ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Wet Air and Related Metal Ion-Catalysed Oxidation Reactions of Methylpyridines

Jacqueline Morris BSc GRSC

A thesis submitted in partial fulfilment of the requirements of Sheffield Hallam University for the degree of Doctor of Philosophy

November 1995

Sponsoring Establishment: Sheffield Hallam University
Collaborating Establishment: Leigh Environmental Plc.

Abstract

The Wet Air Oxidation process has considerable attractions for the disposal of toxic organic wastes. In this thesis, a fundamental study is made of the mechanism of oxidation under wet air and related conditions of a series of well-defined substances known to occur as components of industrial wastes, and which are known to present difficulties in the Wet Air Oxidation process. In the initial stages, the oxidation of a series of simple alkylpyridines, namely 2-, 3-, and 4-methylpyridines, has been studied under simulated Wet Air Oxidation plant conditions in a laboratory autoclave operating at 250°C and 250 atmospheres. The progress of the oxidation was followed by withdrawing samples at intervals and subjecting these to chromatographic analysis, using Gas Chromatography-Mass Spectrometry and High Performance Liquid Chromatography, so as to establish the nature of the oxidation products.

In the autoclave oxidation of 2-, and 4-methylpyridine, a wide range of oxidation products was detected, including a number of compounds which appeared to be derived from the reactions of pyridylalkyl radicals formed from the parent substance, implying that a free radical mechanism was occurring under Wet Air Oxidation conditions. Under these conditions, 3-methylpyridine appeared to be more resistant to oxidation, the only significant oxidation product being the related aldehyde. The literature suggests that the formation of the hydroxyl radical (•OH) under Wet Air Oxidation conditions may be responsible for the initiation of the above reactions, and thus the possibility of catalysis of the above systems by reagents known to generate hydroxyl radicals has been explored. The literature suggests that Fenton's reagent, which is a mixture of iron(II) and hydrogen peroxide, provides a source of hydroxyl radicals. Thus, the oxidation of the methylpyridines using Fenton's reagent at ambient temperature and atmospheric pressure was carried out and it was also used as a catalyst in the autoclave oxidation reactions. The effectiveness of other metal ion/hydrogen peroxide mixtures was explored, e.g. involving iron(III), copper(II), copper(I), titanium(III), and vanadium(IV), as there is considerable evidence from the literature of their involvement in oxidation chemistry. In all of the oxidation reactions investigated, both under autoclave conditions, and at room temperature, evidence of destructive oxidation of the heteroaromatic ring has been gained for all three methylpyridines. However, in addition to ring destruction products, a range of intermediate oxidation products was observed and similarities were found between those products formed in the autoclave and those reactions carried out in the laboratory.

However, recent literature has questioned the formation of hydroxyl radicals by Fenton and related reagents, and so the Fenton catalysed oxidation of each of the methylpyridines was explored further. This was done by the incorporation of appropriate radical trapping agents and complexing agents such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and ethylenediaminetetraacetic acid (EDTA) respectively.

In each of the oxidation reactions studied, attempts have been made to identify as many as possible of the products observed by comparison with known substances. However, it has been necessary to develop procedures for the preparation of some of these compounds, notably a range of dimeric structures derived from the simple alkylpyridines, e.g. dipyridylethenes, dipyridylethanes, and dipyridylmethanes.

Abbreviations

WAO - Wet Air Oxidation

COD - Chemical Oxygen Demand

EPA - Environmental Protection Agency

R - alkyl

Ar - aryl

TBHP - *tert*-butylhydroperoxide

GC - gas chromatography

GC/MS - gas chromatography/mass spectrometry

HPLC - high performance liquid chromatography

LC/MS - liquid chromatography/mass spectrometry

mol - mole

TEMPO - 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical

EDTA - ethylenediaminetetraacetic acid

t_R - retention time

RSD - relative standard deviation

k - rate constant

dmg - dimethylglyoxime

^{1}H NMR - Proton Nuclear Magnetic Resonance

TLC - thin layer chromatography

$CDCl_3$ - deuterated chloroform

Contents

Chapter 1 - Introduction

1.1. Hazardous Waste and Waste Management

Hazardous Waste is generated in vast quantities by industry and there are several methods of disposing of such material[1]. The most common method involves the placement of the waste into drums for burial. Other methods include:-

- incineration
- pooling for evaporation
- placement into lined disposal sites
- spraying into the ground and then mixing with the soil.

However, research is ongoing into waste treatment to make it possible to deal with waste either so that useful components maybe retrieved from it and used again, or so that a threat is not posed to the environment when the waste is stored within it. Such research is therefore involved with the Deactivation of Hazardous Waste.

Hazardous chemical waste maybe either - toxic
reactive
corrosive
radioactive.

A toxic waste is harmful to the environment and to living organisms. It may be carcinogenic, mutagenic, or teratogenic and may ultimately cause death. A reactive hazardous waste may be explosive or it may form a dangerous mixture with water. It may also undergo chemical changes without addition of another substance to give rise to a toxic product. A waste is said to be corrosive if it is aqueous and has a $pH<2$ or a $pH>12$.

factors[10], remembering that the fuel for the process is the aqueous toxic waste itself:-

- the fuel supply
- the air supply
- the water to fuel ratio because of the possible need for dilution of fuels of higher waste concentration
- the ratio of oxygen to nitrogen
- the amount and actual products of oxidation withdrawn, as they will affect the temperature and pressure of the WAO process.

The degree of oxidation in the WAO process is measured in terms of the reduction in the toxicity of the mixture as a result of changes in the chemical structure of toxic compounds. The toxicity of a resultant waste stream treated by WAO is measured in terms of its chemical oxygen demand (COD) value[11]. The COD value represents the oxidisable organic content remaining in the mixture, and the more organics that remain, the higher the chemical oxygen demand is found to be. COD values are measured using an oxidimetric assay based on the consumption of potassium dichromate[11]. Samples are mixed with potassium dichromate before and after WAO treatment, and the residual dichromate is determined by titration with standardised ferrous ammonium sulphate solution. Hence, the amount of potassium dichromate that is used up in the oxidation of the organics in the sample, after WAO treatment, provides an indication of the amount of oxidisable organic content that remains. Therefore, the aim of the WAO process is to reduce the COD value of a particular waste type.

1.2.1. Method for Deactivation by WAO

The WAO process is represented in the following diagram

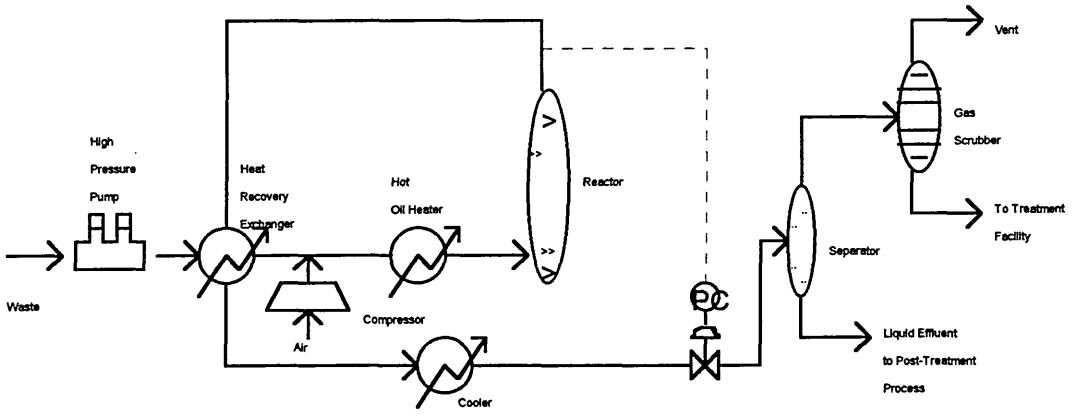


Figure 1 - Simplified schematic of the Wet Air Oxidation Process[2]

An aqueous waste[5], containing organic compounds, is pumped from storage by a high pressure pump. It is then mixed with air before being passed through a heat exchanger on its way to the bottom of the reactor. The reactor is built to withstand high temperatures and pressures, and the corrosive attack of the intermediates and final products of the process.

The oxidation reaction which is occurring in the reactor helps to raise and maintain the temperature of the reactor to the desired maximum value. From the reactor, the mixture enters the separator as a gas and a liquid. The separated liquid, under the high pressure of the reactor, passes through another heat exchanger and then through a valve reducing it to atmospheric pressure. This effluent is then discharged for further purification using conventional biological treatment. The separated steam/gas mixture goes through a turbine expander which then supplies power to the air compressor.

The technology associated with the WAO process is continually being developed to improve the effectiveness of the system. From the literature,

however, there is evidence to illustrate the considerable effectiveness that the process already has. Work carried out by Randall[12] in 1981 illustrated that the toxicity of aqueous organic toxic and hazardous waste can be reduced significantly when subjected to WAO, and this was proved by using *Daphnia Magna* for toxicity testing. The Environmental Protection Agency, EPA, published a list of 65 priority compounds or classes of compounds that need to be eliminated from effluents. From this information Randall selected a variety of compounds and subjected them to the WAO process, in order to determine the effectiveness of the process at destroying them. The results indicate that for aqueous solutions of, for example, 2,4-dinitrotoluene, a destruction in excess of 99% of the original concentration can be achieved. From this study and an earlier study carried out by Randall and Knopp[13] and work done by Baillod et al[14], it was shown that low molecular weight acids such as formic and acetic acid are generated from the WAO of an organic waste stream. These compounds are then readily biodegradable by conventional treatment methods. However, no other attempts were made to identify intermediate oxidation products formed throughout the oxidation process itself.

The literature contains examples of the WAO of other organic systems suspended or dissolved in water[15],[16], including examples of where the technology involved in the WAO process has been applied to a novel system e.g. the use of Wet Air Regeneration for the destruction of phenanthrene adsorbed onto powdered activated carbon[17] involves WAO technology. This work, carried out by Larson et al[17], much later did, however, attempt to identify intermediates formed during the oxidation process, as also did work carried out by Joglekar et al[18] who were considering the oxidation of phenols and substituted phenols using conventional WAO conditions.

Such attempts to identify and characterise intermediate oxidation products lead to proposals for possible degradation mechanisms and to also provide a means of establishing the identity of the oxidation products that are responsible for the resultant toxicity of treated wastes. This enhanced understanding leads to improvements in technology by aiding the development of appropriate catalytic systems which would give rise to a greater degree of oxidation/destruction.

1.2.2. Catalytic WAO

The use of catalysts within the area of waste treatment technology has received some attention. The effectiveness of catalysts on the oxidation of organic contaminants is measured in terms of a greater reduction in COD values, compared with the uncatalysed WAO process. When trying to establish a catalyst the following variables have to be considered:-

- operating temperature
- pH of the system
- reaction time period
- catalyst loading

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 WAO process[19]-[21]. One example is involved with the WAO of oxygen- and nitrogen- containing organic compounds catalysed by the presence of cobalt(III) oxide[19]. The oxidation scheme that was proposed here for simple aliphatic alcohols and amines proceeds via the formation of alkyl radicals, R•. The mechanism for the oxidation process follows the general scheme shown below:-

With alcohols and amines, initial hydrogen atom abstraction occurs at the carbon atom to which the appropriate NH_2 or OH functional groups are attached to form R•CHX where X=OH or NH_2. These radicals can then do one of two things.

They can undergo further elimination of another hydrogen atom from the NH_2 or OH group to give compounds of the following type -

$$CH_3OH \rightarrow \bullet CH_2OH \rightarrow HCHO \quad (1)$$

$$CH_3NH_2 \rightarrow \bullet CH_2NH_2 \rightarrow CH_2{=}NH \quad (2)$$

Alternatively, the radical can undergo β-scission cleavage of a C-C bond (or C-H bond if no C-C bond is present) to give another radical species and an unsaturated molecule.

$$RCH_2\bullet CHOH \rightarrow R\bullet + CH_2{=}CHOH \quad (3)$$

$$RCH_2\bullet CHNH_2 \rightarrow R\bullet + CH_2{=}CHNH_2 \quad (4)$$

Oxidative degradation of the unsaturated species then occurs. For the oxygen-containing compound, the C=C double bond cleaves to give either formic acid or the aldehyde.

$$CH_2{=}CHOH \rightarrow 2HCOOH \quad (5)$$

$$\text{or} \quad CH_2{=}CHOH \rightarrow CH_3CHO \quad (6)$$

For the nitrogen-containing compound, the C=C double bond cleaves to give CO_2 and NH_3 in a two step process.

$$CH_2{=}CHNH_2 \rightarrow CH_2{=}C{=}NH \quad (7)$$

then $CH_2=C=NH \rightarrow 2CO_2 + NH_3$ (8)

The alkyl radicals generated in stages (3) and (4) can undergo oxidative degradation very quickly to give formic acid i.e.

$$R\bullet \rightarrow \rightarrow \rightarrow HCOOH \quad (9)$$

The aldehydes that are formed in (1) and (6) from the oxidation of the alcohols are oxidised further to the corresponding acids as well as to carbon dioxide and further radical species.

$$RCHO \rightarrow RCOOH \quad (10)$$

and $RCHO \rightarrow R\bullet + CO_2$ (11)

In this system, for larger carboxylic acids, hydrogen abstraction occurs initially at either the acid functionality or at the CH_2 group next to the COOH group. The alkyl radical generated can then either decompose completely by a series of sequential oxidations to form formic acid

$$R\bullet \rightarrow \rightarrow \rightarrow HCOOH \quad (12)$$

or can promote degradation

$$CH_3CH_2COOH \xrightarrow{\text{via } CH_3\bullet CHCOOH} CH_3CHO + CO_2 \quad (13)$$

or gives rise to an aldehyde of smaller carbon number

$$RCH_2CH_2COOH \xrightarrow{\text{via } RCH_2\bullet CHCOOH} RCHO + HCOOH + CO_2 \quad (14)$$

The reactions outlined above all have their own individual rates but the following general assumptions were made about each of them:-

- the paths are all first order with respect to the reactants and are independent of all other compounds present. This statement is very simplistic, especially if materials are present in high concentrations, as the surface area of the cobalt(III) oxide catalyst may limit the rate as would be expected in heterogeneous catalysis. However, it should apply for low concentrations of materials such as intermediates.
- there is an excess of oxygen present.

The above is an example of a mechanistic scheme for the WAO of simple organic compounds containing oxygen and nitrogen heteroatoms, in the presence of a catalyst, cobalt(III) oxide. The mechanism is radical in nature as is expected, in view of an earlier study by Baillod et al[14], that illustrated that the WAO process involves the formation of radicals, in particular, hydroxyl radicals •OH. This theory was also supported later by Joglekar et al during their investigation of the WAO of phenols and substituted phenols[18].

An extensive study was carried out by Chowdbury and Ross that also dealt with the use of catalysts as a way of improving the effectiveness of the WAO process[22]. They considered the effects of various mixtures of metal ions and hydrogen peroxide as catalysts. The metal ions that were deemed to be the most effective were iron(II), iron(III), and copper(II). Iron salts in the presence of hydrogen peroxide produce free radicals according to the following two equations

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^{-}OH + {}^{\bullet}OH \qquad (15)$$

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HO_2{}^{\bullet} + H^{+} \qquad (16)$$

In the presence of hydrogen peroxide, copper salts probably behave in the following way

$$Cu^{2+} + H_2O_2 \rightarrow Cu^{3+} + {}^{-}OH + \bullet OH \quad (17)$$

$$Cu^{2+} + H_2O_2 \rightarrow Cu^{+} + HO_2\bullet + H^{+} \quad (18)$$

The use of these catalysts is pH dependent and mixtures of catalysts appear to be more effective at reducing the percentage COD values for an aqueous waste mixture, but during the study no attempt was made to analyse the reaction intermediates or products in any detail. More specialised work, therefore, is required to determine how catalysts, in particular those that were investigated by Chowdbury and Ross[22], are actually involved in the oxidation of organic contaminants and what intermediates and products are actually being formed in the catalysed process.

Another example of the effectiveness of the use of catalysis in the WAO process was illustrated by Randall in his work[12]. He showed that although the WAO process is efficient at deactivating hazardous waste, some compounds require more persuasive methods of deactivation e.g. PCB's, DDT, and pentachlorophenol, these being more environmentally persistent compounds. Such compounds were more difficult to deal with by the conventional WAO process. However, by the use of unspecified cocatalysts, the extent of their degradation could be improved e.g. 1,2-dichlorobenzene undergoes WAO at 275°C to give a 30% yield of carbon dioxide and chloride ions. In the presence of a catalyst however, an 89% yield of carbon dioxide and 98% yield of chloride ions was produced. This provides further evidence, again, of the usefulness of catalysts in the area of WAO treatment for wastes and hence catalysed WAO is worthy of continued investigation.

A detailed understanding of the mechanism of the oxidation processes occurring during WAO is therefore required[23]. The identification of products formed during the reaction will enable more effective post treatment of treated waste. Also, an understanding of the mechanism may enable the manipulation of the process, by the use of appropriate catalysts for example, to provide either a greater degree of destruction or perhaps the preferential formation of a particular product. As indicated earlier, the mechanism for the WAO process is thought to be radical in nature. This suggestion is not an unlikely scenario since at high temperatures under aqueous conditions, the dioxygen (O_2) present may undergo some complex chemical reactions. The formation of oxygen radical atoms could occur at elevated temperatures and this radical species could then react with water and with further oxygen to form systems such as hydrogen peroxide (H_2O_2) or ozone (O_3). The reaction course that an oxygen molecule takes under such conditions is potentially extensive but the important fact is that the fate of the molecule gives rise to the generation of radical systems which are then themselves ultimately responsible for the oxidation reactions taking place. Therefore, the intermediate and final oxidation products formed during the WAO of organic systems are thought to be derived from radical reactions. This suggestion is to be considered and explored in the discussion that is to follow.

1.3. Oxidation Chemistry

This thesis is concerned with a detailed investigation into the mechanism of oxidation of organic compounds and classes of compounds under WAO conditions. A recent text[24] deals in detail with the chemistry associated with molecular oxygen, and is largely concerned with the reactivity of oxygen-containing reagents such as hydrogen peroxide and oxygen radicals e.g. hydroxyl radicals •OH. Also dealt with is the metal-induced activation of

dioxygen and its subsequent behaviour. From the literature, there is evidence that work has been carried out on the oxidation of organic compounds by the use of oxygen or oxygen-containing compounds. This revealed that the use of catalysts is commonly required, metal salts being particularly effective in this area[25]-[39]. However, considering the fact that dioxygen itself is a good oxidant, its reaction with organic compounds is energetically unfavourable[40]. Why is this? The answer to this is related to the electronic configuration of molecular oxygen.

Dioxygen, in its ground state, is a triplet with two unpaired electrons with parallel spins[41]. The first two electronically excited states are both singlets and they are formed by either relocation and/or pairing of the unpaired electrons in the $2p\pi^*$ antibonding molecular orbitals. The half-filled antibonding molecular orbitals of $^3O_2$ can accommodate two additional electrons. The addition of one electron produces the superoxide anion O_2^- and the addition of two electrons gives the peroxide ion O_2^{2-}. The direct reaction of $^3O_2$ with singlet organic molecules to give singlet products is, however, a spin forbidden process with a very low rate. One way of overcoming the energy barrier, however, is to proceed via a free radical pathway:-

$$RH + {}^3O_2 \rightarrow R\bullet + HO_2\bullet \qquad (19)$$

Here, the formation of two doublets i.e. free radicals is a 'spin allowed' process. However, this process is very endothermic and requires the use of highly reactive substrates.

Another way of overcoming the spin conversion obstacle is for $^3O_2$ to combine with a paramagnetic transition metal:-

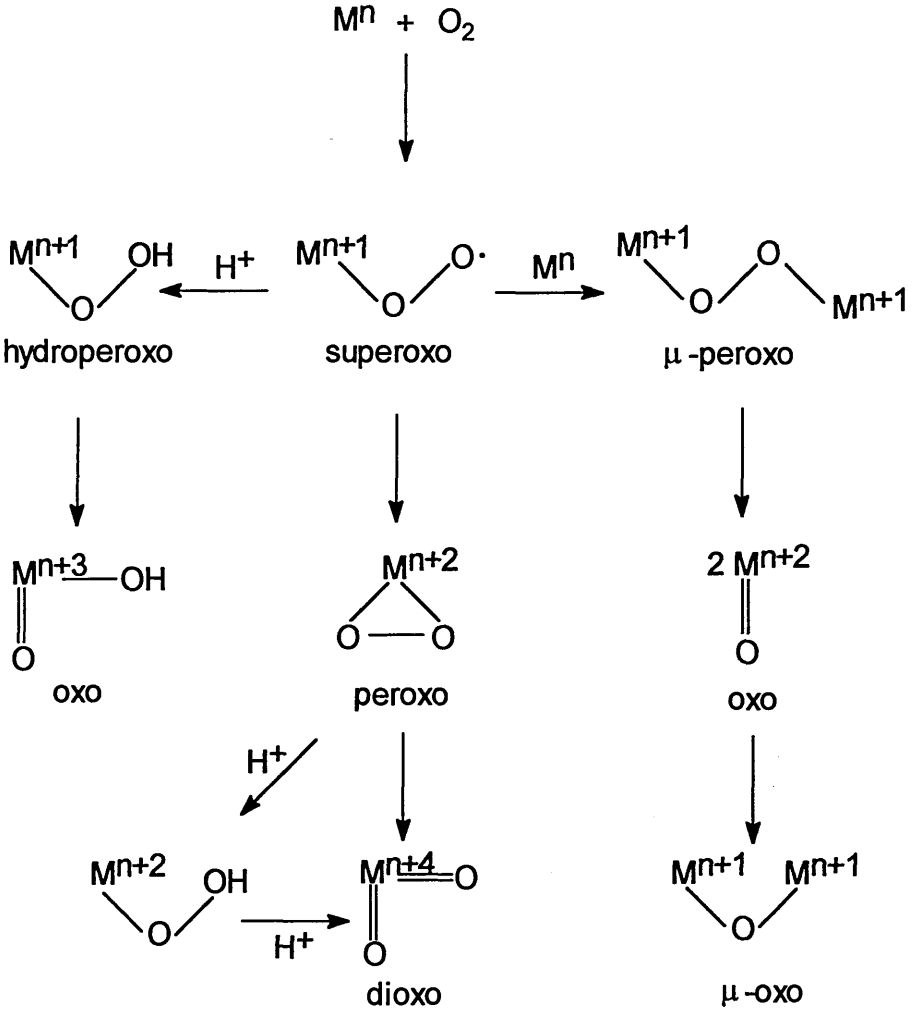
$$M^{n+} + {}^3O_2 \rightarrow \quad M^{n+1}\text{-}O\text{-}O\bullet \qquad (20)$$

where n = the formal oxidation state of the metal.

It is expected that this resulting metal-dioxygen complex will then react, in a selective manner, with organic molecules at more moderate temperatures than the free radical pathway, (19), above.

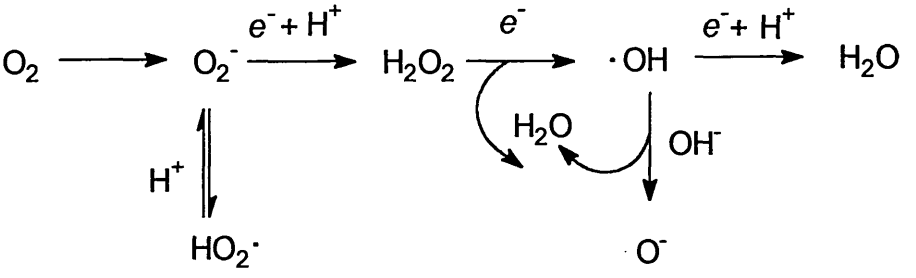
The following scheme illustrates the various possible oxygenated species that may play a role in metal-catalysed oxidations with dioxygen - Scheme 1

Scheme 1



As indicated above in 1.2.2., the interaction of molecular oxygen with water at elevated temperatures and pressures generates hydrogen peroxide and ozone via the formation of oxygen radicals. The presence of transition metal ions will, however, extend this picture and the activation of molecular oxygen can occur as shown in Scheme 1. In effect, the reduction of molecular oxygen is occurring in the following way as shown in Scheme 2[40], via the intermediacy of a metal species, as shown above (Scheme 1).

