 hour with vigorous stirring. The layers were separated, the water phase was extracted with ether and the combined ethereal phases were dried over magnesium sulphate. The resulting mixture was analysed by GC/MS.

GC/MS Analysis

The same instrument and temperature program was used for the analysis as described in section 2.1. The retention time of a major peak was $t_R = 9.92$ indicating the formation of 5-methyl-(3H)-thiophen-2-one and exhibiting an apparent molecular ion at *m/z* 114.

4.2.1.2. Synthesis of 5-methyl-(5H)-thiophen-2-one (30)

A few bubbles of hydrogen chloride were bubbled into 5-methyl-(3H)-thiophen-2 one (**29**) and the mixture was allowed to stand for 24 hour.

GC/MS Analysis

GC/MS analysis revealed the almost complete rearrangement to 5-methyl-(5H)-thiophen-2-one (**30**). A broad peak with a retention time at t_R = 12.46 was observed under the above conditions exhibiting an apparent molecular ion at *m/z* 114. Both retention time and mass spectral fragmentation were identical with the oxidation product of 2-methylthiophene. The GC spectrum of a mixture of components (**29**) and (**30**) has been given in Figure 2.5 in section 2.2.1.2. When the reaction mixture was left for further analysis, e.g. NMR, some white crystalline particles developed which were identified as dimerisation products (**33**), (**34**) and (**35**) [10].

4.2.1.3. Synthesis of 3-methyl-(5H)-thiophen-2-one (58) and 4-methyl-(5H)-thiophen-2-one (59)

For the synthesis of 3-methyl-(5H)-thiophen-2-one and 4-methyl-(5H)-thiophen-2-one, the same experimental procedure was employed as described in section 4.2.1.1 but using 3-methylthiophene. The reaction resulted in the formation of both compounds (**58**) and (**59**). These two isomers were isolated from the reaction mixture by column chromatography using dichloromethane/petroleum ether (3:7) solvent mixtures as eluent. Their chemical characterization was fully accomplished.

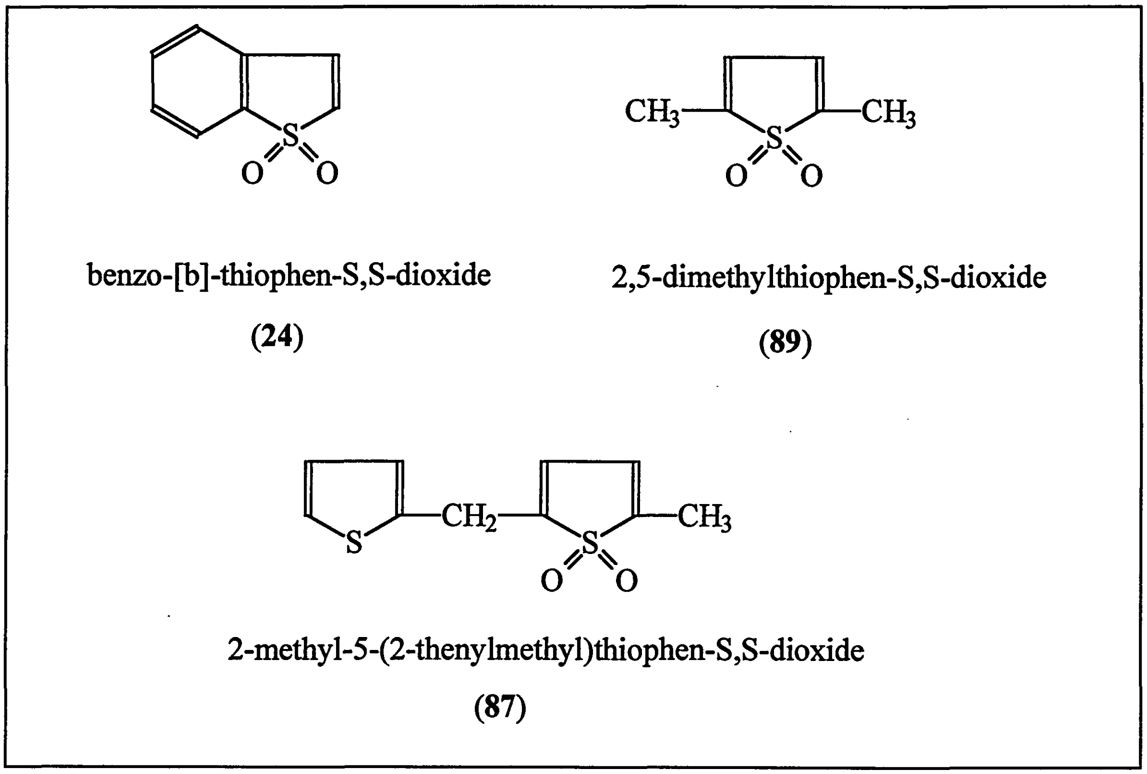
3-methyl-(5H)-thiophen-2-one (58): light yellow oil; δ ^{1}H ($CDCl_3$): 1.93 (s, CH_3); 3.90 (s, 3H), 7.2 (s, 1H) ppm.

4-methyl-(5H)-thiophen-2-one (59); light yellow oil; δ ^{1}H ($CDCl_3$): 2.21 (s, CH_3); 3.95 (s, 3H), 6.09 (s, 1H) ppm.

4.3. Synthesis of Thiophen-S,S-dioxides

A range of thiophen-S,S-dioxide was prepared for comparison with the Fenton-catalysed oxidation products. Benzo-[b]-thiophen-S,S-dioxide (**24**), 2-methyl-5-(2-thienylmethyl)thiophen-S,S-dioxide (**87**) and 2,5-dimethylthiophen-S,S-dioxide (**89**) (Figure 4.3) were prepared by using the methods outlined below.