Scheme 2



All of the oxygen species generated then play an important role in the oxidation of organic compounds. The scheme shown above occurs in nature. This four electron reduction to form water is catalysed by the presence of *Cytochrome oxidase*[42] which is the terminal oxidase of the electron transport chain.

The chemistry in Schemes 1 and 2 is mimicked in the laboratory by using mixtures of metal ions and molecular oxygen. For example, the oxidation of aldehydes to carboxylic acids using molecular oxygen is facilitated in the presence of a cobalt(II) catalyst[34]. This is an example of where the activation of molecular oxygen occurs via complexation with the metal to give oxygen-cobalt complexes. Further literature provides examples of the use of copper salts as catalysts, in the form of both copper(I)[32] and copper(II)[30],[31]. It has been suggested that copper(II) is similar to cobalt(II) in that they both posses an unpaired electron which can interact with ground state dioxygen, in

an electron transfer mode i.e. $M^{2+}+O_2 \rightarrow M^{3+}-O_2^-$. The system formed is a metallo-superoxo entity. The co-ordinated superoxide radical anion is then assumed to interact with organic substances present.

1.3.1. Fenton's Reagent

Fenton's Reagent is a mixture of iron(II) and hydrogen peroxide and it was first recognised as an oxidising agent by H.J.H. Fenton in 1894[43]. Since then, subsequent studies have shown that this mixture is an effective oxidant for a variety of organic compounds[44], and the oxidation process involves the following generalised steps:-

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^-OH + \bullet OH \quad (21)$$

$$Fe^{2+} + HO\bullet \rightarrow Fe^{3+} + {}^-OH \quad (22)$$

$$HO\bullet + R'H \rightarrow H_2O + R'\bullet$$
$$HO\bullet + R''H \rightarrow H_2O + R''\bullet$$
$$HO\bullet + R'''H \rightarrow H_2O + R'''\bullet \quad (23)$$

$$R'\bullet + Fe^{3+} \rightarrow Fe^{2+} + \text{product} \quad (24)$$

$$2R''\bullet \rightarrow \text{product (dimer)} \quad (25)$$

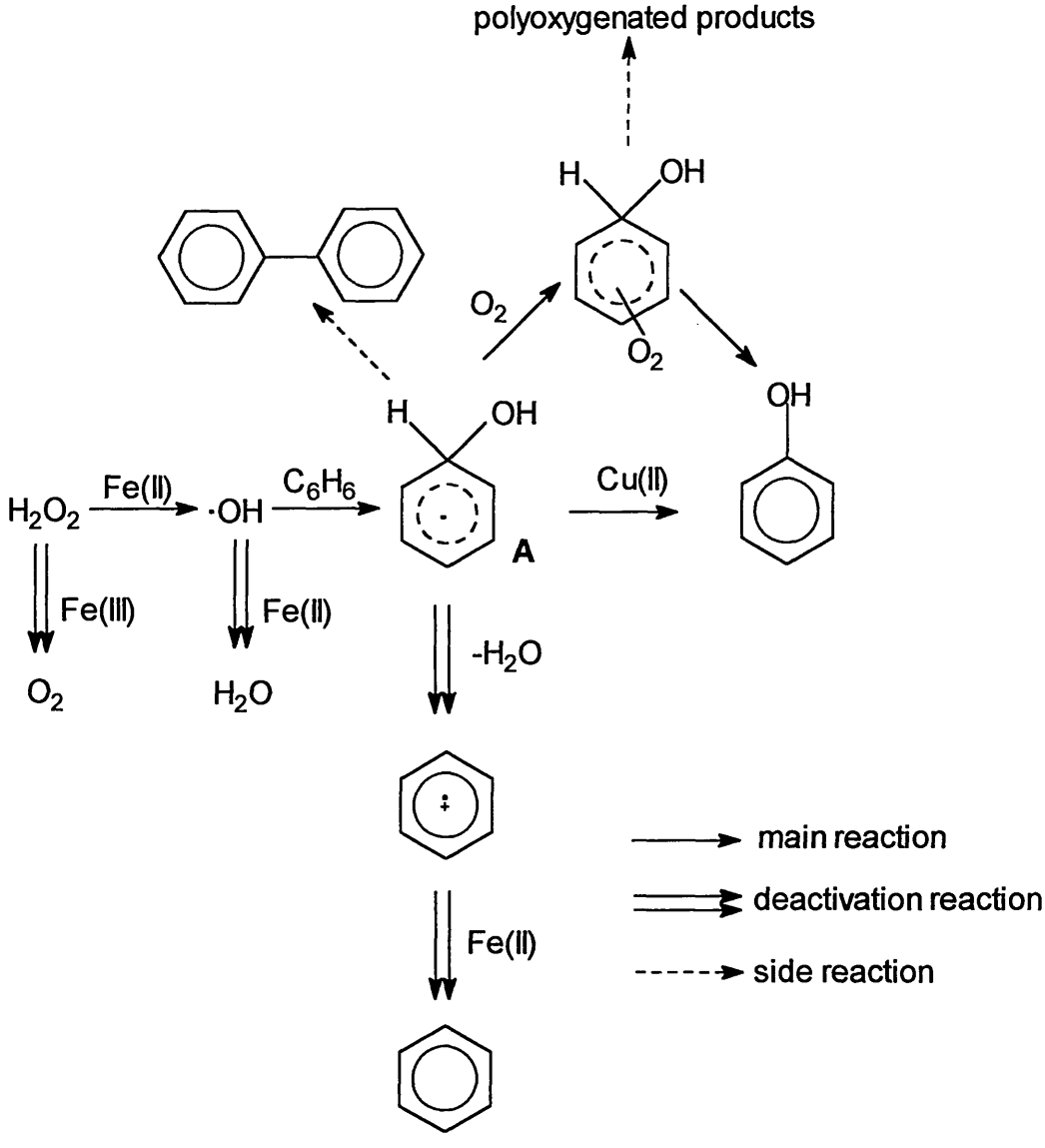
$$R'''\bullet + Fe^{2+} \rightarrow Fe^{3+} + R'''H \quad (26)$$

The radicals formed, R'•, R''•, R'''•, either undergo oxidation, and therefore give rise to the reformation of Fe^{2+}(24), dimerisation(25), or reduction(26) respectively.

Recent papers have documented the use of Fenton's reagent as an oxidant of organic compounds[45]-[57], and how it has proved to be an efficient oxidising

system. Aromatic systems such as benzene[56], [58] have been oxidised using Fenton's reagent to produce phenol, and the mechanism[58] for the process highlights the fact that the oxidising system is a source of hydroxyl radicals, as was previously suggested[44] - Scheme 3.

Scheme 3



The hydroxyl radicals add to the aromatic system and the resulting hydroxycyclohexadienyl radicals **A** are either oxidised to the phenol or they dimerize, or collapse to give radical cations.

Many transition metal ions are known to exhibit oxidative features similar to the traditional Fenton reagent[59]. Therefore, mixtures of these metal ions and hydrogen peroxide were named 'Fenton-like reagents'. Metals that were shown to behave in this way included Cu(I), Ti(III), Cr(II), and Co(II), to name but a few. However in the literature there are publications that are concerned with a more thorough investigation of the nature of the actual oxidising species generated in a Fenton Type system.

A recent publication by Sawyer[60] has suggested that Fenton's reagent does not lead predominantly to the generation of hydroxyl radicals, in contrast to established opinion[44], [58]. Studies carried out implied that reactions of substrates with a hydroxyl radical generated by other means, such as pulse radiolysis, did not behave in the same way when the substrate was exposed to Fenton's reagent. It is thought that no free carbon radicals R• are formed under Fenton conditions and that the formation of free •OH is supposedly not the dominant reactant. It was proposed by Sawyer that the iron(II) is complexed and that it is a complex of the type FeL_4OOH which reacts with the organic substrate present. Thus, Sawyer suggests that Fenton's reagent does not produce

i) free •OH

ii) free carbon radicals (R•)

iii) aryl radical adducts (HO-Ar•)

However, Sawyer was not the first to question the formation of free •OH radicals in a typical Fenton system. Groves et al[57] in 1974 investigated the stereospecific hydroxylation of aliphatic compounds. They found evidence to support the presence of a metal bound oxidant and it was this that was responsible for the oxidation reaction occurring and not free hydroxyl radicals.

Walling first published work in 1975[44] that suggested that Fenton's reagent did produce free hydroxyl radicals by a series of reactions, (21)-(26), that was indicated earlier in 1.3.1. More recent work carried out by him, however, has investigated this suggestion further by considering the oxidation of mandelic acid using Fenton's reagent[61]. The work was aimed at trying to establish the 'primary oxidant' responsible for the reactions taking place. From his earlier work, the evidence generated pointed to the fact that simple hydroxyl radicals, •OH, were responsible. However, in biological systems, those oxidations taking place that involve iron-containing enzymes are thought to involve the formation of high valence iron or iron-oxygen complexes and it is these that are then the 'primary oxidants'[41].

Walling deduced from his work that mandelic acid is oxidised by either 'free' hydroxyl radicals, or an untrappable intermediate formed from a 'cage' reaction between $MA•Fe^{III}$ and •OH which forms products too quickly to be intercepted by an added substrate, S. The reactions that are postulated by him are as shown below:-

$$H_2O_2 + Fe^{II}•MA \rightarrow X \rightarrow \text{products} + Fe^{II} \quad (27)$$

$$H_2O_2 + Fe^{II}•MA \rightarrow Fe^{III}_{Fe^{III}}•MA + HO• \quad (28)$$

$$HO• + MA \rightarrow R• \xrightarrow[Fe^{II}]{} \text{products} + Fe^{II} \quad (29)$$

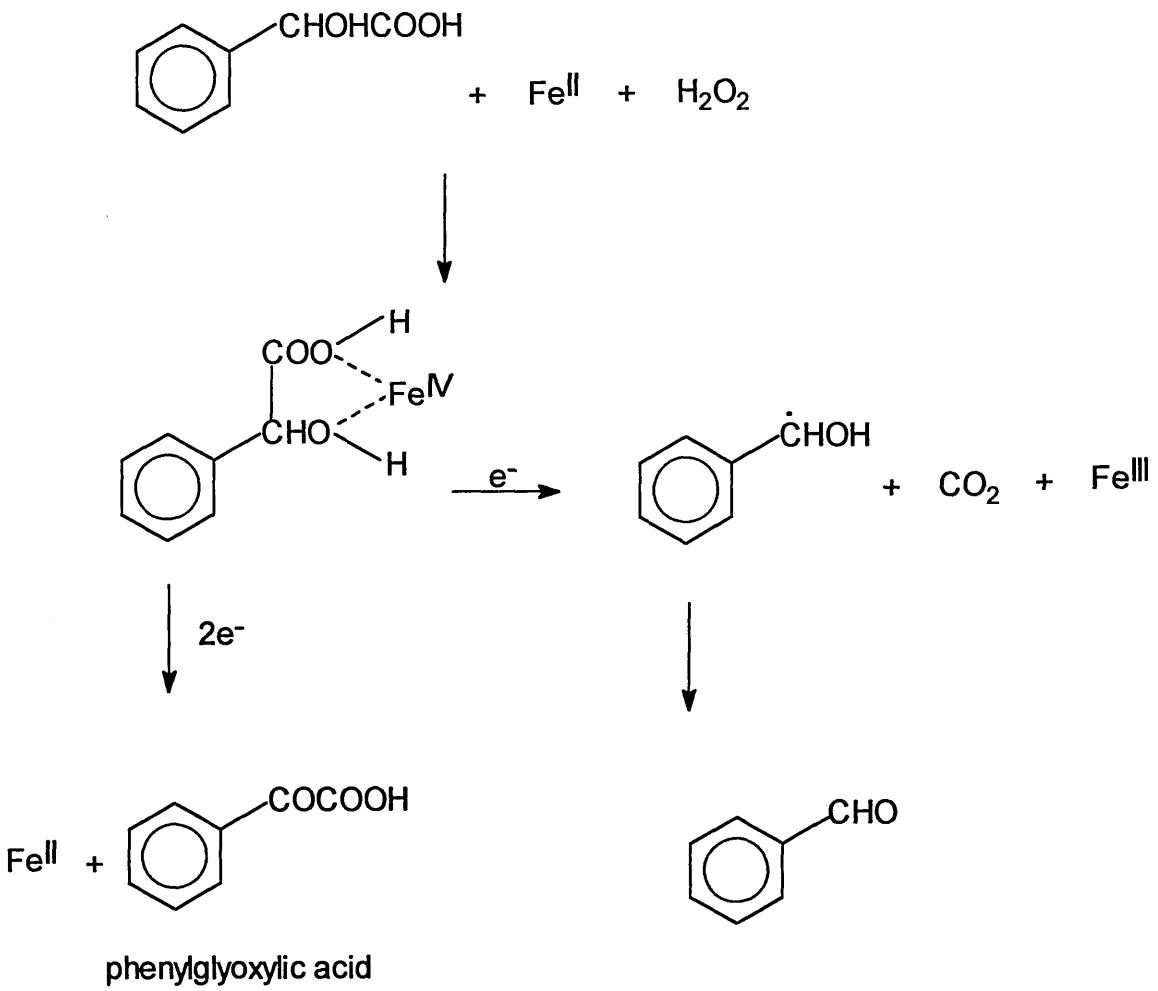
$$HO• + S \rightarrow S• \rightarrow \text{products} + Fe^{III} \quad (30)$$

X represents the untrappable intermediate, MA the total mandelic acid present, and S the added substrate. He found that the addition of a substrate, S, interferes with the oxidation of mandelic acid. Such a substrate will react effectively with hydroxyl radicals but not the intermediate X. An amount of mandelic acid is still oxidised, however, in the presence of the substrate S, and

this apparently represents a 'cage reaction' of newly formed hydroxyl radicals and not an oxidation reaction involving a high oxidation state species such as ferryl Fe^{IV}.

However, Mahapatro et al[62] also considered the oxidation of mandelic acid but they concluded that the Fenton oxidation does proceed via the formation of an Fe^{IV} species, due to the observation of significant amounts of phenylglyoxylic acid in the product mixture. In their studies, they used a radical trap e.g. acetone. A two electron pathway occurs in the Fenton catalysed oxidation of mandelic acid even in the presence of a radical trap (Scheme 4). This was proved by the fact that the yield of phenylglyoxlic acid remained unchanged in the presence of the trapping agent.

Scheme 4



phenylglyoxylic acid

The literature contains other examples of work relevant to this investigation regarding the species actually responsible for the oxidising capabilities of Fenton's reagent[63]-[66]. In some cases the arguments are conflicting and they all revolve around the formation of hydroxyl radicals, and whether or not it is this which is responsible for the subsequent oxidation reactions that take place. Sutton et al[65] suggested that the species generated in a Fenton system has properties that represent both a hydroxyl radical and also the participation of a higher oxidation state of the transition metal e.g. ferryl iron Fe(IV). However, work carried out by Eberhardt et al[67] suggests that a mixture of hydrogen peroxide and transition metal ions, in this case Cu^+, does form hydroxyl radicals, •OH, in what they term a Fenton-like fashion. They

have investigated this theory by considering the course of hydroxylation of a number of aromatic compounds using both Cu^{+}-H_2O_2 and the radiolysis of dilute aqueous solutions. The isomer distributions formed were compared in each case. The isomer distributions formed from the Cu^{+}-H_2O_2 oxidation of fluorobenzene, anisole and nitrobenzene were found to be almost identical to that formed under radiation-induced hydroxylation, Therefore, they conclude that the hydroxyl radical is the major oxidising species in the following general reactions:-

$$Cu^{+} + H_2O_2 \rightarrow Cu^{2+} + OH^{-} + \bullet OH \qquad (31)$$

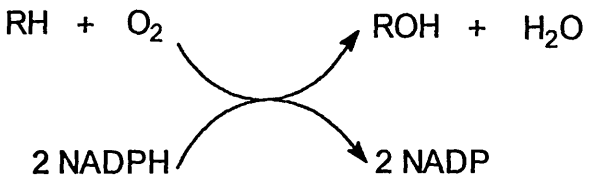
$$ArH + \bullet OH \rightleftharpoons \left[Ar(OH)H \right]^{\bullet} \longrightarrow ArOH \qquad (32)$$

1.3.2. 'Gif' Chemistry

The discussion so far has highlighted the fact that the oxidation of organic compounds using oxygen-containing reagents, catalysed by a variety of transition metals, is an important aim of recent oxidation chemistry. An example of the importance of this aim is found in the development of 'Gif' Chemistry. Barton developed Gif chemistry to provide a means of selectively generating functionalised systems from saturated hydrocarbons. The direct functionalisation of saturated hydrocarbons would usually require quite drastic conditions of high temperatures and pressures[68]. The introduction of functional groups via an oxidative mechanism is therefore an industrially important objective. In order to be able to understand and attempt such an objective, a consideration of biological systems is required as, in Nature, the hydroxylation of non-activated carbon-hydrogen bonds commonly takes place under mild conditions[69]. Such a process is catalysed by the mono-oxygenase enzymes, the best examples of which are the cytochrome P450

mono-oxygenases. This group of mono-oxygenases is one of the most studied and it consists of a series of isozymes which are active in the oxidation of drugs, xenobiotics and endogenous compounds. The oxidation process involves, among many things, the hydroxylation of saturated hydrocarbons and this is represented in Scheme 5, where the cofactor, NADPH, is a source of electrons.

Scheme 5



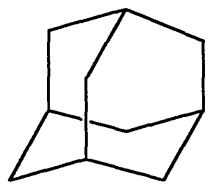
The active site of the enzymes responsible for the oxidation processes consists of an iron porphyrin system. Barton points out that the mechanism of the insertion of oxygen into the C-H bonds of the substrate is not understood but that there is evidence to support the presence of an Fe^{V}=O species.

The first work carried out on the functionalisation of hydrocarbons by Barton appeared in 1983[70] when it was found that it was possible for ketones to be formed from saturated hydrocarbons via an oxidative mechanism. Since this time, Barton has done much work which has involved the catalytic oxidation of organic compounds, specifically saturated hydrocarbons, using a set of systems which he has established[71]. These have been referred to as the Gif and GoAgg systems and are summarised in the Table 2. For each of these reactions, a solution of pyridine and acetic acid is required as the solvent[71].

Table 2

SYSTEM	CATALYST	ELECTRON SOURCE	OXIDANT
Gif (III)	Fe (II)	Fe	O_2
Gif (IV)	Fe (II)	Zn	O_2
GO	Fe (II)	cathode	O_2
GoAgg (I)	Fe (II)	KO_2/Ar	
GoAgg (II)	Fe (III)	H_2O_2	H_2O_2
GoAgg (III)	Fe (III)/picolinic acid	H_2O_2	H_2O_2
GoChAgg	Cu (II)	H_2O_2	H_2O_2
Cu/O_2	Cu (I)	Cu	O_2

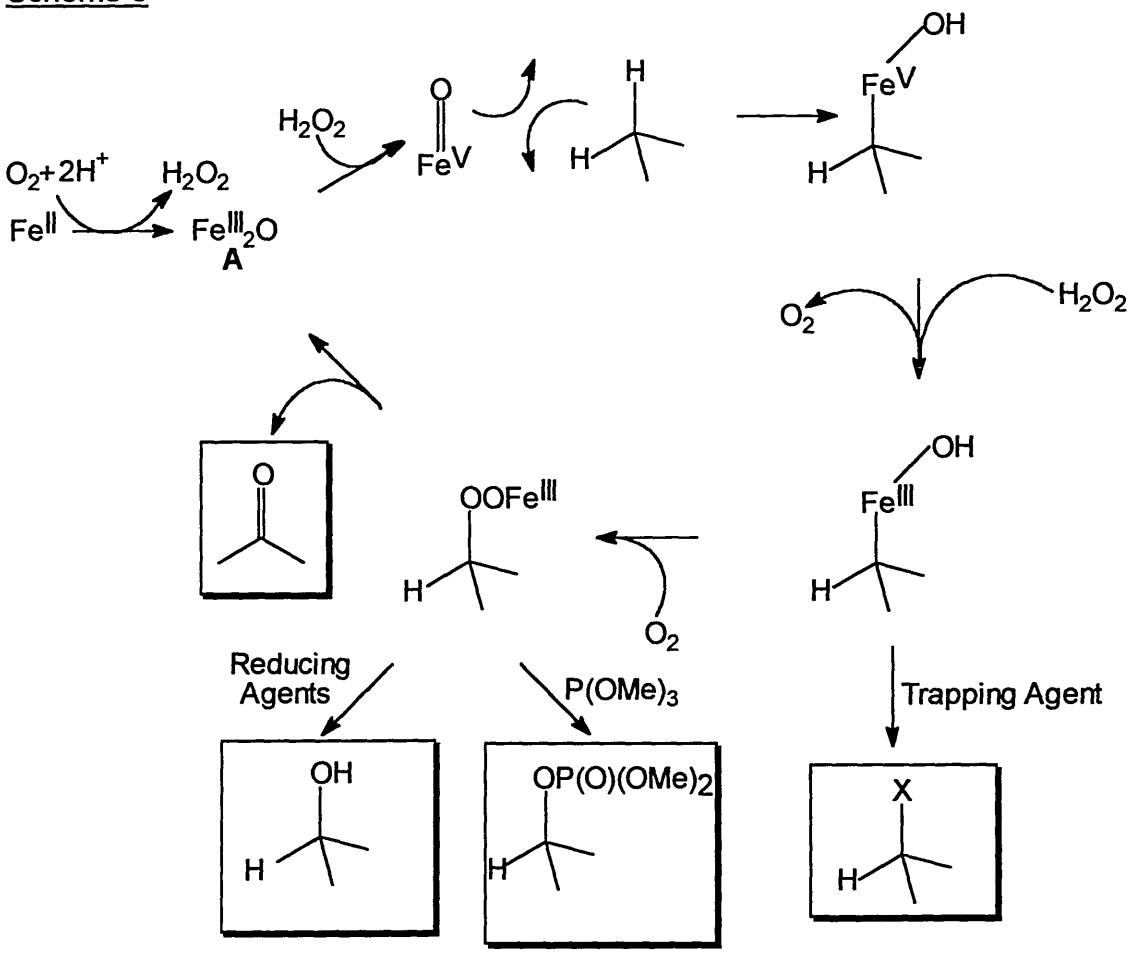
The characteristics of these systems were investigated by determining their effect on the oxidation of a hydrocarbon such as adamantane.



Adamantane was selected as a suitable substrate as it is a spherically symmetrical hydrocarbon possessing four tertiary and twelve secondary carbon-hydrogen bonds[70]. The first effective Gif reagent established, Gif (III), involved the use of Fe (II) as a catalyst, Fe as an electron source and O_2 as the oxidant. This system was able to oxidise adamantane to give a mixture of adamantanone and 1- and 2-adamantanol. It was later discovered that the oxidation could be made more efficient by the use of zinc as an electron source i.e. the Gif (IV) system.

Several other systems have been developed which differ from each other as shown in Table 2. In the GoAgg systems, Gif properties were mimicked by the use of Fe(II) and a superoxide such as potassium superoxide or the use of Fe(III) and hydrogen peroxide. Essentially, Gif catalysts react with alkanes giving rise to ketones, primarily, and small amounts of alcohols and other minor products, depending on the conditions adopted[72]. The mechanism of oxidation occurring under Gif conditions is thought to proceed via the formation of an alkyl hydroperoxide and a catalytic cycle is thought to be involved. This cycle is represented in Scheme 6 which represents the catalytic cycle for GoAgg reactions.

Scheme 6



The Gif mechanism, shown in Scheme 6 does not involve the reaction of O_2 with a ferrous species in any of the important mechanistic steps. The oxygen does, however, oxidise the Fe(II) precatalyst to give a (μ-oxo)diiron (III) compound **A** and hydrogen peroxide. The Fe^{V}=O oxenoid that results from the interaction of Fe^{III}_2O with H_2O_2 in Scheme 6 is then formed, and it is this that then reacts with the C-H bond to give an iron-carbon bond with the structure HO-Fe-C[73]. This pathway for a GoAgg system is equivalent to the widely accepted cytochrome P450 oxidation chemistry[71].

Barton has done much work to support his theory of the mechanism of oxidation occurring when Gif systems are used[74]-[81] i.e. that the oxidation proceeds via the formation of the Fe^{V}=O species. Such a species is formed by using either a mixture of Fe (II) and superoxide or hydrogen peroxide and Fe (III)[75i].

$$Fe^{II} + {}^{-}O_2\bullet \equiv Fe^{III} + H_2O_2 \rightarrow Fe^{III}\!-\!O\!-\!OH \rightarrow Fe^{V}\!=\!O \qquad (29)$$

The chemical reactivity of Gif systems can be summarised in the table shown below[75a]:-

Table 3

GIF CHEMISTRY	KETONES
	- order of reactivity of C-H bond is
$>CH_2 \longrightarrow >C=O$	*sec.> tert.≥ prim.*

Barton suggests that Gif-type reactions do not involve radical chemistry, which is contrary to what might be expected from the use of iron salts in the presence

of oxygen containing species. He suggests that the oxidation reactions proceed via the formation of alkyl hydroperoxides. Therefore, the general process for a Gif Type reaction is[74]

Alkane $\rightarrow$ *Alkyl Hydroperoxide* $\rightarrow$ *Ketone* or *Alcohol.*

It has been established that the main features of all Gif systems are[82]:-

i) the oxidation of *sec.* C-H bonds occurs mainly to ketones and that alcohols are not reaction intermediates

ii) the presence of an excess of alcohols or other easily oxidisable compounds does not suppress the oxidation of alkanes significantly

iii) cyclic olefins are not epoxidised under these conditions, but instead give rise to conjugated ketones

iv) the order of selectivity for the oxidation of C-H bonds is *sec.>tert.≥prim.*

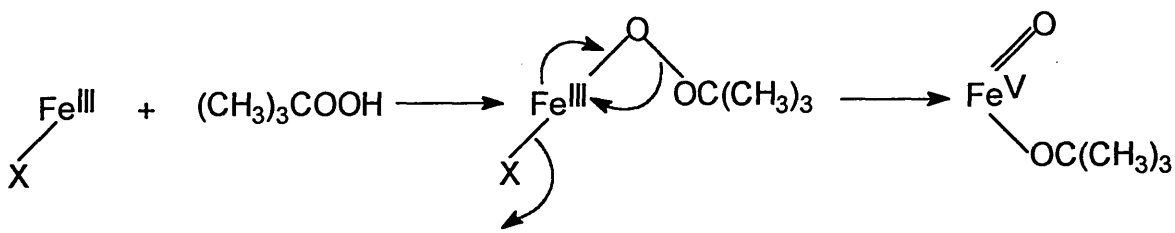
v) *sec.* alkyl radicals are not intermediates in the activation process as the reaction proceeds smoothly even in the presence of different radical trapping agents. Such agents do not interfere with the oxidation process but instead highly functionalised hydrocarbons are formed.

Barton has continued with his study of the oxidation of saturated hydrocarbons. The Gif systems discussed earlier were all based upon the use of an iron-containing catalyst. However, other systems have been developed which involve the use of copper-containing catalysts and such catalysts were also found to exhibit the Gif-type characteristics[82]. Such systems were referred to as GoChAgg as indicated in Table 2. Experiments carried out by Barton suggest that the Cu^{II}-catalysed oxidation of saturated hydrocarbons by H_2O_2 is similar to the Fe^{III}-catalysed process i.e. GoAgg reactions. Continued research into the use of both copper(II) and iron(III) as catalysts does, however, provide evidence to suggest that intermediates formed from each system were actually different. Therefore, Barton has suggested that Gif-type

reactivity is metal-dependent and involves two chemically different non-radical species[83]. This study supported his view that the oxidation process does not involve activation by free •OH.

Barton also considered other primary oxidants instead of hydrogen peroxide[84]. The use of *tert*-butyl hydroperoxide (TBHP) has been used in conjunction with Fe^{III} in a mixture of pyridine and acetic acid and this system was referred to as $GoAgg^{IV}$. The mechanistic pathway for an oxidation reaction involving $GoAgg^{IV}$ is very similar to that seen for other systems in that a high valent Fe^{V}=O species is also formed here - Scheme 7

Scheme 7



X = OAc, OH *etc*

The Fe^{V}=O species has been formed by a rearrangement process which is a plausible explanation as can be seen above in Scheme 7.

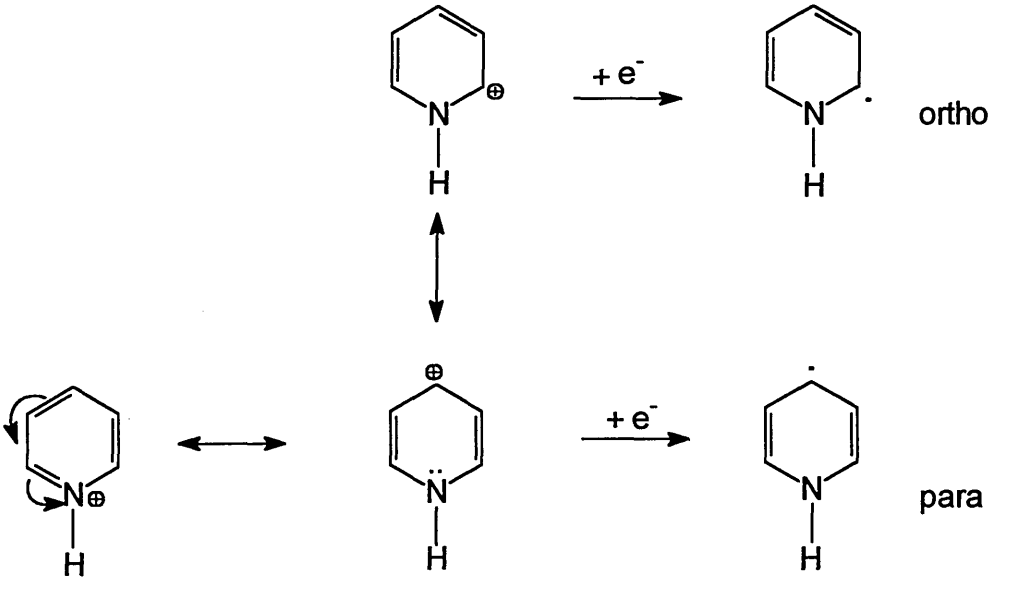
The use of TBHP is a development of the existing Gif systems as it provides a more powerful and selective way of forming the ketone from the oxidation of saturated hydrocarbons[84]. The literature provides examples of the effectiveness of this and other new systems, e.g. $GoAgg^{V}$, developed by Barton et al[85]-[87].

The work carried out by Barton clearly suggests the need for a greater understanding of the mechanism of the oxidation of organic compounds, with a view to achieving regio-selective oxidation of hydrocarbons.

Although Barton has suggested that the Gif mechanism of oxidation proceeds in a non-radical fashion, a publication in 1987 detailed an investigation carried out by his group that dealt with the observation of bipyridines and pyridine-hydrocarbon coupling products in Gif oxidation products[88] using GC/MS techniques.

Although Barton has shown that several organic acids may replace the acetic acid used in the solvent system for Gif reactions, pyridine is essential for the Gif-system oxidation to occur[81]. During the oxidation of adamantane, the ketone derived from the hydrocarbon has been observed together with an equivalent amount of a coupling product formed between a *tert*-adamantyl radical and a pyridyl radical. Several isomeric bipyridines were also observed.

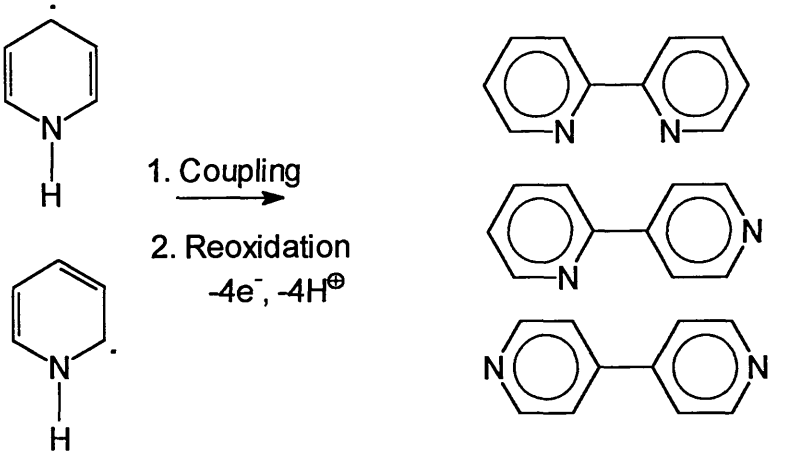
Scheme 8



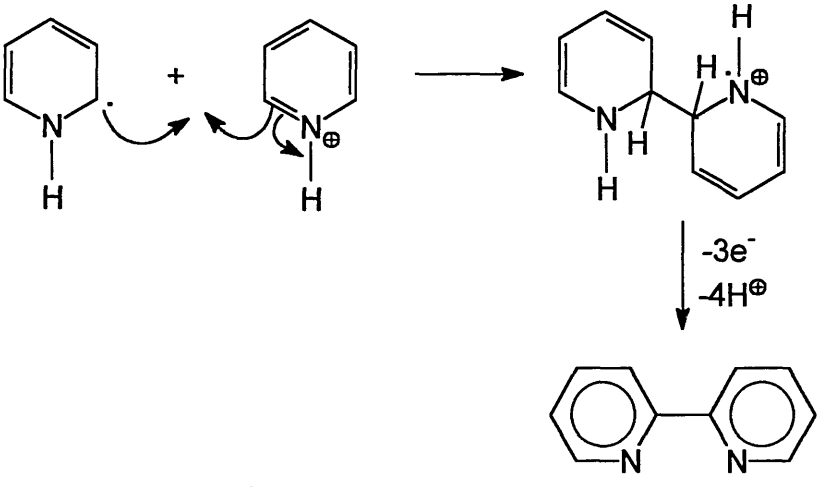
Scheme 8 shows the formation of two possible pyridyl radicals. Scheme 9 then shows how the bipyridine structures are formed by either the coupling of the two radicals (A) to give three isomeric structures, or from the coupling of one of the pyridyl radicals and a protonated pyridine compound (B).

Scheme 9

A. Radical-Radical Coupling

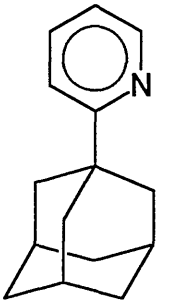


B. Radical-Protonated Pyridine Coupling



Schemes 8 and 9 above illustrate the formation of 2,2'-, 4-4'-, and 2,4'-bipyridines, which are only a few of the bipyridyl structures that could be

possibly formed. The schemes, however, do illustrate the radical nature of their formation. Radical reactions would also be responsible for the formation of the coupling product between the *tert*-adamantyl radical and a pyridyl radical to give structures of the type shown below.



Such structures may also arise from the coupling of the pyridine in the 4-position and also where the radical coupling reaction takes place via the protonated pyridine as shown in Scheme 9 (B).

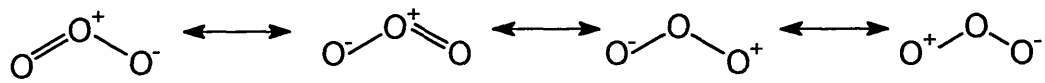
The investigation carried out by Barton went on to discuss the nature of the formation of other bipyridyl structures. Therefore, when using the Gif IV system, the evidence clearly points to a radical reaction occurring *in conjunction with* the formation of the appropriate ketone via a non-radical route, as discussed earlier in this section. It would seem appropriate to suggest that a Gif oxidation reaction involves two mechanistic routes even though the radical route is the result of a side reaction involving the solvent.

1.4. Other Treatments for Hazardous Waste

The treatment of hazardous waste using WAO technology has been considered in 1.2. However, there are many other ways of oxidising aqueous organic compounds which are commonly found in industrial wastes, with the aim of destroying them e.g. the use of potassium permanganate, chlorine dioxide and ozone[89]. All of these processes involve the chemical oxidation of organic compounds in waste waters. Ozone is particularly effective for

disinfection, odour and colour removal, and the destruction of cyanides and toxic organic compounds in water[90].

Ozone, O_3, is an allotropic form of oxygen and its structure has been explained as a resonance hybrid of the following four canonical structures[91]:-

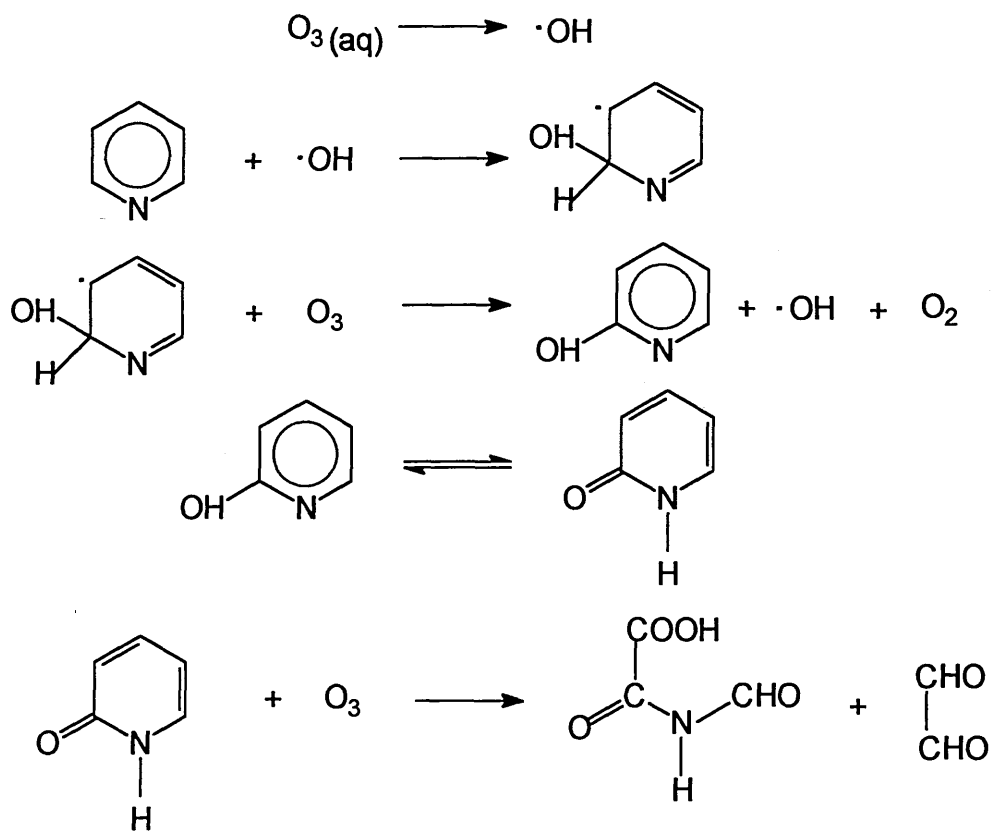


The reaction of ozone depends strongly on pH, temperature and the rate of ozone decomposition. At lower pH values, the ozone molecule reacts directly with organic molecules. At higher pH values, however, the ozone decomposes to form hydroxyl radical intermediates. Such radicals are then themselves more reactive with certain organic compounds than ozone itself e.g. the reaction with benzene. Therefore, careful control of conditions is required for the effective ozonation of certain organic compounds.

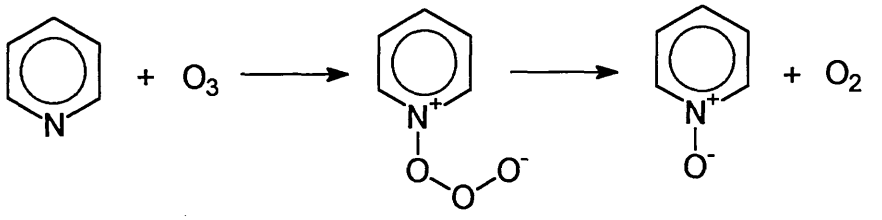
Balloid et al[14] in 1983 discussed the effectiveness of the use of ozonation for the oxidation of organic compounds in water. Ozone reacts with aromatic compounds to produce catechol and hydroquinone followed by muconic, maleic, glyoxylic, glycolic, oxalic and formic acids, with the corresponding aldehydes being frequently detected as precursors of these acids. The rate of total organic carbon removal, however, was found to decrease with time as the lower molecular weight acids react more slowly than their parent compounds. They went on to suggest that hydroxyl radicals play an important role in the ozonation of organic compounds.

The interest in ozonation in the context of this discussion is due to this suggestion that hydroxyl radicals play an important role in the ozonation oxidation process, under certain conditions. Work carried out by Andreozzi et al[92] provides an example of this in the oxidation of pyridine involving the use of ozone as the oxidising reagent. They showed that the pyridine ring is destroyed in a stepwise fashion and that the process is initiated by the presence of hydroxyl radicals generated from the decomposition of ozone - Scheme 10. The mechanism shown in Scheme 10 is suggested due to the observation of N-formyloxamic acid among the ozonation products. This mechanism occurs if the ozone undergoes decomposition in the absence of any radical scavengers. If radical scavengers <u>are</u> present, then the ozone reacts directly with the pyridine, with the mechanism of attack being mostly directed towards the nitrogen atom - Scheme 11.

<u>Scheme 10</u>

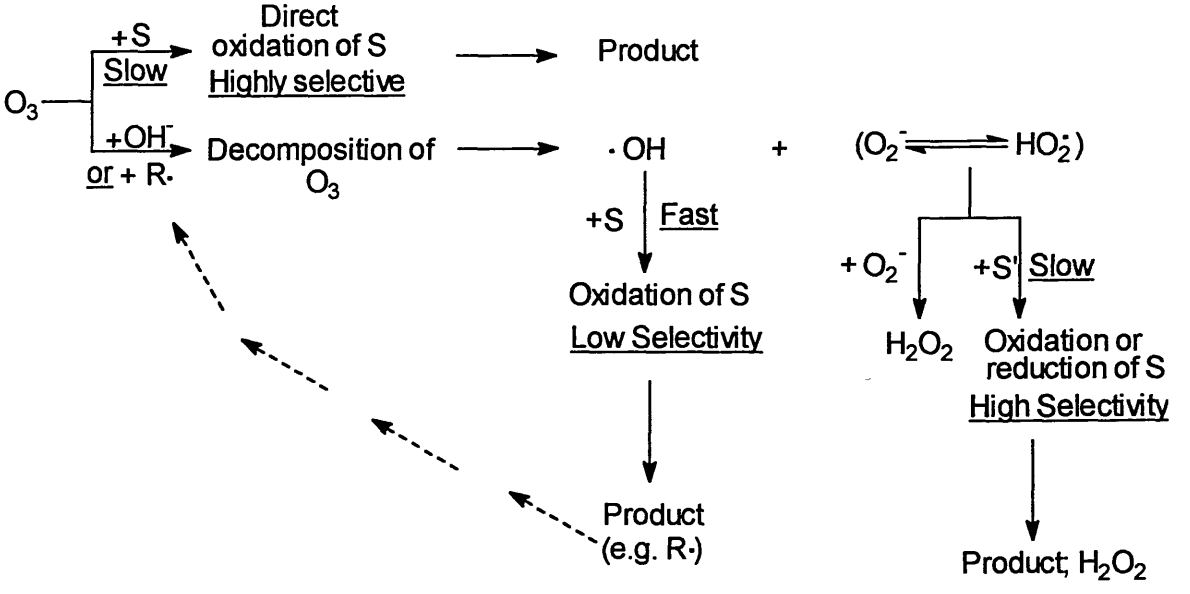


Scheme 11



The fact that ozone has a dual role during ozonation processes was also suggested by Hoigne et al[93]. This study illustrated the effect pH has on the ozonation process and that, about a critical pH, the ozonation proceeds either via direct attack of ozone on the substrate, or by decomposition products of ozone such as the hydroxyl radical. This is summarised in Scheme 12, where S is the substrate.

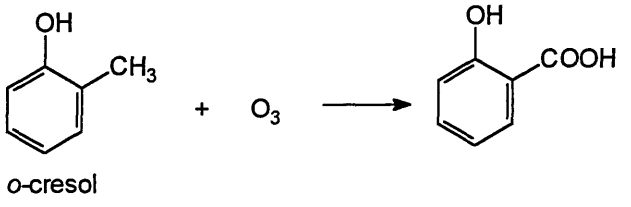
Scheme 12



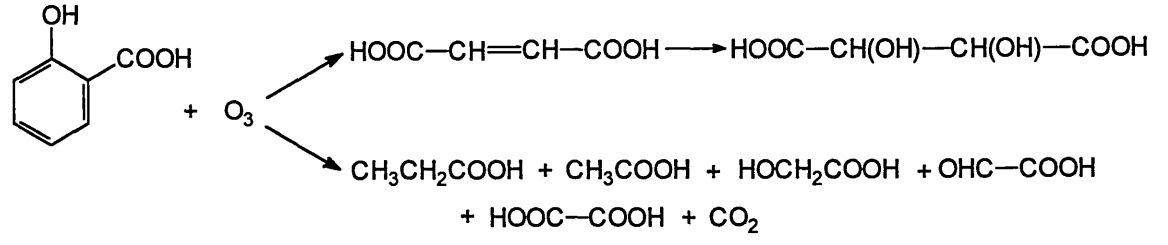
A more recent example of the use of ozone as an oxidising system was carried out by Zheng et al in 1993[94]. Here the oxidation between ozone and cresols was investigated and the oxidation, with complete conversion to various intermediate products, was found to be very rapid. Further reactions of those

intermediates resulted in the rupturing of the aromatic ring to produce carbon dioxide, acetic and other acids. A general scheme for the fate of cresols is illustrated in Scheme 13.

Scheme 13



o-cresol



The formation of the various acidic compounds via the rupturing of the aromatic ring is very similar to the fate of the pyridine in Scheme 10.

Essentially, the oxidising species responsible for the oxidation process occurring during ozonation is thought to be a hydroxyl radical, depending upon the conditions adopted for the process. Therefore the chemistry associated with ozonation could be related to Fenton chemistry and those radical reactions taking place in Gif chemistry.

1.5. Kinetic Studies of the Oxidation of Organic Compounds

In any oxidation reaction being considered, a kinetic study provides a means of investigating the process taking place in more detail. During a kinetic study, two aspects have to be considered:-

1) molecular interactions involving the collision of two molecules to produce one or more species, which are called elementary reactions

2) the sequence of elementary reactions that constitutes the overall chemical transformation[95].

The second aspect involves measurements of how the rate of a reaction depends on the concentrations of the reagents. Such results are then expressed in the form of a rate equation. This equation represents the dependence of the rate at a given temperature on the concentration of the reagents. Many reactions have rates that, at a given temperature, are proportional to the concentration of one or two of the reactants, with each of the reactant concentration terms raised to a small integral power, Therefore for the reaction

$$aA + bB \rightarrow cC + dD$$

the simple rate equations could be

Rate of reaction = $k[A]$			first order
Rate of reaction = $k[A]^2$	or	$k[A][B]$	second order.

In the rate equation, k is the rate constant, and by determining this value for any system, it is possible to investigate and ultimately improve a reaction process.

Kinetic studies of the WAO of some organic compounds have been carried out[96], [97]. In these studies, the rates of destruction of each of the organic compounds being considered were measured with respect to the reduction in substrate concentration and with respect to the reduction in COD values. In the studies carried out by Joglekar et al[18] and by Mishara et al[96], the WAO

reaction was found to be first order with respect to substrate concentration. However, these studies only relate to specific substrates. There is an example in the literature, though, which deals with the development of a generalised kinetic model that is applicable to a variety of organic compounds[97]. Again, the oxidation is found to be statistically first order with respect to the concentration of the substrate organic compounds.

The use of kinetic data enables the possibility of improving the conditions of the WAO process. The determination of rate constants for individual reactions provides a means of optimising the process, by establishing the limiting factors in the reaction. This is an essential requirement when considering reactions that are required to be efficient. For the treatment of wastes, the aim is to establish an efficient oxidising system as the quicker the destruction of the organic compounds occurs, the more economical the process is found to be.