Figure 4.3. Thiophen-S,S-dioxides



benzo-[b]-thiophen-S,S-dioxide

(24)

2,5-dimethylthiophen-S,S-dioxide

(89)

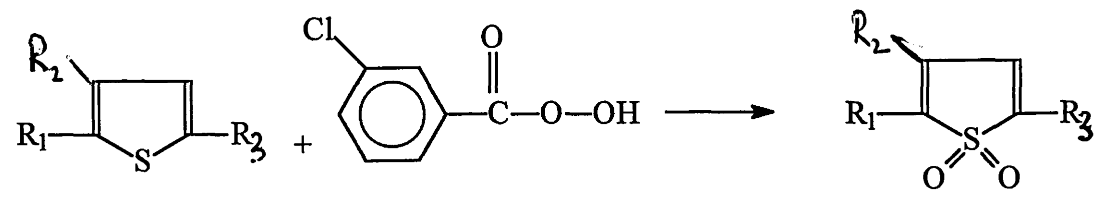
2-methyl-5-(2-thenylmethyl)thiophen-S,S-dioxide

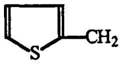
(87)

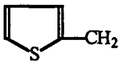
4.3.1. Method 1

The corresponding thiophene was oxidized by excess m-chloroperbenzoic acid to thiophen-S,S-dioxide in a high yields. All thiophen-S,S-dioxides were succesfully prepared with this method (Scheme 4.8).

Scheme 4.8.



	R1	R2	R3
77.	n-C_6H_4		H
45.		H	CH_3
88.	CH_3	H	CH_3

	R1	R2	R3
24.	n-C_6H_4		H
87.		H	CH_3
89.	CH_3	H	CH_3

4.3.2. Method 2

Components (**24**), (**87**) and (**89**) were also prepared by using either hydrogen peroxide or sodium perborate in acetic acid. Sodium perborate is highly reactive and has been shown to be selective for the conversion of a variety of sulphur heterocycles to the corresponding S,S-dioxides [11].

4.3.3. Experimental

4.3.3.1. Synthesis of Benzo-[b]-thiophen-S,S-dioxide Method 1

Benzo-[b]-thiophene (1.34 g, 0.01 mol) and m-chloroperbenzoic acid (6.84 g, 4.4 mol from 55% pure) were dissolved in dichloromethane (100 cm^3) and reaction mixture was left stirring overnight. Then the reaction mixture was transferred to a separation funnel, shaken with dilute sodium bicarbonate (100 cm^3) to destroy excess oxidant and the organic layer was separated, washed with water and dried. Excess dichloromethane was evaporated, resulting in white crystals of benzo-[b]-thiophen-S,S-dioxide. GC/MS analysis revaled that all benzo-[b]-thiophene was converted to S,S-dioxide (t_R=30.96, *m/z* 166).

4.3.3.2. Synthesis of Benzo-[b]-thiophen-S,S-dioxide Method 2

Sodium perborate tetrahydrate (7.69 g, 0.05 mol) or hydrogen peroxide (24.8 cm^3, 0.05 mol from 27%) was added portionwise during 20 min. to a stirred solution of the benzo-[b]-thiophene (1.34 g, 0.01 mol) in glacial acetic acid (40 cm^3) held at 45-50 °C, and stirring was continued at this temperature until TLC analysis indicated completion of reaction. The acetic acid was then removed by evaporation under reduced pressure and the residue stirred with water (100 cm^3). The crude product which separated was collected by filtration, washed with water and dried.

4.3.3.3. Synthesis of 2-Methyl-5-(2-thienylmethyl)thiophen-S,S-dioxide Method 1

2-Methyl-5-(2-thienylmethyl)thiophene (0.194 g, 0.001 mol) was oxidized with m-chloroperbenzoic acid (0.68 g, 0.004 mol) under the same conditions as described in section 4.3.3.1. Component **(87)** was isolated from the reaction mixture by flash column chromatography using petroleum-dichloromethane (1:1) as eluent, giving white crystals of 2-methyl-5-(2-thienylmethyl)thiophen-S,S-dioxide in 50 % yield. GC/MS analysis gave a peak at t_R=32.43 and an apparent molecular ion at *m/z* 226. Its NMR results are given below:

2-Methyl-5-(2-thienylmethyl)thiophen-S,S-dioxide (87): white crystals; δ ^{1}H (CDCl$_3$): 2.25 (s, 3H); 4.1 (s, 2H), 6.28 (d, 1H); 6.40 (d, 1H); 6.98 (dd, 1H); 7.08 (dd, 1H) and 7.35 (dd, 1H) ppm.

4.3.3.4. Synthesis of 2,5-Dimethylthiophen-S,S-dioxide Method 1

2,5-Dimethylthiophene (0.96 g, 0.01 mol) was oxidized with m-chloroperbenzoic acid (6.8 g, 0.04 mol) under the same conditions as described in section 4.3.3.1. Component (**89**) was isolated from the reaction mixture by flash column chromatography using petroleum-dichloromethane (1:1) as eluent, giving white crystals of 2,5-dimethylthiophen-S,S-dioxide in 70 % yield. GC/MS analysis gave a peak at t_R=16.62 and an apparent molecular ion at *m/z* 144. Its NMR results are given below:

2,5-Dimethylthiophen-S,S-dioxide (89): white crystals, δ ^{1}H (CDCl$_3$): 2.11 (s, 6H); 6.29 (s, 2H)ppm.

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