1.6. Purpose of the Present Study

WAO is the process adopted for the destruction of waste materials by Leigh Environmental Ltd. and others, and it was decided that a greater understanding of the chemistry of the process was required as earlier work does not provide sufficient detail. A more extensive study is necessary in order to optimise conditions for the process and to achieve better results with difficult contaminants.

The suggested initial approach involved taking a typical waste stream and analysing it to determine its contents. Having established the content of the sample, WAO followed by determination of the products of the oxidation process might have aided an understanding of degradation pathways. Improvements in the process, for example, as a result of introducing an appropriate catalyst might then follow. The major problem with this approach would be the determination of the exact content of a typical waste stream, even with the extensive analytical techniques that are to hand. A typical approach to the analysis of such samples is to study them by chromatography, in particular gas- and liquid-chromatography. With the samples proposed, however, the initial contents of a waste stream would be completely unknown and therefore appropriate conditions for the chromatographic determinations would be difficult to establish e.g. depending on whether the contaminants are volatile or involatile, polar or non-polar will have an effect on the analytical technique adopted.

Interactions between compounds in a typical waste stream have also to be considered. For example, the WAO of a compound may occur in the presence of acetic acid, a common product from the oxidation of organic compounds. However, in the absence of the acid the oxidation of that particular compound

may not occur. This process is referred to as co-oxidation[98]. Such interactions, between individual components of a typical multicomponent waste stream, may ultimately confuse our understanding of the basic chemistry that is occurring in the WAO process.

Thus, it was felt necessary to narrow the scope of the study by considering the fate of individual compounds under the conditions of WAO, thereby facilitating the analysis of the oxidation products formed. The study has therefore involved an investigation of the WAO of nitrogen-containing compounds, particularly aromatic nitrogen compounds such as the alkylpyridines, which are known to be difficult to oxidise, and which are commonly found in effluent streams from coking plants[99].

Oxidation reactions involving oxygen- or oxygen-containing compounds as the means of oxidation are extensive and, therefore, an understanding of the mechanism of the oxidation is required. Since WAO is a process that involves the use of oxygen as an oxidising system, the chemistry involved can be linked to that of other oxidising systems which involve the use of oxygen- or oxygen-containing compounds e.g. Fenton chemistry (1.3.1.) and Gif chemistry (1.3.2.). Also, the use of catalysis within WAO technology has involved the use of mixtures of metal salts and hydrogen peroxide i.e. Fenton-like reagents[59]. Thus a detailed study of the oxidation of 2-, 3-, and 4-methylpyridine under WAO conditions, and also in the presence of other reagents of the Fenton-Type, will hopefully add to the information regarding the mechanism of oxidation using oxygen reagents. The background chemistry associated with Gif chemistry illustrates the extent of the need for a greater understanding of the course of the oxidation of organic compounds. However, the information already provided by Barton et al and others will help our understanding of the observations made in the study which is described in this thesis.

1.6.1. Aims of the Research Study

The aims of the study were as follows:-

1. To investigate the oxidation of 2-, 3-, and 4-methylpyridines under simulated WAO conditions in the laboratory, under both uncatalysed and catalysed conditions.
2. To investigate and compare the oxidation of 2-, 3-, and 4-methylpyridine using some of the various oxidising systems of the Fenton-Type that have been discussed in this chapter.
3. To investigate the kinetics associated with the oxidation of 2-methylpyridine using Fenton's reagent as the oxidising system.
4. To synthesise and characterise some of the intermediate oxidation products formed during the oxidation of 2-, 3-, and 4-methylpyridines.

1.7. References

1. Tucker S.P. & Carson G.A., Deactivation of Hazardous Chemical Wastes, *Environ. Sci. Technol.*, 1985, **19**, 215-220.
2. Jackman A.P. & Powell R.P., Hazardous Waste Treatment Technologies, Noyes Publications, 1991, 90-134, and references therein.
3. Mishara V.S., Mahajani V.V. & Joshi J.B., Wet Air Oxidation - A Review, *Ind. Eng. Chem. Res.*, 1995, **34**, 2-48, and references therein.
4. Copa W.M., Randall T.L. & Wilhelmi A.R., Wet Air Oxidation of Hazardous Wastes, *Ency. of Environ. & Control Tech.*, 1989, **1**, 314-332.
5. Heimbuch J.A. & Wilhelmi A.R., Wet Air Oxidation - A Treatment Means for Aqueous Hazardous Waste Streams, *J. Hazardous Materials*, 1985, **12**, 187-200.
6. Baillod C.R., Lamparter R.A. & Barna B.A., Wet Oxidation for Industrial Waste Treatment, *Chem. Eng. Prog.*, August 1985, 52-56.
7. Laughlin R.G.W., Gallo T. & Robey H., Wet Air Oxidation for Hazardous Waste Control, *J. Hazardous Materials*, 1983, **8**, 1-9.
8. Wilhelmi A.R. & Knopp P.V., Pollution Control Practices: Wet Air Oxidation - An Alternative to Incineration, *Chem. Eng. Prog.*, August 1979, 46-52.
9. Pruden B.B. & Le H., Wet Air Oxidation of Soluble Components in Waste Water, *The Canadian Journal of Chemical Engineering*, August 1976, **54**, 319-325.
10. Othmer D.F., Earth+Water+Air = Fire. The Wet Air Oxidation WAO of Wastes, *Mechanical Engineering*, December 1979, 30-37.
11. Chemical Oxygen Demand (Dichromate Value) of Polluted and Waste Waters 1986 (Second Edition), Methods for the Examination of Waters and Associated Materials, Published by London: Her Majesty's Stationary Office.

12. Randall T.L., Wet Oxidation of Toxic and Hazardous Compounds, *Procs. 15th Mid-Atl. Conf. Indust. Waste*, 1981, 501-508.

13. Randall T.L. & Knopp P.V., Detoxification of Specific Organic Substances by Wet Oxidation, *Journal WPCF*, 1980, **52**, 2117-2130.

14. Baillod C.R., Faith B.M. & Masi O., Fate of Specific Pollutants during Wet Oxidation and Ozonation, *Environmental Progress*, 1982, **1**, 217-226.

15. Daoyi B.I. & Jianhua H.A.N., Study on Treatment of Oil Shale Retorting Waste Water by WAO, *Procs. Oil Shale Symposium - USA*, 1990, 169-172.

16. Dubois M.A., Huard T. & Massiani C., Wet Oxidation of Non Water - Soluble Polymers, *Environmental Technology*, 1993, **14**, 195-200.

17. Larson R.A., Ju H-L., Snoeyink V.L., Recktenwalt M.A. & Dowd P.A., Some Intermediates in the Wet Air Oxidation of Phenanthrene Adsorbed on Powdered Activated Carbon, *Water Research*, 1988, **22**, 337-342.

18. Joglekar H.S., Samant S.D. & Joshi J.B., Kinetics of Wet Air Oxidation of Phenol and Substituted Phenols, *Water Research*, 1991, **25**, 135-145.

19. Masato M.I., Akita K. & Inoue H., Wet Oxidation of Oxygen- and Nitrogen-Containing Organic Compounds Catalysed by Cobalt(III) Oxide, *Ind. Eng. Chem. Res.*, 1989, **28**, 894-899.

20. Imamura S-I., Hirano A. & Kawabata N., Wet Oxidation of Acetic Acid Catalysed by Co-Bi Complex Oxides, *Ind. Eng. Chem. Prod. Res. Dev.*, 1982, **21**, 570-575.

21. Miller R.A., Fox R.D. & Pitts D.M., Evaluation of Catalysed Wet Oxidation for Treating Hazardous Waste, *Procs. American EPA 7th Ann. Research Symposium (Philadelphia)*, March 1981, **2**, 272-276.

22. Chowdbury A.K. & Ross L.W., Catalytic Wet Oxidation of Strong Waste Waters, *AIChE Symposium Series - Water 1975*, **71**,151, 46-58.

23. Devlin H.R. & Harris I.J., Mechanism of the Oxidation of Aqueous Phenol with Dissolved Oxygen, *Ind. Eng. Chem., Fundam.*, 1984, **23**, 387-392.

24. Sawyer D.T., Oxygen Chemistry, Oxford University Press, 1991.

25. Mukaiyama T. & Yamada T., Recent Advances in Aerobic Oxygenation, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 17-35.

26. Baciocchi E., d'Acunzo F., Galli C. & Ioele M., Oxidation of Isopropylbenzene by Iron Tetraphenylporphyrin: Evidence for the Interaction of the Cumyl Radical with Oxygen Donors, *J. Chem. Soc., Chem. Commun.*, 1995, 429-430.

27. Lanfranchi M., Prati L., Rossi M. & Tiripicchio A., The Oxidation of Ethane-1,2-diol resulting from Molecular Oxygen Activation by Copper: Formation of an Oxoethanoate Complex precedes Carbon-Carbon Bond Cleavage, *J. Chem. Soc., Chem. Commun.*, 1993, 1698-1699.

28. Lee D.G. & Gai H., Kinetics and Mechanism of the Oxidation of Alcohols by Ferrate Ion, *Can. J. Chem.*, 1993, **71**, 1394-1400.

29. Murahashi S-I., Naota T. & Hirai N., Aerobic Oxidation of Alcohols with Ruthenium-Cobalt Bimetallic Catalyst in the Presence of Aldehydes, *J. Org. Chem.*, 1993, **58**, 7318-7319.

30. Aihara K., Urano Y., Higuchi T. & Hirobe M., Mechanistic Studies of Selective Catechol Formation from *o*-Methoxyphenols using a Copper(II)-Ascorbic Acid-Dioxygen System, *J. Chem. Soc., Perkin Trans. 2*, 1993, 2165-2170.

31. Murahasi S-I., Oda Y., Naota T. & Komiya N., Aerobic Oxidations of Alkanes and Alkenes in the Presence of Aldehydes Catalysed by Copper Salts, *J. Chem. Soc., Chem. Commun.*, 1993, 139-140.

32. Sobkowiak A., Qui A., Liu X., Llobet A. & Sawyer D.T., Copper(I)/(*t*-BuOOH)-Induced Activation of Dioxygen for the Ketonization of Methylenic Carbons, *J. Am. Chem. Soc.*, 1993, **115**, 609-614.

33. Capdevielle P., Sparfel D., Baranne-Lafont J., Cuong N.K. & Maumy M., Efficient Catalytic Dehydrogenation of Alcohols by the 2,2'-Bipyridine-Copper(I) Chloride-Dioxygen System in Acetonitrile. A Mechanistic Study with Deuterium Isotope Effects, *J. Chem. Research (S)*, 1993, 10-11.

34. Bhatia B. & Iqbal J., Cobalt(II) Catalysed Oxidation of Aldehydes to Carboxylic Acid with Molecular Oxygen, *Tetrahedron Letters*, 1992, **33**, 7961-7964.

35. (a) Szeverenyi Z. & Simandi L.I., Oxidation of a Methyl Group in 2,3-dihydro-2,2,4,-trimethyl-1H-1,5-benzodiazepine by O_2 in the Presence of Metal Ions, pp 65-69, (b) Drago R.S., The Activation of Molecular Oxygen by Transition Metal Complexes, pp 83-91, (c) Sasaki K., Kunai A., Kuroda Y. & Kitano T., Oxidation of Naphthalene on Palladium Based Catalyst, pp137-145, (d) Balla J. & Kiss T., The Copper(II)-Catalysed Autoxidation of Catechol in Aqueous Solution, pp189-194, (e) Tyeklar Z. & Karlin K.D., Biomimetic Binding and Activation of Dioxygen with Copper Complexes, pp 237-248, (f) Takehira K., Shimizu M., Hayakawa T. & Orita H., Novel Oxidation of Phenols by a Copper(II) Complex Catalyst/O_2 System, pp 279-284, (g) Buijs W., Offermanns R. & Frijns L., Catalytic Cu(II) Induced Reactions, pp 595-601, (h) Maumy M. & Capdevielle P., Oxo Transfer from Amines N-oxides to Copper Salts: Resulting Copper(III) Mediated Oxidation of Organic Ligands, pp 665-673, Dioxygen Activation and Homogeneous Catalytic Oxidation, edited by Simandi L.I., Elsevier Science Publishers, 1991.

36. Kurusu Y. & Neckers D.C., Functionalisation of Silica Gel: Application for the Catalytic Oxidation of Alkanes, *J. Org. Chem.*, 1991, **56**, 1981-1983.

37. Ito S., Kunai A., Okada H. & Sasaki K., Direct Conversion of Benzene to Hydroquinone. Cooperative Action of Cu(I) Ion and Dioxygen, *J. Org. Chem.*, 1988, **53**, 296-300.

38. Ito S., Yamasaki T., Okada H., Okino S. & Sasaki K., Oxidation of Benzene to Phenols with Molecular Oxygen Promoted by Copper(I) Chloride, *J. Chem. Soc., Perkin Trans. 2*, 1988, 285-293.

39. Sadana A. & Katzer J.R., Catalytic Oxidation of Phenol in Aqueous Solution over Copper Oxide, *Ind. Eng. Chem., Fundam.*, 1974, 13, 127-134.

40. Goldstein S., Czapski G., Transition Metal Ions and Oxygen Radicals, *Int. Rev. Exp. Pathol.*, 1990, **31**, 153-164.

41. Sheldon R.A., A History of Oxygen Activation: 1773-1993, pp 9-30, in The Activation of Dioxygen and Homogeneous Catalytic Oxidation, edited by Barton D.H.R., Martell A.E. & Sawyer D.T., Plenum Press, New York, 1993.

42. Aust S.D., Morehouse L.A. & Thomas C.E., Role of Metals in Oxygen Radical Reactions, *J. Free Radicals Biol. Med.*, 1985, **1**, 1-25.

43. Fenton H.J.H., *J. Chem. Soc.*, 1894, **65**, 899.

44. Walling C., Fenton's Reagent Revisited, *Acc. Chem. Res.*, 1975, **8**, 125-131.

45. Wink D.A., Nims R.W., Saavedra J.E., Desrosiers M.F. & Ford P.C., Oxidation of Alkylnitrosamines via the Fenton Reagent, *ACS Symposium Series*, 1994, 553, 324-327.

46. Mohanty N.R. & Wei I.W., Oxidation of 2,4-Dinitrotoluene using Fenton's Reagent: Reaction Mechanisms and their Practical Applications, *Hazardous Waste and Hazardous Materials*, 1993, **10**, 171-183.

47. Mckehnie M., Nonhebel D.C. & Scullion I., Oxidative Coupling of 2,4,6-Trimethylphenol with Fenton's Reagent, *J. Chem. Research (S)*, 1993, 286-287.

48. Eberhardt M.K., Formation of cis-1,2-Dibenzoylethylene from 2,5-Diphenylfuran by Fenton's Reagent and by Peroxydisulfate. Effect of Oxygen, *J. Org. Chem.*, 1993, **58**, 497-498.

49. Leung S.W., Watts R.J. & Miller G.C., Degradation of Perchloroethylene by Fenton's Reagent: Speciation and Pathway, *J. Environmental Quality*, 1992, **21**, 377-381.

50. Sedlak D.L. & Andren A.W., Oxidation of Chlorobenzene with Fenton's Reagent, *Environ. Sci. Technol.*, 1991, **25**, 777-782.

51. Lipczynska-Kochany E., Degradation of Aqueous Nitrophenols and Nitrobenzene by means of the Fenton Reaction, *Chemosphere*, 1991, **22**, 529-536.

52. Sheu C., Sobkowiak A., Zhang L., Ozbalik N., Barton D.H.R. & Sawyer D.T., Iron-Hydroperoxide-Induced Phenylselenization of Hydrocarbons (Fenton Chemistry), *J. Am. Chem. Soc.*, 1989, **111**, 8030-8032.

53. Vile G.F., Winterbourn C.C. & Sutton H.C., Radical-Driven Fenton Reactions: Studies with Paraquat, Adriamycin, and Anthraquinone 6-Sulphonate and Citrate, ATP, ADP, and Pyrophosphate Iron Chelates, *Archives of Biochemistry and Biophysics*, 1987, **259**, 616-626.

54. Kunai A., Hata S., Ito S. & Sasaki K., The Role of Oxygen in the Hydroxylation of Benzene with Fenton's Reagent. ^{18}O Tracer Study, *J. Am. Chem. Soc.*, 1986, **108**, 6012-6016.

55. Sugimoto H. & Sawyer D.T., Iron(II)-Induced Activation of Hydroperoxides for the Dehydrogenation and Monooxygenation of Organic Substrates in Acetonitrile, *J. Am. Chem. Soc.*, 1985, **107**, 5712-5716.

56. Goldwalling C. & Johnson R.A., Fenton's Reagent. V. Hydroxylation and Side-Chain Cleavage of Aromatics, *J. Am. Chem. Soc.*, 1975, **97**, 363-367.

57. Groves J.T. & Van Der Puy M., Stereospecific Aliphatic Hydroxylation by an Iron-Based Oxidant, *J. Am. Chem. Soc.*, 1974, **96**, 5274-5275.

58. Ito S., Mitarai A., Hikino K., Hirama M. & Sasaki K., Deactivation Reaction in the Hydroxylation of Benzene with Fenton's Reagent, *J. Org. Chem.*, 1992, **57**, 6937-6941.

59. Goldstein S., Meyerstein D. & Czapski G., The Fenton Reagents, *Free Radical Biology and Medicine*, 1993, **15**, 435-445.

60. Sawyer D.T., Kang C., Liobet A. & Redman C., Fenton Reagents (1:1 $Fe^{II}L_X$/HOOH) React via $[L_XFe^{II}OOH(BH^+)]$ (1) as Hydroxylases (RH→ROH), not as Generators of Free Hydroxyl Radicals (HO•), *J. Am. Chem. Soc.*, 1993, **115**, 5817-5818.

61. Walling C. & Amarnath K., Oxidation of Mandelic Acid by Fenton's Reagent, *J. Am. Chem. Soc.*, 1982, **104**, 1185-1189.

62. Mahapatro S.N., Panigrahi A.K., Panda R. & Patro D.M., Mechanism of Oxidation of Mandelic Acid by Fenton's Reagent, *Inorg. Chem.*, 1984, **23**, 4119-4120.

63. Wink D.A., Wink C.B., Nims R.W. & Ford P.C., Oxidising Intermediates Generated in the Fenton Reagent: Kinetic Arguments Against the Intermediacy of the Hydroxyl Radical, *Environmental Health Perspectives*, 1994, **102**, 11-15.

64. Yamazaki I. & Piette L.H., EPR Spin-Trapping Study on the Oxidising Species Formed in the Reaction of the Ferrous Ion with Hydrogen Peroxide, *J. Am. Chem. Soc.*, 1991, **113**, 7588-7593.

65. Sutton H.C. & Winterbourn C.C., On the Participation of Higher Oxidation States of Iron and Copper in Fenton Reactions, *Free Radical Biology and Medicine*, 1989, **6**, 53-60.

66. Koppenol W.H., The Reaction of Ferrous EDTA with Hydrogen Peroxide: Evidence Against Hydroxyl Radical Formation, *J. Free Radicals in Biology and Medicine*, 1985, **1**, 281-285.

67. Eberhardt M.K., Ramirez G. & Ayala E., Does the Reaction of Cu^{+} with H_2O_2 Give OH Radicals? A Study of Aromatic Hydroxylation, *J. Org. Chem.*, 1989, **54**, 5922-5926.

68. Leddy B.P., McKervey M.A. & McSweeny P., Some Comments on the Thermal Stability of Substituted Ammonium, Phosphonium, and Arsonium Permanganates and Their use in Alkane Oxidation, *Tetrahedron Letters*, 1980, **21**, 2261-2264.

69. Barton D.H.R., Boivin J., Gastiger M., Morzycki J., Hay-Motherwell R.S., Motherwell W.B., Ozbalik N. & Schwartzentruber K.M., Functionalisation of Saturated Hydrocarbons. Part 4. [1]The Gif System for Selective Oxidation using Molecular Oxygen, *J. Chem. Soc., Perkin Trans 1*, 1986, 947-955.

70. Barton D.H.R., Gastiger M.J. & Motherwell W.B., A New Procedure for the Oxidation of Saturated Hydrocarbons, *J. Chem. Soc., Chem. Commun.*, 1983, 41-43.

71. Barton D.H.R. & Doller D., The Selective Functionalisation of Saturated Hydrocarbons: Gif Chemistry, *Acc. Chem. Res.*, 1992, **25**, 504-512.

72. Feig A.L. & Lippard S.J., Reactions of Non-Heme Iron(II) Centres with Dioxygen in Biology and Chemistry, *Chem. Rev.*, 1994, **94**, 759-805.

73. Barton D.H.R., Halley F., Ozbalik N., Schmitt M., Young E. & Balavoine, Functionalisation of Saturated Hydrocarbons. 14. Further Studies on the Mechanism of Gif-Type Systems, *J. Am. Chem. Soc.*, 1989, **111**, 7144-7149.

74. Barton D.H.R., Beviere S.D., Chavasiri W., Csuhai E., Doller D. & Liu W-G., The Functionalisation of Saturated Hydrocarbons. Part 20.$^{+}$ Alkyl Hydroperoxides: Reaction Intermediates in the Oxidation of Saturated Hydrocarbons by Gif-Type Reactions and Mechanistic Studies on Their Formation, *J. Am. Chem. Soc.*, 1992, **114**, 2147-2156.

75. (a) Barton D.H.R. & Doller D., The Selective Functionalisation of Saturated Hydrocarbons. Gif and All That, pp 1-10, (b) Lee K.W., Choi K.Y., Jun K.W. & Barton D.H.R., Selective Oxidation of Hydrocarbons, pp 55-64, in Dioxygen Activation and Homogeneous Catalytic Oxidation, edited by Simandi L.I., Elsevier Science Publishers, 1991.

76. Barton D.H.R., Beviere S.D. & Doller D., An Unprecedented Chemical Transformation: the Oxidation of Alkanes to Alkyl Dimethyl Phosphates, *Tetrahedron Letters*, 1991, **32**, 4671-4674.

77. Balavoine G., Barton D.H.R., Gref A. & Lellouche I., The Insertion of Sulphur into the Non-Activated C-H Bond. A Possible Model for Penicillin Cyclase and Biotin Synthase, *Tetrahedron Letters*, 1991, **32**, 2351-2354.

78. Barton D.H.R., Csuhai E., Doller D., Ozbalik N. & Senglet N., Comparison of Gif-Type Reactivity Towards Alkanes with Standard Radical Reaction

Selectivity. Gif Oxidation of n-Butane and Propane, *Tetrahedron Letters*, 1990, **31**, 3097-3100.

79. Barton D.H.R., Lee K.W., Mehl W., Ozbalik N. Zhang L., Functionalisation of Saturated Hydrocarbons. Part XVII.[1] Reactivity of Carbon-Carbon Double Bonds, *Tetrahedron*, 1990, **46**, 3753-3768.

80. Barton D.H.R., Halley F., Ozbalik N. & Young E., On the Mechanism of the Gif-Orsay Systems for the Selective Substitution of Saturated Hydrocarbons, *New J. Chem.*, 1989, **13**, 177-182.

81. Barton D.H.R., Boivin J., Motherwell W.B., Ozbalik N. & Schwartzentruber K.M., Functionalisation of Saturated Hydrocarbons. Part V[1]. Studies of the Catalytic Gif System for Oxidation with Molecular Oxygen and a Working Hypothesis on the Mechanism, *New J. Chem.*, 1986, **10**, 387-398.

82. Barton D.H.R., Csuhai E., Doller D. & Geletti Y.V., The Functionalisation of Saturated Hydrocarbons. Part XIX^{+}. Oxidation of Alkanes by H_2O_2 in Pyridine Catalysed by Copper(II) Complexes. A Gif-Type Reaction, *Tetrahedron*, 1991, **47**, 6561-6570.

83. Barton D.H.R., Beviere S.D., Chavasiri W., Csuhai E. & Doller D., The Functionalisation of Saturated Hydrocarbons. Part XXI^{+}. The Fe(III)-Catalysed and the Cu(II)-Catalysed Oxidation of Saturated Hydrocarbons by Hydrogen Peroxide: A Comparative Study, *Tetrahedron*, 1992, **48**, 2895-2910.

84. Barton D.H.R. & Chavasiri W., The Functionalisation of Saturated Hydrocarbons. Part 24.$^{+}$ The Use of *tert*-Butyl Hydroperoxide: GoAgg^{IV} and GoAgg^{V}, *Tetrahedron*, 1994, **50**, 19-30.

85. Barton D.H.R., Beviere S.D. & Chavasiri W., The Functionalisation of Saturated Hydrocarbons. Part 25.$^{+}$ Ionic Substitution Reactions in GoAgg^{IV} Chemistry: The Formation of Carbon-Halogen Bonds, *Tetrahedron*, 1994, **50**, 31-46.

86. Barton D.H.R. & Chavasiri W., The Functionalisation of Saturated Hydrocarbons. Part 26.[+] Ionic Substitution Reactions in $GoAgg^{IV}$ Chemistry: The Construction of C-N, C-S, and C-C Bonds, *Tetrahedron*, 1994, **50**, 47-60.

87. Barton D.H.R. & Wang T-L., The Selective Functionalisation of Saturated Hydrocarbons. Part 28[1]. The Activation of Benzylic Methylene Groups Under $GoAgg^{IV}$ and $GoAgg^{V}$ Conditions, *Tetrahedron*, 1994, **50**, 1011-1032.

88. Barton D.H.R., Boivin J., Schwartzentruber K., Ozbalik N., Gaudin D. & Jankowski K., GC-MS Study of Gif-Oxidation System. GC-MS Contribution to Elucidation of Gif-Oxidation Mechanism on the Formation of Bipyridines and Coupled Pyridines, *Spectroscopy Letters*, 1987, **20**, 963-981.

89. Vella P.A. & Munder J.A., Toxic Pollutant Destruction. Comparison of the Oxidants Potassium Permanganate, Fenton's Reagent, and Chlorine Dioxide on the Toxicity of Substituted Phenols, *ACS Symposium Series*, 1993, **518**, 85-105.

90. Jackman A.P. & Powell R.L., Hazardous Waste Treatment Technologies, Noyes Publications, 1991, 214-276.

91. Ledon H., Why not Ozone?, pp 603-610, in Dioxygen Activation and Homogeneous Catalytic Oxidation, edited by Simandi L.I., Elsevier Science Publishers, 1991.

92. Andreozzi R., Insola A., Caprio V. & D'Amore M.G., Ozonation of Pyridine in Aqueous Solution: Mechanistic and Kinetic Aspects, *Water Research*, 1991, **25**, 655-659.

93. Hoigne J. & Bader H., The Role of Hydroxyl Radical Reactions in Ozonation Processes in Aqueous Solutions, *Water Research*, 1976, **10**, 377-386.

94. Zheng Y., Hill D.O. & Kuo C.H., Destruction of Cresols by Chemical Oxidation, *J. Hazardous Materials*, 1993, **34**, 245-260.

95. Barrow G.M., Physical Chemistry, McGraw-Hill International Editions, Fifth Edition, chapter 18, pp 691.

96. Mishara V.S., Joshi J.B. & Mahajani V.V., Kinetics of Wet Air Oxidation of Diethanolamine and Morpholine, *Water Research*, 1994, **28**, 1601-1608.

97. Li L., Chen P. & Gloyna E.F., Generalised Kinetic Model For Wet Oxidation of Organic Compounds, *J. AIChE.*, 1991, **37**, 1687-1697.

98. Kawabata N. & Urano H., Improvement of Biodegradability of Organic Compounds by Wet Oxidation, *Memoirs of the Faculty of Eng. and Design*, 1985, **34**, 64-71.

99. Pelizzari E.D., Castillo N.P., Willis S., Smith D. & Bursey J.T., Measurement of Organic Pollutants in Water and Waste Water, ASTM STP 686, American Society for Testing and Materials, Philadelphia 1979, pp 256-274.

Chapter 2

The Oxidation of 2-, 3-, and 4-Methylpyridines under Simulated WAO Conditions

CHAPTER 2 - The Oxidation of 2-, 3-, and 4-Methylpyridines under Simulated Wet Air Oxidation (WAO) Conditions

The oxidation of 2-, 3-, and 4-methylpyridines was carried out under WAO conditions that were simulated by using a laboratory autoclave, both in the absence and presence of catalysts. All of the methylpyridines were supplied by Aldrich.

2.1. Experimental Conditions

Samples of 2-, 3-, and 4-methylpyridines were submitted to Leigh Environmental where they were subjected to WAO using a laboratory autoclave. The autoclave oxidation reactions were carried out by John Matthews at Leigh. The autoclave simulated those conditions that Leigh Environmental uses on site for the destruction of organic waste by the WAO process.

2.1.1.i) Uncatalysed Autoclave Conditions

An aqueous solution of each of the methylpyridines (0.54 mol dm^{-3}, 1 dm^3) was heated to an operating temperature of 250°C over a 1 hour period under an air pressure of 250 atmospheres. The autoclave was then maintained under these conditions for 2 hours and the reaction mixture was stirred. The pH of the oxidation reaction mixture was adjusted to an acidic pH by the addition of dilute sulphuric acid (1 mol dm^{-3}), and it was maintained in the region of 3.5-5.5 during the course of the reaction.

Samples of the aqueous mixture were taken at designated time intervals during the reaction. The initial reaction time, T_0, was the time at which the reaction mixture reached the desired operating temperature of 250°C. Samples were then taken at T_1, T_2, T_3, and T_4. At T_1, the reaction had been held at 250°C for 30 minutes, T_2 for a further half hour and so on.

2.1.1.ii) Catalysed Autoclave Conditions

Various individual catalysts have been used in the catalysed autoclave oxidation of 2-, 3-, and 4-methylpyridines, following suggestions regarding the effectiveness of certain systems in the WAO of organic compounds in water[1]. They included the following:-

Iron(II) sulphate ($3x10^{-3}$ mol)/hydrogen peroxide

Iron(III) sulphate ($3x10^{-3}$ mol)/hydrogen peroxide

Copper(II) sulphate ($2x10^{-3}$ mol)

Copper(II) sulphate ($3x10^{-3}$ mol)/hydrogen peroxide

Copper(I) chloride ($3x10^{-3}$ mol).

The hydrogen peroxide used in the catalysed autoclave reactions was a 30% w/v solution of the peroxide in water, supplied by Aldrich.

The appropriate amount of metal salt was added to the aqueous mixture containing each of the methylpyridines (0.54 mol dm^{-3}, 1 dm^3). This mixture was then stirred and the pH adjusted to and maintained in the region of 2-5, by the addition of dilute sulphuric acid (1 mol dm^{-3}), during the course of the reaction. The reaction mixture was heated to 250°C over a 1 hour period under an air pressure of 250 atmospheres. The autoclave was then maintained under these conditions for 2 hours and during this time three aliquots of hydrogen peroxide were added. The first aliquot of 30 cm^3 was added after the reaction

mixture had been held at 250°C for 15 minutes; the second aliquot of 30 cm^3 was added after a further 45 minutes and the final aliquot of 35 cm^3 was added after a 75 minute interval had elapsed at a temperature of 250°C. Samples of the reaction mixture were taken at regular time intervals from T_0 to T_4 in the same way as those taken in 2.1.1.i above.

2.1.2 Sample Preparation

A 5 cm^3 aliquot of each of the samples, taken from the above reaction mixtures, was extracted with 4 x 10 cm^3 of either dichloromethane or diethyl ether, after first adjusting the pH of the aqueous mixture to approximately 7, by addition of sodium hydroxide (2 mol dm^{-3}). After drying over magnesium sulphate, the extract was then evaporated to approximately 2 cm^3 under reduced pressure. The dichloromethane/diethyl ether-insoluble products remaining in the aqueous phase were then isolated by removing the excess water on a rotary evaporator. The residue that remained was then extracted with methanol.

2.1.3 Sample Analysis

The literature provides examples of the analysis of organic compounds in water, involving the use of Gas Chromatography (GC) techniques[2], [3] and, in particular, Gas Chromatography-Mass Spectrometry (GC-MS)[4], [5] as the mass spectrometer detector provides a means of "fingerprinting" components of a sample mixture. Since 2-, 3-, and 4-methylpyridines are volatile enough to be detected by GC methods, the analysis of the oxidation products generated from these precursors initially involved GC techniques.

GC-MS - the volatile oxidation products present in both the ethereal and methanolic extracts were analysed using GC-MS techniques. Two instruments were used, during the study, for the analysis of the volatile oxidation products formed in the autoclave reactions. Instrument 1 was a VG Trio 1 quadrupole MS system fitted with a Hewlett Packard 5890 gas chromatograph. This instrument was operated under the following conditions:-

Column	50 m x 0.32 mm i.d. Supelcowax
Carrier gas	Helium
Temperature programme 1	40-250°C at 10°C min^{-1}
Temperature programme 2	70-250°C at 10°C min^{-1}
Injection volume	1 mm^3 splitless
Ion source	Electron impact (70eV)
Source current	150 μA
Source temperature	200°C
Scan rate	1 s $scan^{-1}$
Scan range	20-300 daltons.

Instrument 2 was a VG Micromass double focusing MS system coupled to a Carlo Erba 2150 gas chromatograph. The instrument was operated under the same conditions as instrument 1 above.

However, it could not be assumed that all of the oxidation products generated from the oxidation of each of the methylpyridines would be sufficiently volatile to be detected by GC. A method of analysis was required which would enable the detection of the less volatile components generated from the oxidation of 2, 3-, and 4-methylpyridines i.e. High Performance Liquid Chromatography (HPLC).

HPLC - this method of analysis requires no sample preparation and provides a means of detecting the presence of involatile oxidation products. A literature method[6] was found which described the separation of pyridinecarboxylic acids by HPLC. The separation of 2-, 3-, and 4-pyridinecarboxylic acids was achieved using a Zipax SCZ column and an aqueous mobile phase which contained sodium nitrate (0.1 mol dm^{-3}) and phosphoric acid (0.3 mol dm^{-3}). This is an example of Cationic Exchange Chromatography and the conditions used in the analysis of oxidation products, formed from the autoclave oxidation reactions, were as follows:-

Injection volume	20 μl (fixed injection loop)
Column type	Adsorbosphere SCX 5U
Detector	Philips Pye Unicam LC-UV detector
Data collection	HP340 desk top integrator
Flow rate	1 ml min^{-1}
Wavelength	254 nm
Mobile Phase	50:50 0.1 mol dm^{-3} sodium nitrate/0.3 mol dm^{-3} phosphoric acid (suggested in the literature for this column type)

The suggested mobile phase for this column type contained a mixture of phosphoric acid and sodium nitrate. Since phosphoric acid is not amenable to use in conjunction with a detector such as a mass spectrometer, modification of the suggested mobile phase was required. A method was therefore developed to analyse, by HPLC, the oxidation products formed in the autoclave which could then be used to determine the identity of sample components using techniques such as Liquid Chromatography-Mass Spectrometry (LC-MS).

An aqueous mixture containing ammonium acetate and acetic acid was initially considered as a possible mobile phase which would be suitable for analysis using LC-MS. Pyridine-2-carboxylic acid was then used as a reference compound, in order to compare the retention time of the acid on the column using each of the different mobile phases. This would indicate the effectiveness of the experimental mobile phase at carrying the samples of interest through the column.

Retention time values for pyridine-2-carboxylic acid:-

1) Suggested mobile phase - 5.50 minutes

(50:50 0.1 mol dm^{-3} sodium nitrate/0.3 mol dm^{-3} phosphoric acid)

2) Experimental mobile phase - 5.01 minutes

(50:50 0.1 mol dm^{-3} ammonium acetate/0.1 mol dm^{-3} acetic acid)

Since the retention time of pyridine-2-carboxylic acid is very similar using each of the different mobile phases, the use of the experimental mobile phase was adopted so that methods of separation, developed by HPLC, could be linked to other means of detection other than a UV detector.

2.1.4. Summary

In all of the autoclave oxidation reactions of the methylpyridines, unchanged starting material was observed at the end of the reaction, in different amounts. However, in each case, a variety of oxidation products was observed. Their structures were either identified, or possible structures were suggested from the molecular ions and fragmentation patterns observed in their mass spectra. The oxidation products formed in each reaction are summarised and discussed in the sections that follow in this chapter.

It is also important to note at this point that different GC temperature programme ramps and different instruments were used to investigate these oxidation reactions, and aid in the determination of the nature of the oxidation products formed in each case. Therefore, any differences noted in retention time values for the same compounds have to be considered with reference to the precise analytical conditions used for each of the samples analysed. Hence, more accurate comparisons can be made between the products of oxidation of each of the methylpyridines in the various reactions investigated.

2.2. The Effect of WAO on 2-, 3-, and 4-Methylpyridines

2.2.1. 2-Methylpyridine

a) Analysis by GC-MS

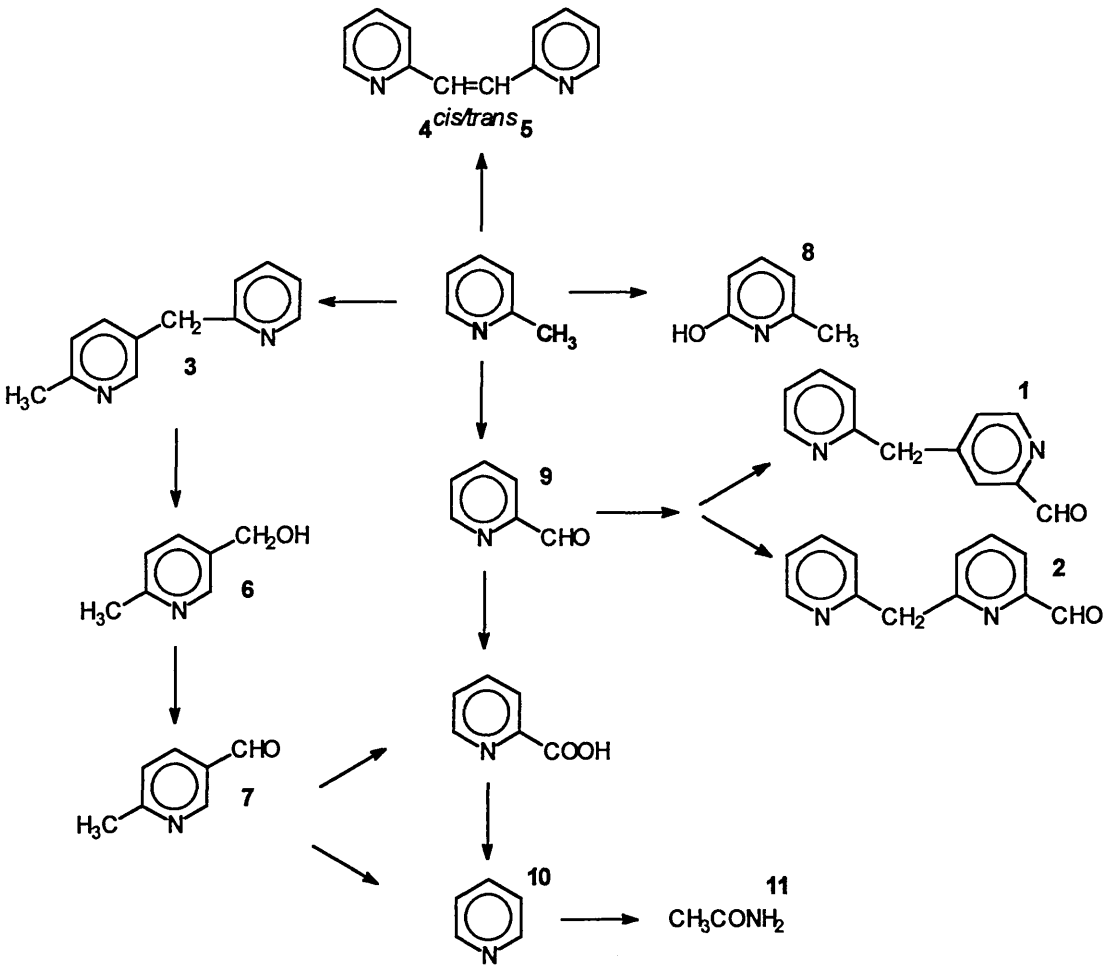
The oxidation of 2-methylpyridine led to the formation of a range of oxidation products - Appendix 1. Some of those species formed have been identified by comparison with authentic standards, and the structures of other species formed have been deduced from mass spectral and retention time (t_R) data. Table 1 summarises those oxidation products formed, that were identified by GC-MS analysis using temperature programme 1 and instrument 1, and the possible pathway for their formation is summarised in Figure 1.

Table 1 Oxidation products arising from the uncatalysed autoclave oxidation of 2- methylpyridine

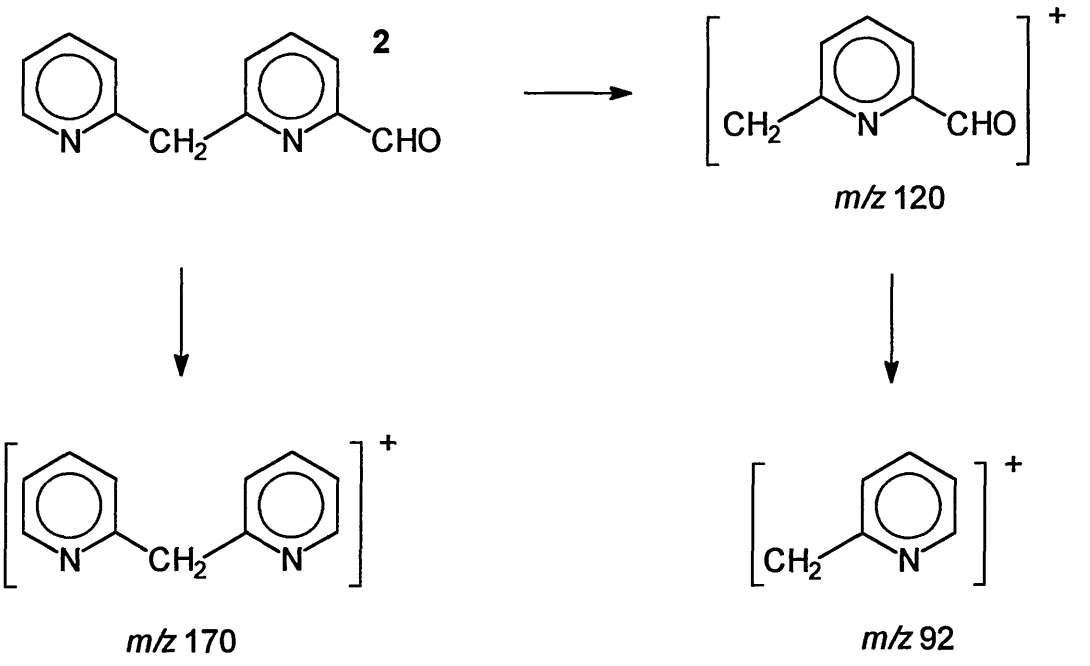
Component	t_R	RMM	Proposed structure
1*	18.55	198	4-(2-pyridylmethyl)pyridine-2-carboxaldehyde
2*	21.48	198	6-(2-pyridylmethyl)pyridine-2-carboxaldehyde
3*	31.01	184	2-methyl-5-(2-pyridylmethyl)pyridine
4	22.18	182	*cis*-1,2-bis-(2-pyridyl)ethene
5	31.12	182	*trans*-1,2-bis-(2-pyridyl)ethene
6*	22.82	123	5-hydroxymethyl-2-methylpyridine
7*	13.68	121	6-methylpyridine-3-carboxaldehyde
8	21.49	109	2-hydroxy-6-methylpyridine
9	13.06	107	pyridine-2-carboxaldehyde
10	7.53	79	pyridine
11	15.61	59	acetamide

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

Figure 1

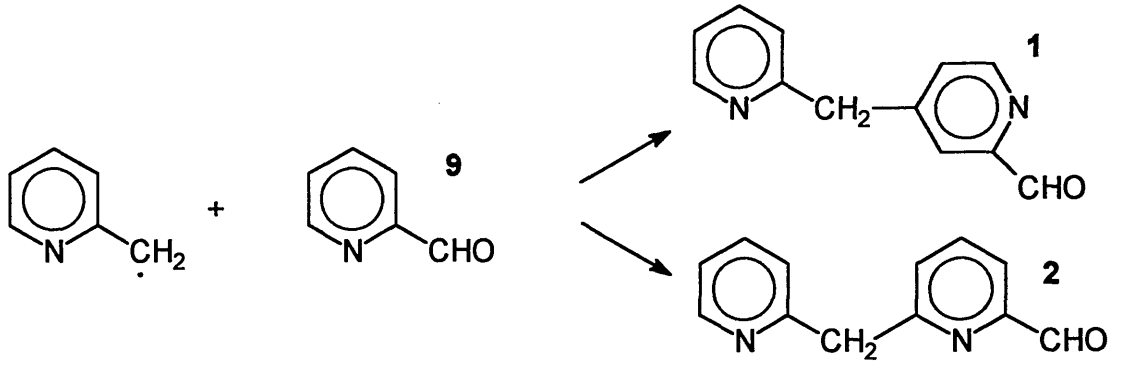


A wide range of oxidation products was observed. Components **1** and **2** were first observed at T_0 but they were destroyed during the oxidation reaction and were not found at T_4. Their structures have still not been identified definitely but their mass spectra were similar to each other in that the same fragment ions were observed in each spectrum, but at different intensities, and both exhibited the same apparent molecular ion of 198. The mass spectrum for component **2** contained stable fragment ions at *m/z* 170, 120, and 92. Therefore its structure was thought to be that of 6-(2-pyridylmethyl)pyridine-2-carboxaldehyde as such a structure could fragment in two ways to give the following stable fragment ions:-



Component **2** would have arisen via a radical substitution reaction, as shown in Scheme 1, occurring between a 2-pyridylmethyl radical and pyridine-2-carboxaldehyde **9** which is itself an observed oxidation product.

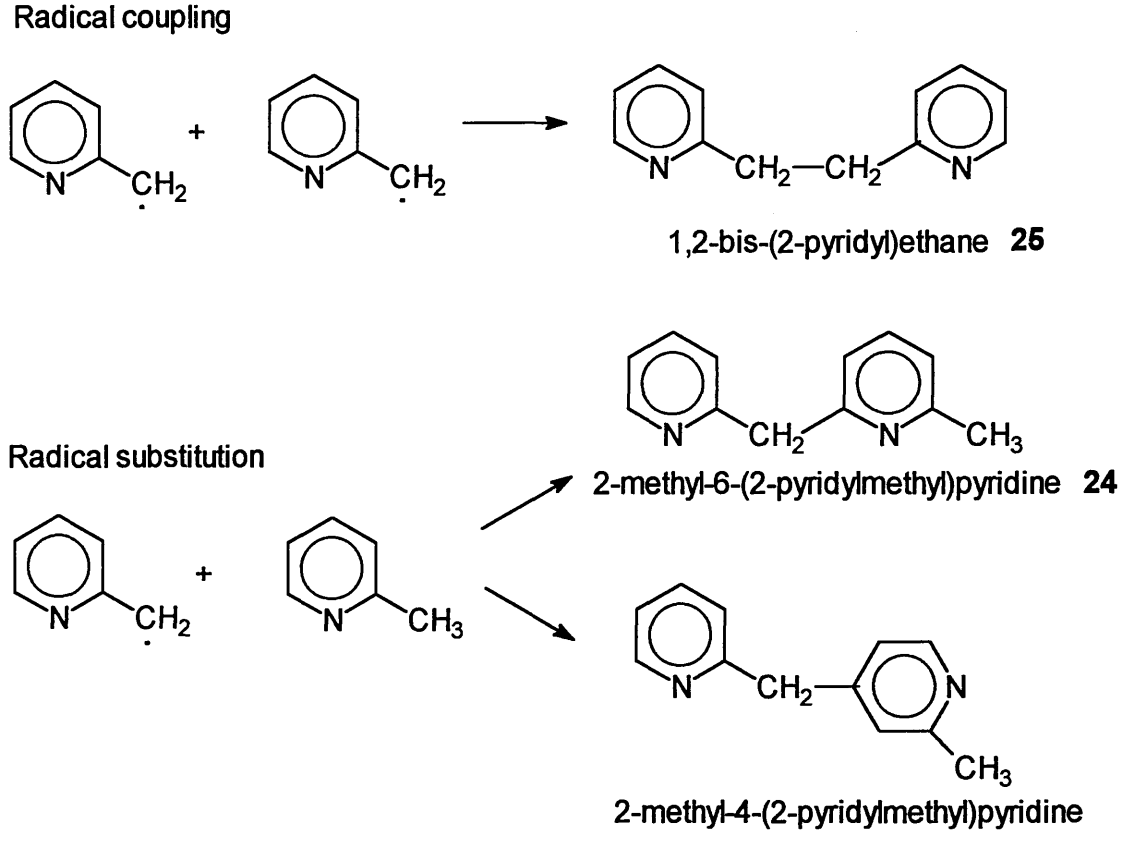
Scheme 1



Scheme 1 also illustrates the formation of component 1, which is thought to be an isomeric form of component 2, due to similarities observed in the fragmentation pattern of each of the mass spectra.

The true identity of component **3** is also unknown, but this is also thought to arise as a result of a radical process. The observation of the apparent molecular ion of 184 implies the formation of a saturated dimeric structure, where either the coupling of two pyridylmethyl radicals has occurred, or a pyridylmethyl radical has undergone substitution in the pyridine ring of the parent substrate, 2-methylpyridine. The relative molecular mass of the product of such radical reactions is 184 and since the WAO process is thought to involve radical reactions[7], then Scheme 2 is a possible scenario.

Scheme 2

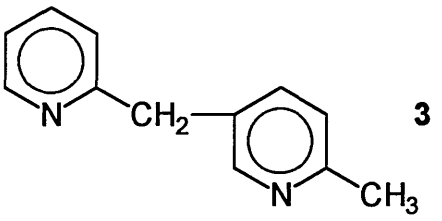


All of the dimeric structures observed in Scheme 2 have been prepared as standard reference compounds and component **3** was not identified as any of them. However, in the above scheme, the radicals have been shown to couple,

or undergo substitution reactions, in ways that are considered to be the most favourable.

It is known that pyridines, along with other nitrogen heterocycles such as quinolines, diazines and imidazoles, undergo reactions with nucleophilic radicals selectively at positions α- and γ- to the nitrogen, resulting in replacement of a hydrogen atom[8]. The radical reactions require an acidic medium as *N*-protonation of the heterocycle is needed, as this promotes reactivity and regioselectivity towards a nucleophilic radical. These radical reactions are termed Minisci reactions. In the case of pyridine as the substrate, control of the reaction with nucleophilic radicals in a regioselective manner is difficult, considering the availability of more than one reactive position. In order to overcome this problem, regarding control of regioselectivity, radical substitution reactions need to be taken to full conversion and control of pH is important.

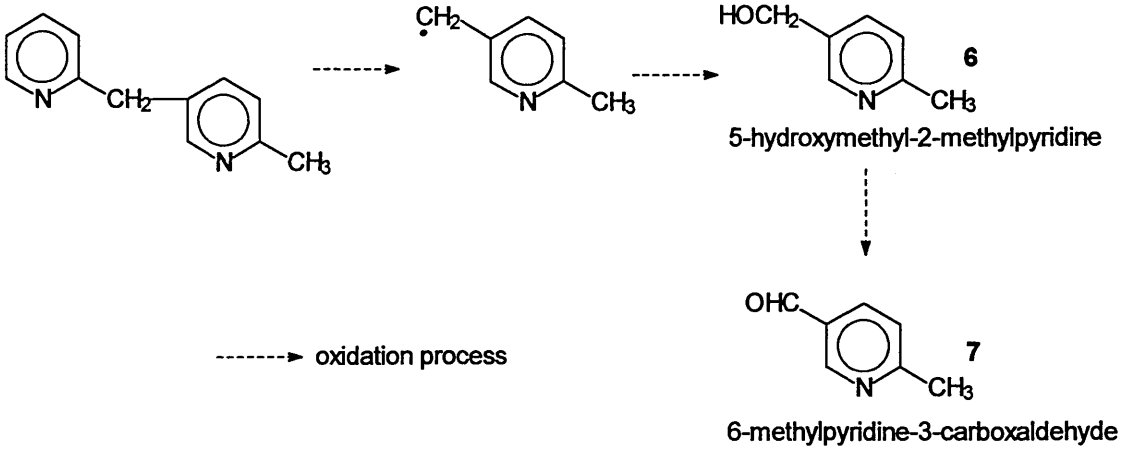
Since the structure of component **3** is not as indicated in Scheme 2, substitution reactions involving the pyridylmethyl radical must have occurred, at the pyridine ring of another methylpyridine molecule, at a position other than α- and γ- to the nitrogen atom. This lack of regioselectivity could be related to the fact that a significant amount of starting material remains at the end of the autoclave oxidation reaction, possibly influencing the radical reactions taking place. Also the pH is not controlled in a precise manner, as the reaction mixtures are only maintained within an acidic range. Therefore, considering steric effects to be the next controlling factor on the structure of component **3**, then a possible structure which would be favoured is 2-methyl-5-(2-pyridylmethyl)pyridine **3**. Although it has not been possible to synthesise this compound as yet, it is this structure which is indicated in Table 1 as a possible oxidation product.



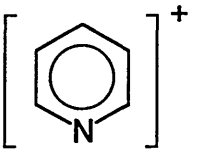
3

Components **6** and **7** have been assigned structures that may have resulted from the oxidation of 2-methyl-5-(2-pyridylmethyl)pyridine **3**. The oxidation of such a dimer would first result in the loss of the pyridine ring and the remaining structure could then undergo oxidation of the alkyl chain to give component **6** followed by further oxidation to give **7** - Scheme 3.

Scheme 3

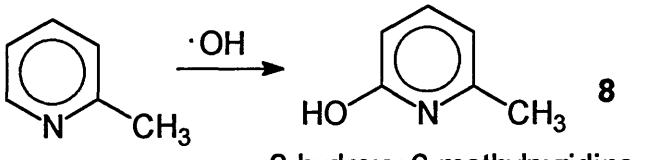


The structures of components **6** and **7** are thought to be very similar as the mass spectra for both structures contains a base peak at *m/z* 79 indicating the formation of the stable ion shown below, forming as a result of loss of the branches on the pyridine ring.



The observation of component **8** was very interesting as this compound compares very well in terms of the mass spectral fragmentation pattern with that of the synthetic standard 2-hydroxy-6-methylpyridine - Appendix 2. The mass spectrum for the standard has a base peak at *m/z* 80, and the apparent molecular ion was observed at *m/z* 109. This is identical with component **8**. The formation of this oxidation product could only have resulted from substitution at the pyridine ring by a hydroxyl radical •OH.

Scheme 4



8

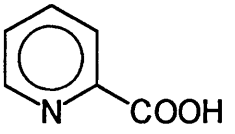
2-hydroxy-6-methylpyridine

Component **9** was identified as pyridine-2-carboxaldehyde by comparison with the authentic standard. This component will have been formed by the oxidation of the methyl group, attached to the ring, in 2-methylpyridine.

The formation of components **10** and **11** was an interesting observation. Both of these components were only observed at T_4, towards the end of the autoclave process. The formation of pyridine **10** was observed in significant amounts whereas the formation of acetamide **11** only occurred on a very small scale. The formation of pyridine from 2-methylpyridine is thought to be a significant observation - see (b) below.

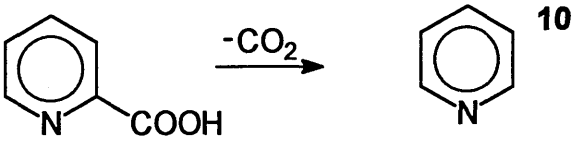
b) Analysis by HPLC

The identification of involatile oxidation products requires the use of HPLC techniques. An expected oxidation product from the oxidation of 2-methylpyridine is the related carboxylic acid shown below.



pyridine-2-carboxylic acid

The autoclave sample, taken from the oxidation reaction at T_4, was analysed using the HPLC method outlined in 2.1.3. The chromatogram that was obtained identified the presence of a mixture of components, the largest of which was unchanged 2-methylpyridine. A large peak was observed at t_R=12.51, but this component has not yet been identified. The presence of pyridine-2-carboxylic acid was not detected. As only the sample taken at T_4 was analysed, the carboxylic acid may have been formed earlier in the oxidation reaction and have undergone subsequent decarboxylation, considering the severity of the conditions imposed in the autoclave. This could account for the formation of pyridine **10** as an oxidation product, detected in the GC-MS analysis of the oxidation products.



None of the various peaks observed in this chromatogram, generated from the oxidation products present at T_4, have been identified. Due to the complexity of the mixture of components observed, the need for a detector such as a mass spectrometer is required in order to enable an attempt at the

identification of possible structures for the various components. Analysis of this reaction mixture has not yet been carried out by HPLC/MS, but it would be possible to use the method developed in section 2.1.3. in such circumstances.

2.2.2. 3-Methylpyridine

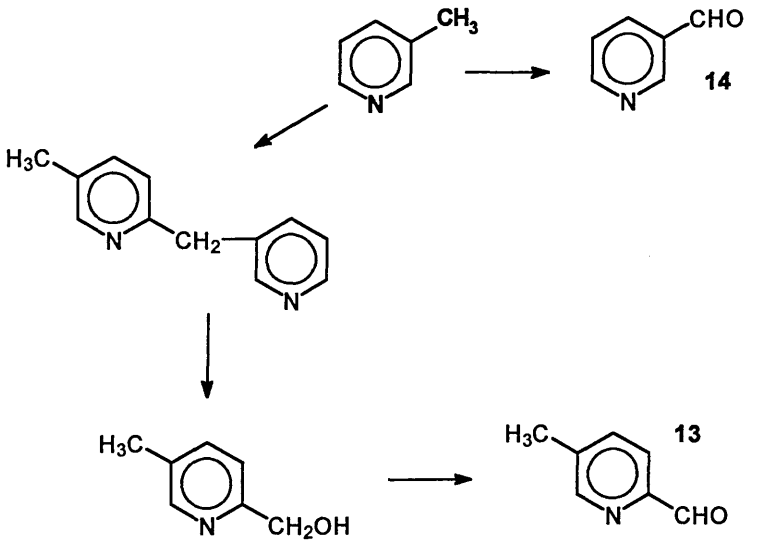
The oxidation products generated from the autoclave oxidation of 3-methylpyridine were analysed using GC-MS techniques which involved the use of instrument 1 and temperature programme 1. In contrast to that of the 2-isomer, the oxidation reaction did not give rise to an extensive array of products. The only significant GC-volatile oxidation product formed was pyridine-3-carboxaldehyde **14**, together with only trace amounts of other oxidation products. They are summarised in Table 2 and the possible pathway for their formation is represented in Figure 2 .

Table 2 Oxidation products arising from the uncatalysed autoclave oxidation of 3-methylpyridine

Component	t_R	RMM	Proposed structure
12	15.07	137	unknown
13*	15.90	121	5-methylpyridine-2-carboxaldehyde
14	14.80	107	pyridine-3-carboxaldehyde

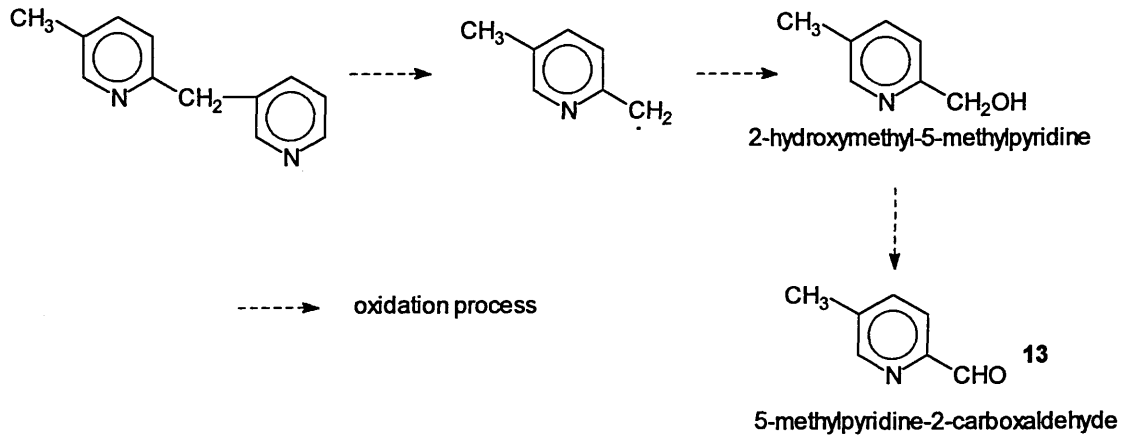
* indicates that proposed structure has not been proved by comparison with the authentic substance

Figure 2

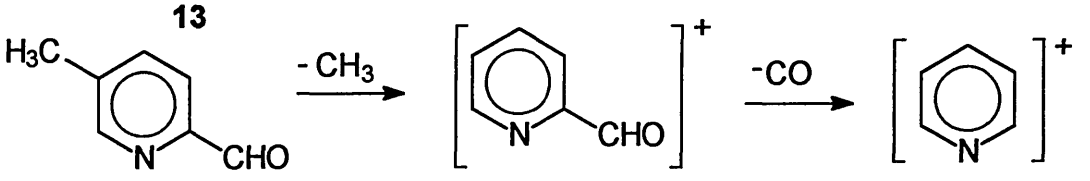


On comparing the reaction stages $T_0 \rightarrow T_4$, the oxidation reaction appeared to have progressed. Evidence for this was provided by the formation of component **14** in larger quantities at T_4 than at T_0, in comparison with the amount of unchanged 3-methylpyridine that remained. The structure of component **13** was deduced by analogy with those observations made in 2.2.1. above for the autoclave oxidation of 2-methylpyridine. Although no dimeric structures were observed as oxidation products in the autoclave oxidation of 3-methylpyridine, this is not necessarily evidence that they were not formed at some stage. Component **13** was only observed in trace amounts in relation to the amount of pyridine-3-carboxaldehyde that was formed. Therefore trace amounts of dimeric structures may have been formed, in a similar fashion to either the radical coupling or radical substitution reactions shown in Scheme 2, and destroyed immediately in the oxidation reaction. Component **13** could have been formed from the oxidation of a dimeric structure such as 3-methyl-6-(3-pyridylmethyl)pyridine, via the initial formation of 2-hydroxymethyl-5-methylpyridine - Scheme 5.

Scheme 5



The mass spectrum generated for component **13** contains stable fragment ions at *m/z* 106 and *m/z* 78. Such stable fragment ions can be accounted for by considering the fragmentation of **13**.



The structure of component **12** is unknown.

2.2.3. 4-Methylpyridine

The autoclave oxidation of 4-methylpyridine produced a range of oxidation products very similar to that observed in 2.2.1. for the autoclave oxidation of 2-methylpyridine. The compounds formed have been analysed using GC-MS techniques involving the use of instrument 1 and temperature programme 1, and they have then been identified by comparison with standards, where possible. The observations made are summarised in Table 3 and the possible

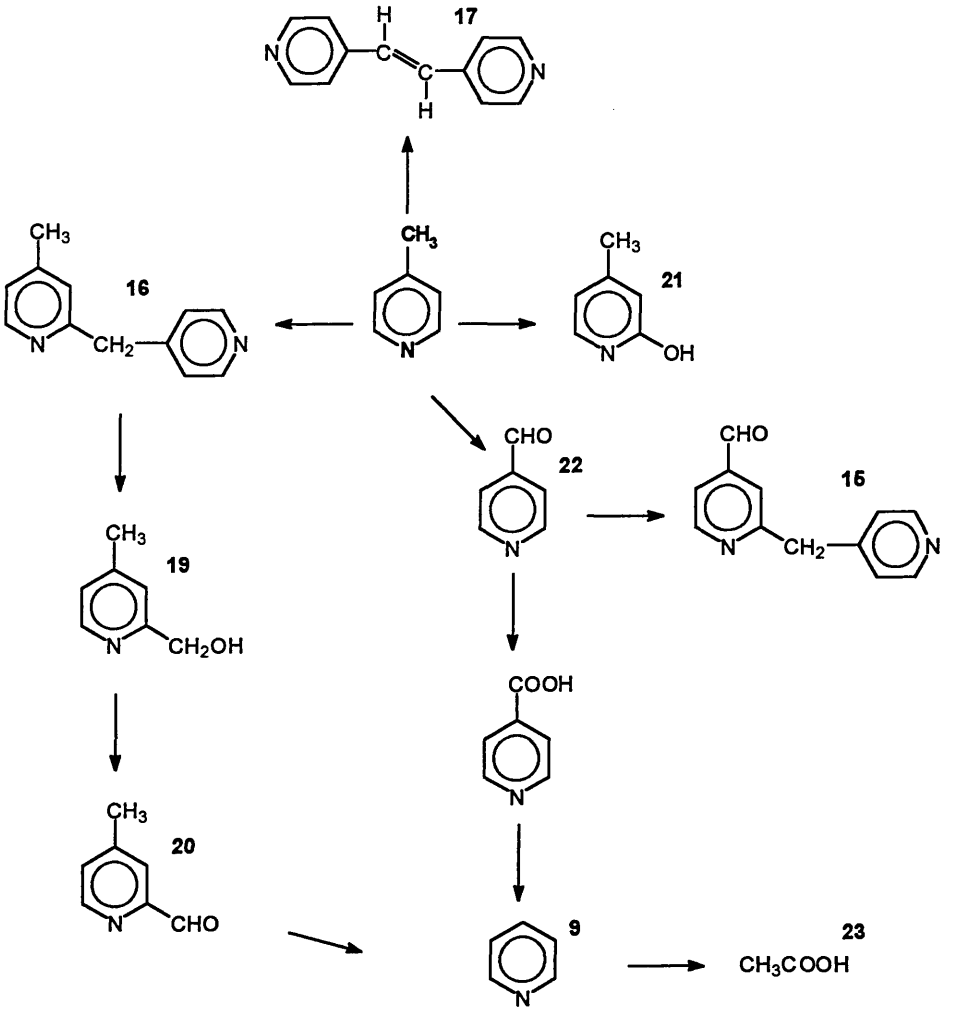
pathway for the formation of each of the oxidation products is represented in Figure 3.

Table 3 Oxidation products arising from the uncatalysed autoclave oxidation of 4-methylpyridine

Component	t_R	RMM	Proposed structure
15*	29.39	198	2-(4-pyridylmethyl)pyridine-4-carboxaldehyde
16*	27.06	184	4-methyl-2-(4-pyridylmethyl)pyridine
17	35.20	182	*trans*-1,2-bis(4-pyridyl)ethene
18	14.98	137	unknown
19*	26.25	123	2-hydroxymethyl-4-methylpyridine
20*	15.84	121	4-methylpyridine-2-carboxaldehyde
21	24.28	109	2-hydroxy-4-methylpyridine
22	14.06	107	pyridine-4-carboxaldehyde
10	7.13	79	pyridine
23	10.84	60	acetic acid

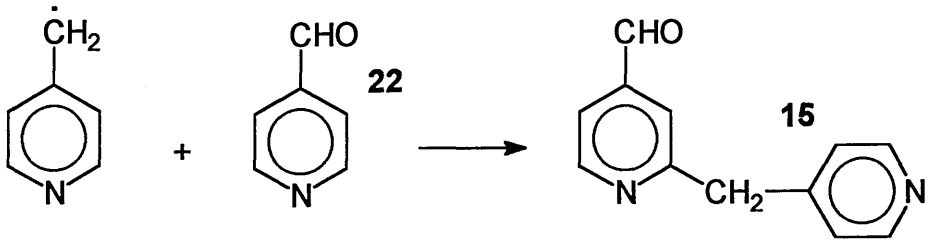
*indicates that proposed structure has not been proved by comparison with the authentic substance

Figure 3

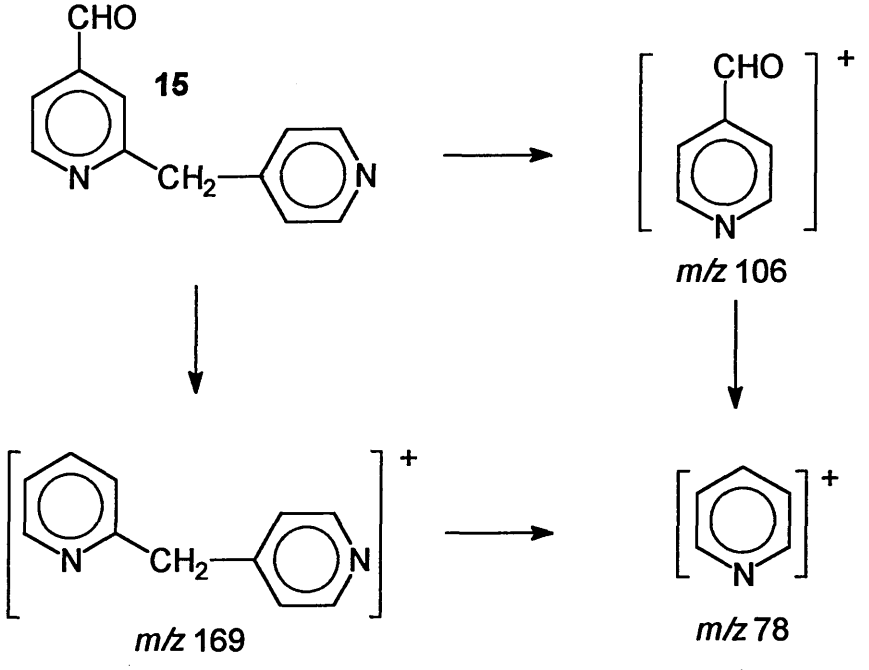


The structure of component **15** has not been identified by comparison with an authentic substance. However, its structure is thought to have been formed as a result of a radical substitution reaction between a 4-pyridylmethyl radical and pyridine-4-carboxaldehyde **22** which is itself an observed oxidation product - Scheme 6.

Scheme 6



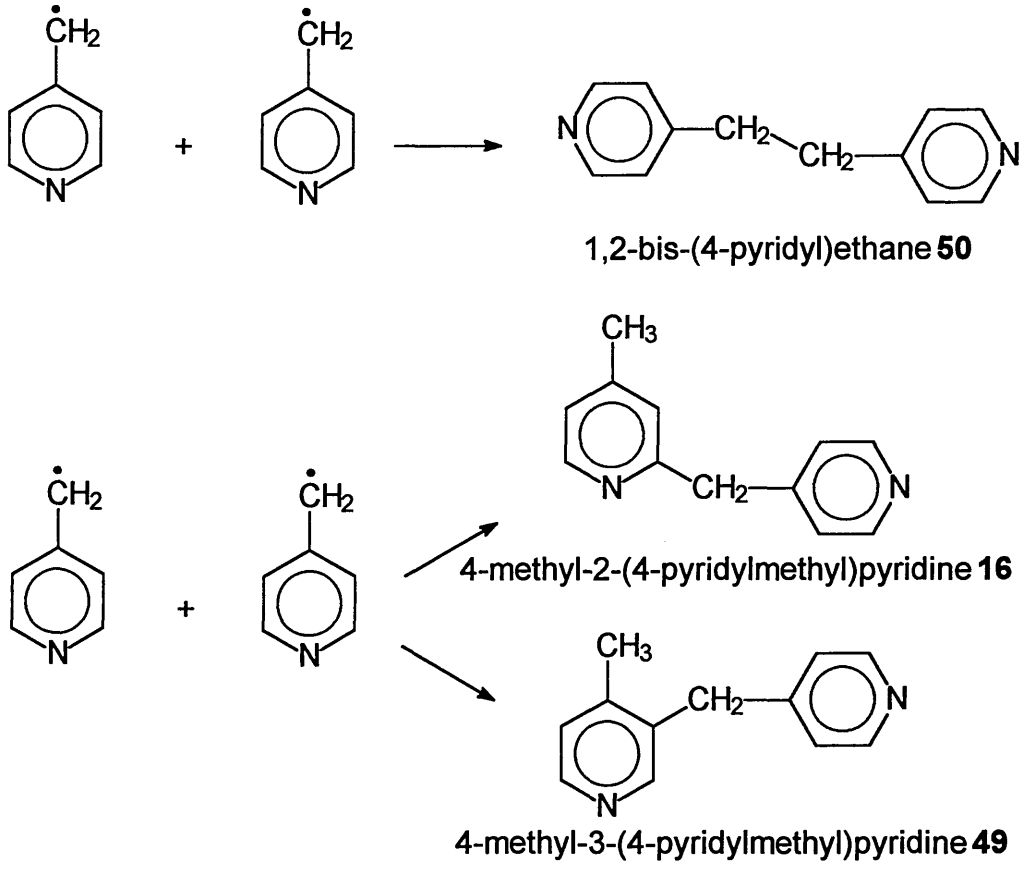
This structure was suggested for component 15 as the mass spectrum of this component exhibited stable fragment ions at m/z 169, 106, and 78.



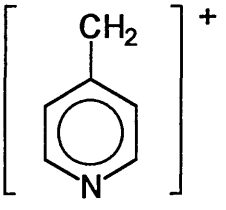
The structure of component **16** is thought to be a saturated dimer due to the observation of the apparent molecular ion at *m/z* 184 in its mass spectrum, and its formation could have occurred by either the coupling of 4-pyridylmethyl radicals or radical substitution by the latter with 4-methylpyridine. The mechanism of the formation of **16** would be similar to those mechanisms seen in Scheme 2, which were involved with the formation of saturated dimeric structures in the autoclave oxidation of 2-methylpyridine. The dimeric

structures that are possible from the autoclave oxidation of 4-methylpyridine are shown below - Scheme 7.

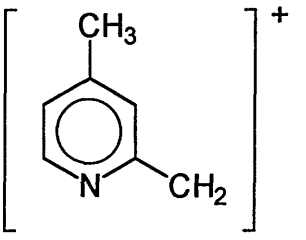
Scheme 7



Component **16** is not 1,2-bis-(4-pyridyl)ethane since, when compared with the authentic standard, the mass spectral fragmentation patterns and t_R are different - Appendix 3. The standard exhibits a base peak at *m/z* 92 which could correspond to the formation of the following stable fragment

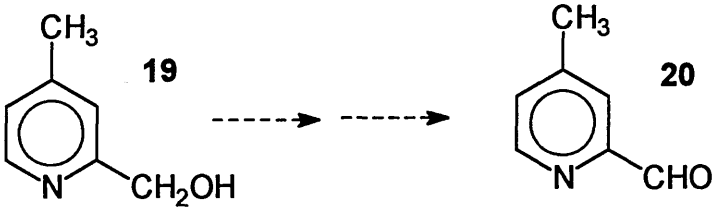


However, component **16** generated a base peak at *m/z* 106, indicating the possible formation of the fragment ion shown below.



Therefore, the structure of **16** is likely to be one of the other possible isomeric dimeric structures. Due to the expected regioselective attack at the pyridine ring occurring at the α- position to the nitrogen atom, the formation of 4-methyl-2-(4-pyridylmethyl)pyridine is indicated in Table 3. This structure appeared to be fairly resistant to oxidation as its presence was still detected in the reaction mixture at T_4.

Components **19** and **20** are thought to be generated from the destructive oxidation of 4-methyl-2-(4-pyridylmethyl)pyridine **16**, the saturated dimeric structure. The course of destruction is similar to that seen in Scheme 3, and therefore the formation of 2-hydroxymethyl-4-methylpyridine **19** would occur first, followed by the formation of 4-methylpyridine-2-carboxaldehyde **20**, after a pyridine ring has been lost from component **16**.

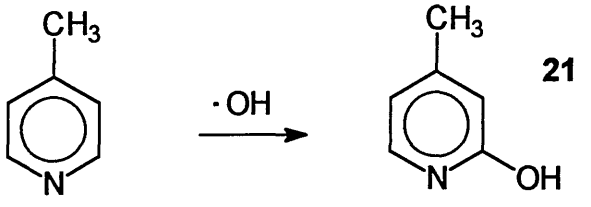


The mass spectrum of component **20** exhibits stable fragment ions at *m/z* 106 and 78 indicating loss of the methyl group followed by loss of -CO, and an apparent molecular ion at *m/z* 121. Component **19** also exhibits similar

fragment ions, but the stability of these ions is different as they occur with different intensities relative to the intensity of the apparent molecular ion which is observed at m/z 123.

The mass spectrum of component **21** has been compared with standards. The mass spectra of authentic 2-hydroxy-6-methylpyridine and 3-hydroxy-6-methylpyridine both exhibit a stable fragment ion at *m/z* 80, and the stable fragment in the region of the molecular ion is *m/z* 109. The mass spectrum for component **21** also exhibits two stable fragment peaks at *m/z* 80 and *m/z* 109 therefore indicating that **21** has also been formed as a result of substitution at the pyridine ring by a hydroxyl radical. Scheme 8 shows that **21** has been formed as a result of substitution by a hydroxyl radical at the α- position to the nitrogen, which is the expected product, as this is the more reactive site in comparison with the available β- site.

Scheme 8



2-hydroxy-4-methylpyridine

Component **22** is pyridine-4-carboxaldehyde which is an expected oxidation intermediate, observed at T_0, as the oxidation of the methyl group would be relatively easy under such conditions imposed in the autoclave. The formation of pyridine, **10**, could have been formed from either the continued oxidative destruction of component **20** by loss of both the methyl and aldehyde groups, or the decarboxylation of the appropriate carboxylic acid, as illustrated in the autoclave oxidation of 2-methylpyridine. The formation of acetic acid,

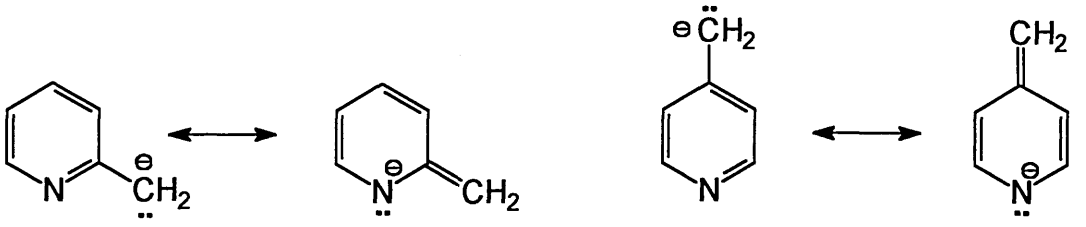
component **23**, is also expected as WAO conditions are known to generate this substance from organic compounds[7], [9].

The identity of component **18** is unknown but the mass spectrum and retention time of this component match that of component **12**, formed in the oxidation of 3-methylpyridine. Therefore, it appears that this component is an impurity in both reactions and is not related to the oxidation of each of the methylpyridines.

2.2.4. Summary

The autoclave oxidation, simulating WAO conditions, of both 2- and 4-methylpyridine generated an extensive range of oxidation products. In both cases there is evidence to support the involvement of radical chemistry, leading to the formation of dimeric structures and compounds such as 2-hydroxy-6-methylpyridine **8**. However, the formation of pyridine-4-carboxaldehyde, for example, also indicates that some other oxidation reaction has taken place. There is also evidence of destructive oxidation, as pyridine and acetamide are formed in the oxidation of 2-methylpyridine, and pyridine and acetic acid in the oxidation of 4-methylpyridine.

In contrast, under WAO conditions, 3-methylpyridine appears to undergo much less change, which is consistent with the general lower reactivity of the 3-isomer relative to 2-, and 4-methylpyridines. This may be related to the ease of deprotonation of the alkyl group that is attached to the ring[8]. The enhanced ease of deprotonation of the 2- and 4-isomers is due to the resonance stabilisation of the anion generated involving the ring nitrogen. This is not possible with the 3-isomer.



2.3. The Effect of Catalysed WAO on 2-, 3-, and 4-Methylpyridines

2.3.1. The use of iron-containing catalysts

The autoclave oxidation of 2-, 3-, and 4-methylpyridines was carried out in the presence of two types of iron-containing catalysts. The first was a mixture of iron(II) sulphate and hydrogen peroxide i.e. Fenton's reagent[10], and the second was a mixture of iron(III) sulphate and hydrogen peroxide i.e. Barton's GoAgg (II) system[11].

2.3.1.1. 2-Methylpyridine

An extensive array of oxidation products were formed from the use of both catalysts and they were analysed using GC-MS techniques, involving the use of instrument 1 and temperature programme 2. The observations made are summarised in Table 4 and a possible pathway for the formation of the oxidation products generated is shown in Figure 4.

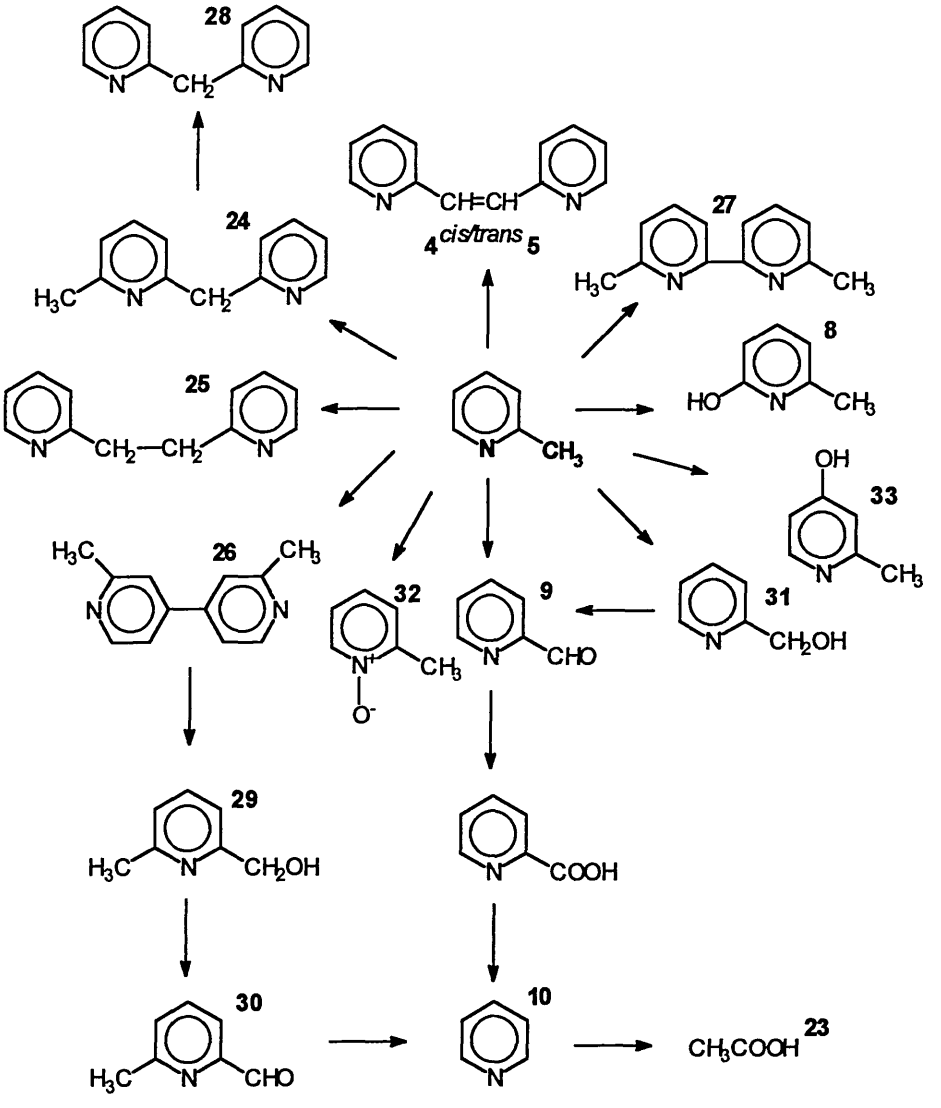
Table 4 Oxidation products arising from the iron catalysed autoclave oxidation of 2-methylpyridine

Component	t_R		RMM	Proposed structure
	Fe(II)	Fe(III)		
24	-	18.50	184	2-methyl-6-(2-pyridylmethyl)pyridine
25	-	19.32	184	1,2-bis-(2-pyridyl)ethane
26*	-	19.98	184	2,2'-dimethyl-4,4'-bipyridine
27*	-	20.57	184	2,2'-dimethyl-6,6'-bipyridine
4	-	21.49	182	*cis*-1,2-bis-(2-pyridyl)ethene
5	27.79	26.09	182	*trans*-1,2-bis-(2-pyridyl)ethene
28*	-	20.13	170	2-(2-pyridylmethyl) pyridine
29*	18.50	18.76	123	2-hydroxymethyl-6-methylpyridine
30*	10.96	9.96	121	2-methylpyridine-6-carboxaldehyde
31	-	13.16	109	2-hydroxymethylpyridine
32	-	16.50	109	2-methylpyridine-N-oxide
33*	-	17.55	109	4-hydroxy-2-methylpyridine
8	19.96	18.79	109	2-hydroxy-6-methylpyridine

9	10.30	9.35	107	pyridine-2-carboxaldehyde
10	4.73	-	79	pyridine
23	8.58	7.74	60	acetic acid

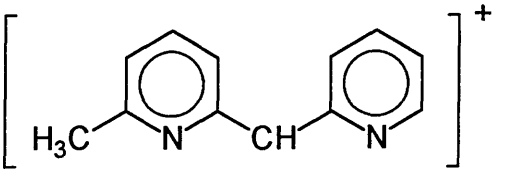
*indicates that proposed structure has not been proved by comparison with the authentic substance

Figure 4

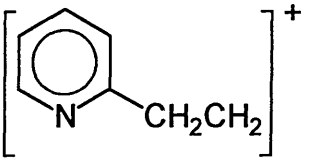


Components **24**, **25**, **26**, and **27** are only produced in the oxidation of 2-methylpyridine where iron(III) is used as the catalyst, and their formation provides evidence to support the fact that some form of radical chemistry is

taking place. Components **24** and **25** have been identified by comparison with standard materials - Appendix 4. The standard 2-methyl-6-(2-pyridylmethyl)pyridine gives a mass spectrum which has a base peak at *m/z* 183 indicating the possible formation of the stable ion shown below.



The other fragment ions are very small and this spectrum compares well with that of component **24**, along with t_R. The formation of **24** could only arise as a result of radical substitution of a pyridylmethyl radical at the pyridine ring of 2-methylpyridine - Scheme 2. The formation of **25** also occurs as a result of a radical reaction, involving the coupling of radicals, as shown in Scheme 2. The standard 1,2-bis-(2-pyridyl)ethane gives a mass spectrum that shows a base peak at *m/z* 106 due to the formation of the stable fragment ion shown below.

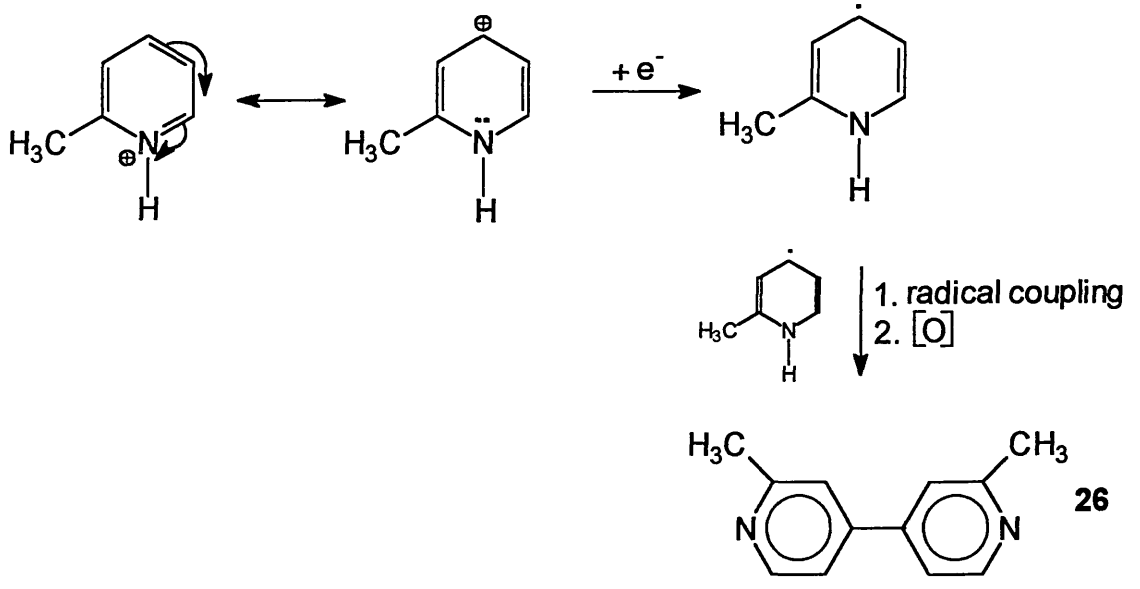


This compares well with the mass spectrum generated by component **25**.

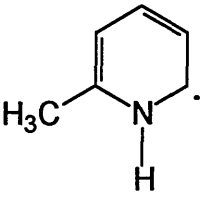
Several other oxidation products were also observed that all possessed the same apparent molecular ion at *m/z* 184. From comparison with those standards prepared that have a relative molecular mass of 184 indicated in Scheme 2, no positive identification was possible on comparison of **26** and **27** with them. However, the mass spectrum for the standard 4,4'-dimethyl-2,2'-bipyridine was obtained and the base peak was found at *m/z* 184. No other stable fragments were observed in the spectrum, and this compares well with

those spectra obtained for components **26** and **27** - Appendix 5. The formation of 2,2'-dimethyl-4,4'-bipyridine **26** and 2,2'-dimethyl-6,6'-bipyridine **27** could only occur as a result of initial radical formation as shown in Scheme 8 in Chapter 1. The coupling of the methylpyridyl radicals could then occur in a similar fashion to that shown in Chapter 1, Scheme 9, to produce the reaction shown in Scheme 9 here, which represents the formation of 2,2'-dimethyl-4,4'-bipyridine **26**.

Scheme 9



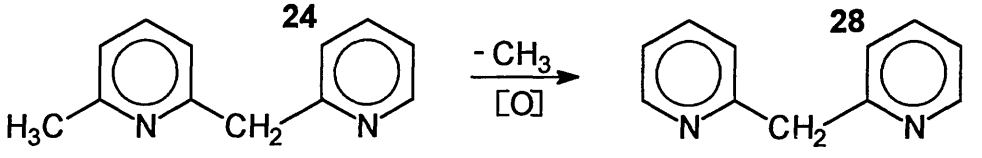
The 2-methylpyridine would be protonated under the autoclave oxidising conditions used and such a mechanism for the coupling of pyridine rings in this manner was suggested by Barton et al[12]. By a similar mechanism to that shown in Scheme 9, it is also possible to generate component **27** via the formation of the radical shown below.



This range of dimeric structures was first observed at T_1 but these compounds did not appear to be very stable under the oxidising conditions used, as they were not observed at the end of the reaction at T_4.

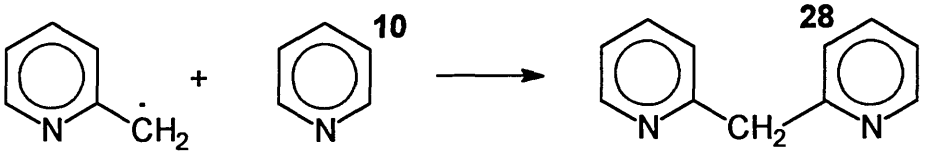
Component **28** is thought to be formed from the oxidation of either 2-methyl-6-(2-pyridylmethyl)pyridine **24**, or any of the other saturated dimeric structures observed as oxidation products by loss of a methyl group. Scheme 10 illustrates the formation of component **28** by loss of a methyl group from component **24**.

Scheme 10



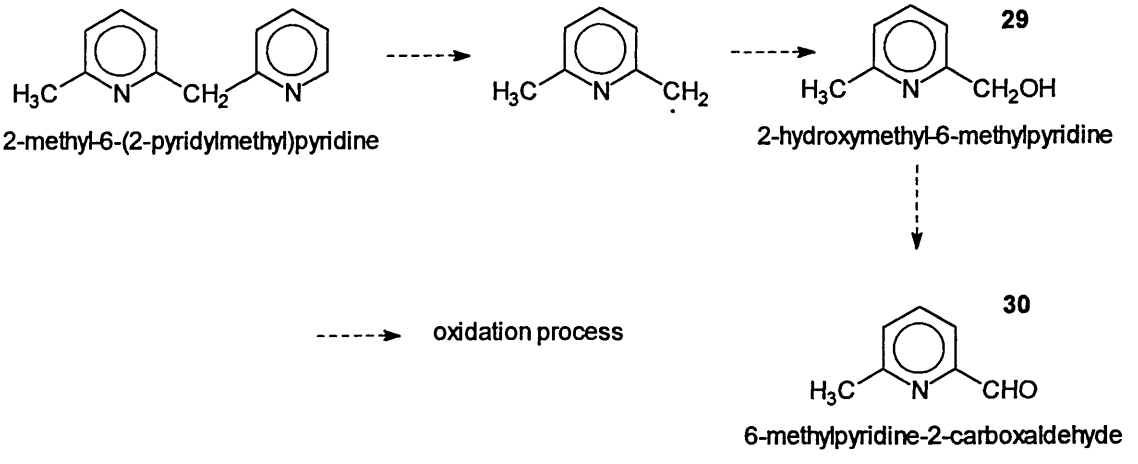
The oxidation of components **26** and **27** may also have occurred in a similar fashion, but only one oxidation product exhibiting an apparent molecular ion at *m/z* 170 was observed and that was represented as component **28**. Component **28** could also have been formed via a radical substitution reaction occurring between a pyridylmethyl radical and pyridine which is itself observed as an oxidation product - Scheme 10a.

Scheme 10a



Components **4** and **5** in Table 7 have been identified as the *cis* and *trans* forms of 1,2-bis-(2-pyridyl)ethene, and the *trans* form of this unsaturated dimeric structure was observed in the oxidation of 2-methylpyridine in the presence of both iron containing catalysts. Components **29** and **30** were also identified in both of the iron-catalysed oxidation reactions considered here. The structures of these components have only been tentatively assigned as 2-hydroxymethyl-6-methylpyridine **29** and 6-methylpyridine-2-carboxaldehyde **30**, respectively. They are thought to be formed as a result of the oxidation of a dimeric structure that was observed at T_1 in the iron(III) catalysed reaction according to Scheme 11 below.

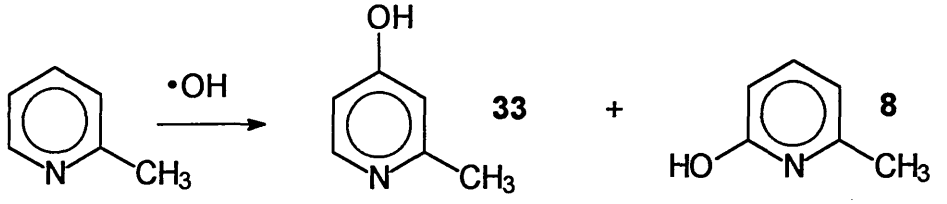
Scheme 11



Although no dimeric structures were observed as oxidation products in the iron(II) catalysed oxidation of 2-methylpyridine, this is not conclusive evidence that they were not formed. It may have been that, following their formation, they were destroyed quickly by the oxidising conditions imposed to give rise to the formation of first component **29** and then **30**, as both of these components were observed at T_1.

Various components all exhibiting the same apparent molecular ion of 109 were observed as oxidation products. For the iron(III)-catalysed oxidation reaction, both 2-hydroxymethylpyridine **31** and 2-methylpyridine-N-oxide **32** were identified as oxidation products. Components **33** and **8** also exhibited apparent molecular ions at *m/z* 109 and they have been assigned structures that result from substitution occurring at the pyridine ring by a hydroxyl radical. Component **8** has been identified as 2-hydroxy-6-methylpyridine by comparison with the standard material. There were similarities in the mass spectra of components **33** and **8** as both exhibited a stable fragment ion at *m/z* 80 and a base peak at *m/z* 109 - Appendix 2 & 6. Therefore, the structure of **33** is thought to be an isomer of **8** formed via a similar radical reaction - Scheme 12.

Scheme 12



Component **8** was observed in both of the iron-catalysed oxidation reactions indicating the presence of hydroxyl radicals in both systems.

Other oxidation products observed included pyridine-2-carboxaldehyde **9** and acetic acid **23** and they were identified in both of the iron-catalysed reactions. Component **10**, identified as pyridine, was only observed in the iron(II) catalysed oxidation reaction. Its formation could have occurred via decarboxylation of pyridine-2-carboxylic acid, which is itself an expected

oxidation product, as in the uncatalysed autoclave oxidation of 2-methylpyridine discussed earlier in this chapter.

2.3.1.2. 3-Methylpyridine

The autoclave oxidation of 3-methylpyridine was carried out in the presence of both iron(II)- and iron(III)-containing catalysts. The oxidation products were analysed using GC-MS techniques which involved the use of instrument 1 and temperature programme 1 for the iron(II)-catalysed reactions and temperature programme 2 for the iron(III)-catalysed reactions. The structures of the products that have been identified, together with those whose identity is, as yet, uncertain are summarised in Table 5, and Figure 5 illustrates a possible pathway for the formation of the oxidation products indicated in the table below.

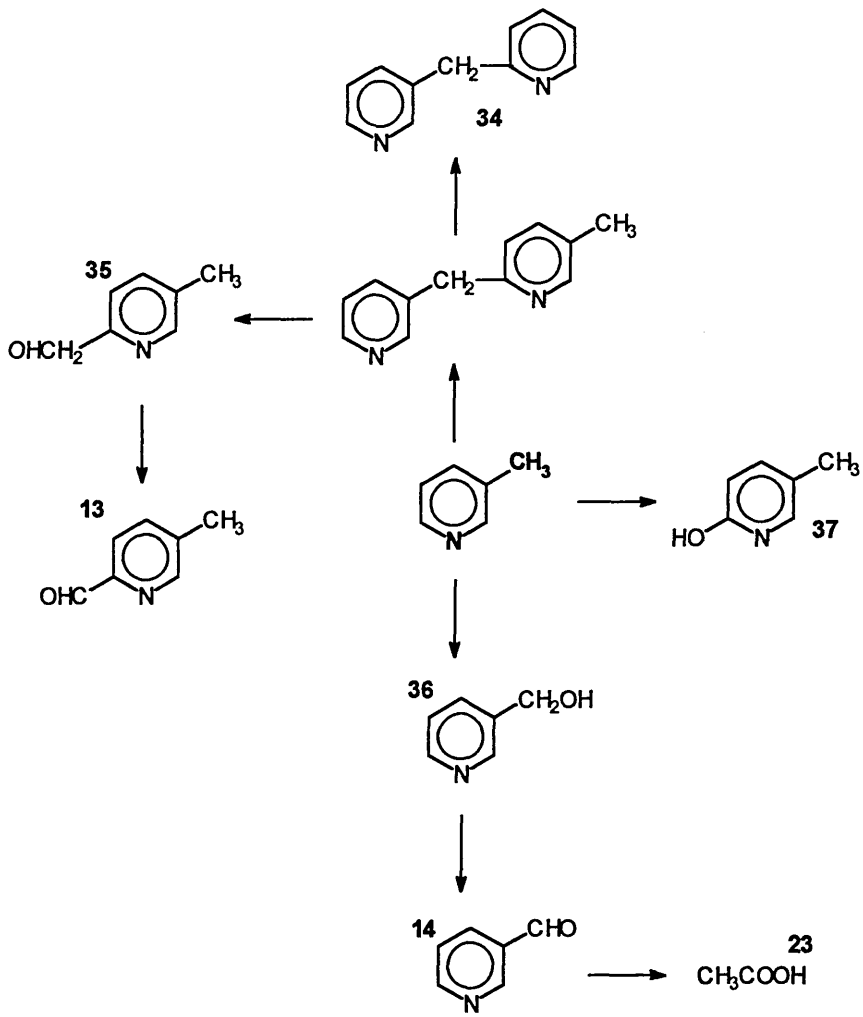
Table 5 Oxidation products arising from the iron catalysed autoclave oxidation of 3-methylpyridine

Component	t_R		RMM	Proposed structure
	Fe(II)	Fe(III)		
34*	23.56	-	170	2-(3-pyridylmethyl) pyridine
35*	-	22.50	123	2-hydroxymethyl-5-methylpyridine
13*	16.28	12.76	121	5-methylpyridine-2-carboxaldehyde
36	20.37	16.92	109	3-hydroxymethylpyridine

37*	23.16	19.67	109	2-hydroxy-5-methylpyridine
14	14.81	11.37	107	pyridine-3-carboxaldehyde
23	10.74	7.54	60	acetic acid

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

Figure 5

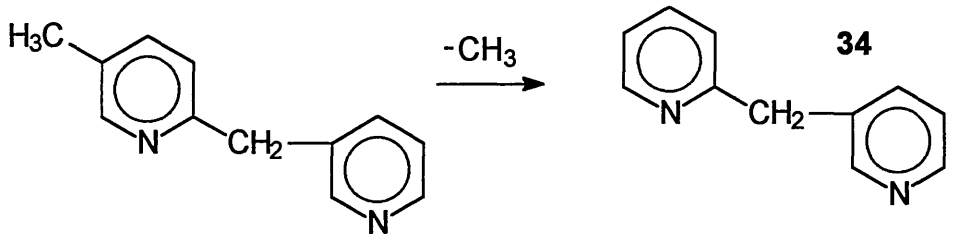


The oxidation of 3-methylpyridine in the autoclave, in the presence of iron-containing catalysts, produces a much more extensive array of oxidation products when compared with the uncatalysed oxidation reaction. The major

oxidation product observed in each of the iron catalysed autoclave reactions is pyridine-3-carboxaldehyde **14**. This was observed at T_0, in each case, and the amount formed appeared to increase over the course of both of the oxidation reactions.

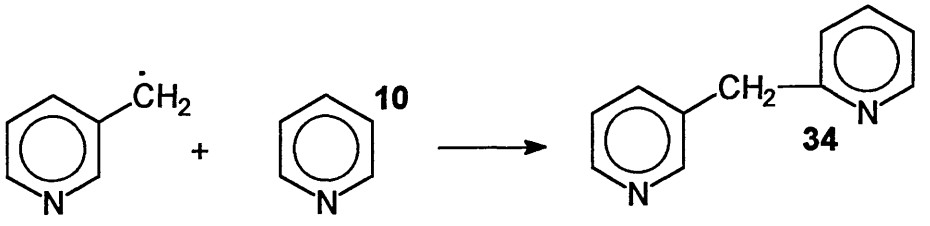
The formation of component **34** occurred at T_2 and it appeared to be fairly resistant to oxidation as it was still detected at T_4. This component has a mass spectrum that is very similar to that generated for component **28**, formed in the iron(III)-catalysed oxidation of 2-methylpyridine. The mass spectrum of component **28** exhibited a base peak at *m/z* 170. A similar picture was observed for **34**, which also had an apparent molecular ion at *m/z* 170, but here the base peak was *m/z* 169 and no other stable fragments were observed. Thus, component **34** could have been formed in a similar way to **28** via the destructive oxidation of a dimeric structure, involving loss of a methyl group (Scheme 10), or via a radical substitution reaction (Scheme 10a). Such a radical reaction would have required a 3-pyridylmethyl radical and pyridine which is not itself observed as an oxidation product here. No appropriate dimeric structures, such as 3-methyl-6-(3-methylpyridyl)pyridine were observed. This structure presumably arises from a radical substitution reaction occurring at the 6-position of 3-methylpyridine with a 3-pyridylmethyl radical. However, this is not conclusive evidence that such dimeric structures have not been formed as intermediates in the reaction. Also, although pyridine was not observed as an oxidation product, this is not evidence that it was not formed at some stage in the oxidation reaction. The structure of **34** is suggested to be 2-(3-pyridylmethyl)pyridine and its possible formation is summarised in Scheme 13 and Scheme 13a.

Scheme 13



5-methyl-2-(3-methylpyridyl)pyridine 2-(3-pyridylmethyl)pyridine

Scheme 13a

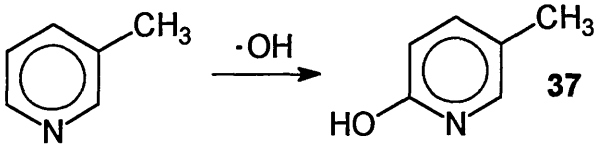


Components **35** and **13** are also thought to occur as a result of the destructive oxidation of a compound such as 5-methyl-2-(3-methylpyridyl)pyridine, to form 2-hydroxymethyl-5-methylpyridine **35**, followed by 5-methylpyridine-2-carboxaldehyde **13**. The likely origin of their formation was shown earlier in Scheme 5. Component **35** was only observed in the oxidation of 3-methylpyridine where an iron(II)-containing catalyst was used and it was evident only at the end of the oxidation process at T_4. Component **13** was formed in both iron-catalysed oxidation reactions here but again it was not observed until T_4.

A structure exhibiting an apparent molecular ion at *m/z* 109 was formed in the oxidation of 3-methylpyridine using both iron(II)- and iron(III)-containing catalysts. Component **37** is thought to have been formed from hydroxyl radical substitution at the pyridine ring of the parent methylpyridine, to form 2-hydroxy-5-methylpyridine **37**, as its mass spectral fragmentation pattern compares well

with that of the known 2-hydroxy-6-methylpyridine **8**. The formation of component **37** is represented in Scheme 14.

Scheme 14



Component **37** was observed at the beginning of the process at T_0 and T_1 and it appeared to be very stable under the oxidising conditions imposed as it was still present at T_4 in both of the oxidation reactions.

Component **36** was formed in both of the oxidation reactions, and was identified as 3-hydroxymethylpyridine by comparison with the standard material. The presence of acetic acid **23** was detected in both oxidation reactions, again an expected product of oxidation under the catalysed WAO conditions imposed.

2.3.1.3. 4-Methylpyridine

The autoclave oxidation of 4-methylpyridine was also carried out in the presence of both iron(II)- and iron(III)-containing catalysts. The reaction mixtures were analysed by GC-MS techniques using instrument 1 and temperature programme 1 for the analysis of the iron(II)-catalysed reaction mixtures, and temperature programme 2 for the analysis of the iron(III)-catalysed reaction mixtures. The observations made, together with structural assignments, are summarised in Table 6, and Figure 6 represents a possible

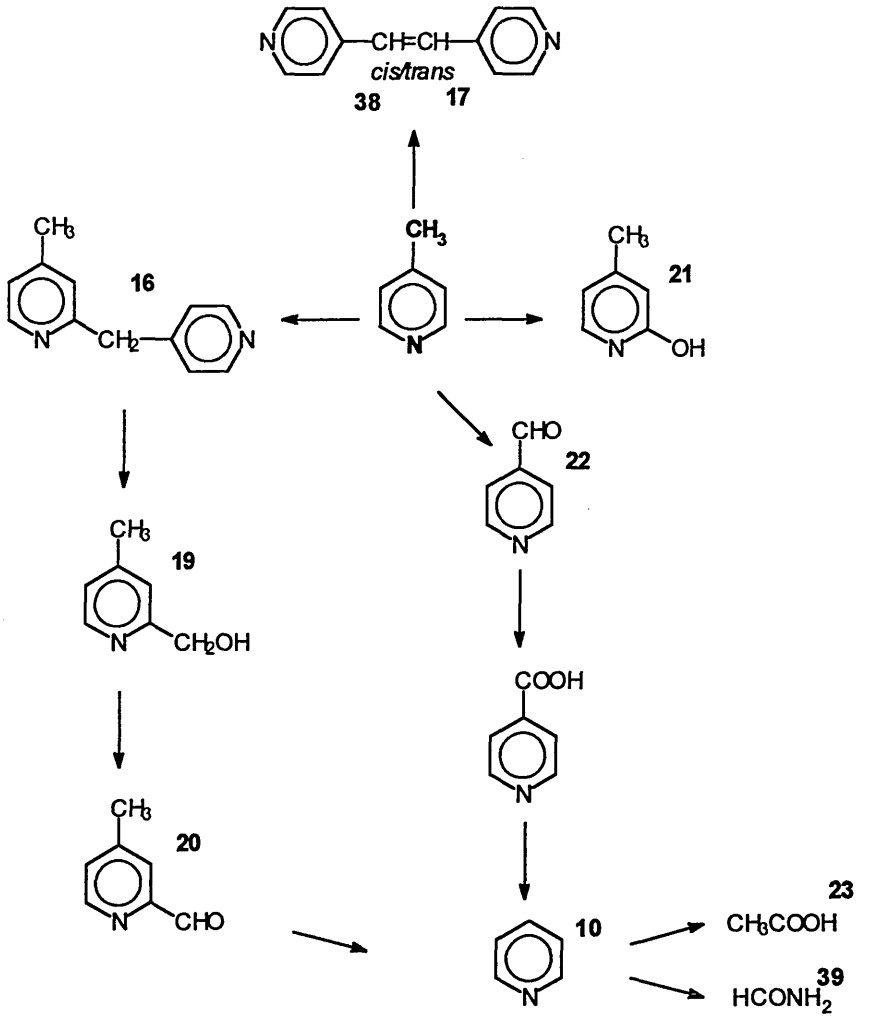
pathway for the formation of the oxidation products indicated in the table below.

Table 6 Oxidation products arising from the iron catalysed autoclave oxidation of 4-methylpyridine

Component	t_R		RMM	Proposed structure
	Fe(II)	Fe(III)		
16*	26.97	-	184	4-methyl-2-(4-pyridylmethyl)pyridine
38	21.91	-	182	*cis*-1,2-bis-(4-pyridyl)ethene
17	35.35	30.80	182	*trans*-1,2-bis(4-pyridyl)ethene
19*	26.49	-	123	2-hydroxymethyl-4-methylpyridine
20*	15.79	12.38	121	4-methylpyridine-2-carboxaldehyde
21*	24.13	-	109	2-hydroxy-4-methylpyridine
22	14.01	10.62	107	pyridine-4-carboxaldehyde
10	7.11	-	79	pyridine
23	10.76	7.85	60	acetic acid
39	-	7.70	45	formamide

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

Figure 6



The first observation to be made from Table 6 is that the range of oxidation products is more extensive when an iron(II)-containing catalyst is used in the oxidation of 4-methylpyridine. This is in contrast to those observations made in the iron-catalysed autoclave oxidation of 2-methylpyridine.

Component **16** was first observed as an oxidation product in the uncatalysed autoclave oxidation of 4-methylpyridine. The structure of this component was earlier suggested to be 4-methyl-2-(4-pyridylmethyl)pyridine, being formed as a result of a reaction involving radical substitution - Scheme 7. This component

was fairly resistant to oxidation as it was observed at T_1 and was still present at T_4.

Components **38** and **17** were identified, by comparison with standards, as being the *cis*- and *trans*- forms of 1,2-bis-(4-pyridyl)ethene, respectively. Component **17** was identified in the oxidation reactions involving the use of each of the iron catalysts, but in both reactions, these compounds were destroyed in the course of the oxidation reaction as they were not identified at T_4.

The formation of components **19** and **20** was also noted in the uncatalysed process. As indicated in 2.2.2. earlier, these components are thought to be formed from the oxidation of a saturated dimeric structure, such as 4-methyl-2-(4-pyridylmethyl)pyridine **16**. The oxidation of **16** could occur by initial loss of a pyridine ring and then the oxidation of the alkyl chain to generate 2-hydroxymethyl-4-methylpyridine **19** first, followed by the further oxidation of the alcohol to generate 4-methylpyridine-2-carboxaldehyde **20**.

Component **21**, with a relative molecular mass of 109, was observed in the oxidation reaction involving iron(II). This component had also been observed in the uncatalysed autoclave oxidation reaction of 4-methylpyridine, and its structure was suggested as being 2-hydroxy-4-methylpyridine, arising via hydroxyl radical substitution at the pyridine ring of 4-methylpyridine, as seen in Scheme 8.

Pyridine-4-carboxaldehyde **22** was observed as an oxidation product in both reactions during the initial stages. Acetic acid **23** was also formed in both cases and this is an expected oxidation product under such conditions. The oxidation of 4-methylpyridine, in the presence of iron(II), generated pyridine **10**

and this could have been formed by a decarboxylation process similar to that seen in the autoclave oxidation of 2-methylpyridine in 2.1.2. (b). The formation of formamide **39** was observed in the iron(III)-catalysed reaction, indicating that destruction of the pyridine ring has occurred.

2.3.2. The use of copper containing catalysts

The autoclave oxidation of 2-, 3-, and 4-methylpyridine was carried out in the presence of three types of copper-containing catalysts. The first was copper(II) sulphate ($Cu(II)_A$), the second was a mixture of copper(II) sulphate and hydrogen peroxide ($Cu(II)_B$) which is presumed to behave in a similar fashion to Fenton's reagent[13], and the third was a mixture of copper(I) chloride and hydrogen peroxide, which is termed a Fenton-like reagent[14].

2.3.2.1. 2-Methylpyridine

The autoclave oxidation of 2-methylpyridine in the presence of all three catalytic systems generated a wide range of oxidation products. They were investigated using GC-MS techniques and temperature programme 2 . The autoclave oxidation reactions involving $copper(II)_A$ were analysed using instrument 1 and the other two copper catalysed reactions were analysed using instrument 2. The observations made are summarised in Table 7, and Figure 7 represents a possible pathway for the formation of those oxidation products indicated in the table below.

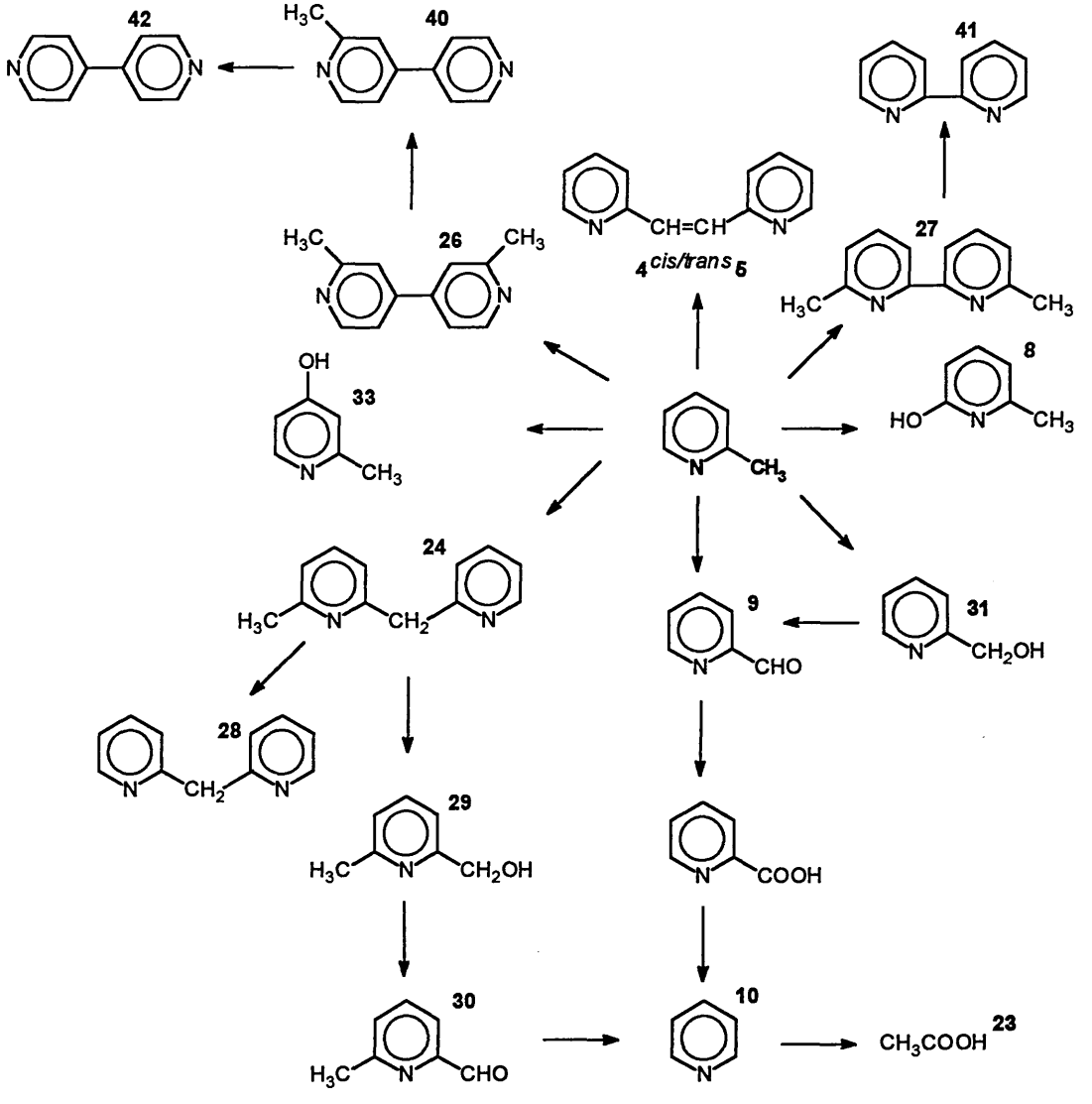
Table 7 Oxidation products arising from the copper catalysed autoclave oxidation of 2-methylpyridine

Component	t_R			RMM	Proposed structure
	$Cu(II)_A$	$Cu(II)_B$	Cu(I)		
26	-	19.32	-	184	2,2'-dimethyl-4,4'-bipyridine
4	-	-	23.09	182	*cis*-1,2-bis-(2-pyridyl)ethene
5	26.03	26.17	-	182	*trans*-1,2-bis-(2-pyridyl)ethene
40*	-	19.09	18.03	170	2-methyl-4-(4-pyridyl) pyridine
28*	-	20.43	19.06	170	2-(2-pyridylmethyl) pyridine
41	-	16.16	-	156	2,2'-bipyridine
42	19.75	19.24	18.17	156	4,4'-bipyridine
29*	18.76	18.14	17.09	123	2-hydroxymethyl-6-methylpyridine
30*	9.94	8.17	8.05	121	6-methylpyridine-2-carboxaldehyde
31	13.20	11.56	-	109	2-hydroxymethylpyridine
33*	-	17.00	16.10	109	4-hydroxy-2-methylpyridine
8	-	18.31	17.28	109	2-hydroxy-6-methylpyridine
9	9.35	7.42	7.31	107	pyridine-2-carboxaldehyde

10	4.77	3.17	3.13	79	pyridine
23	7.50	6.34	6.52	60	acetic acid

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

Figure 7

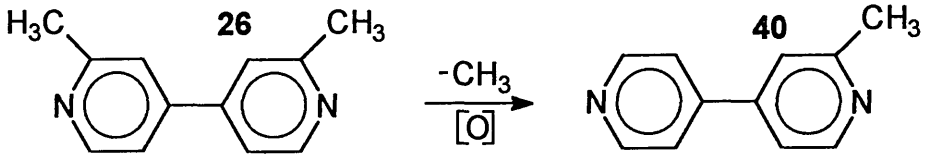


The first observation to be made from Table 7 concerns the extent of the oxidation products formed in all of the copper catalysed reactions. The only saturated dimeric structure observed of relative molecular mass 184 (**26**) was formed in the copper(II)$_B$-catalysed autoclave oxidation at T_0. 2,2'- Dimethyl-

4,4'-bipyridine **26** was also observed in the iron(III)-catalysed oxidation of 2-methylpyridine and therefore must have been formed via a similar process to that seen in Scheme 9. The formation of component **26** in the copper(II)$_B$-catalysed reaction is again an indication that some form of radical chemistry is taking place. Unsaturated dimeric structures in the form of *cis*- **4** and *trans*- **5** 1,2-bis-(2-pyridyl)pyridine were observed both here and in the earlier iron catalysed autoclave oxidation reactions.

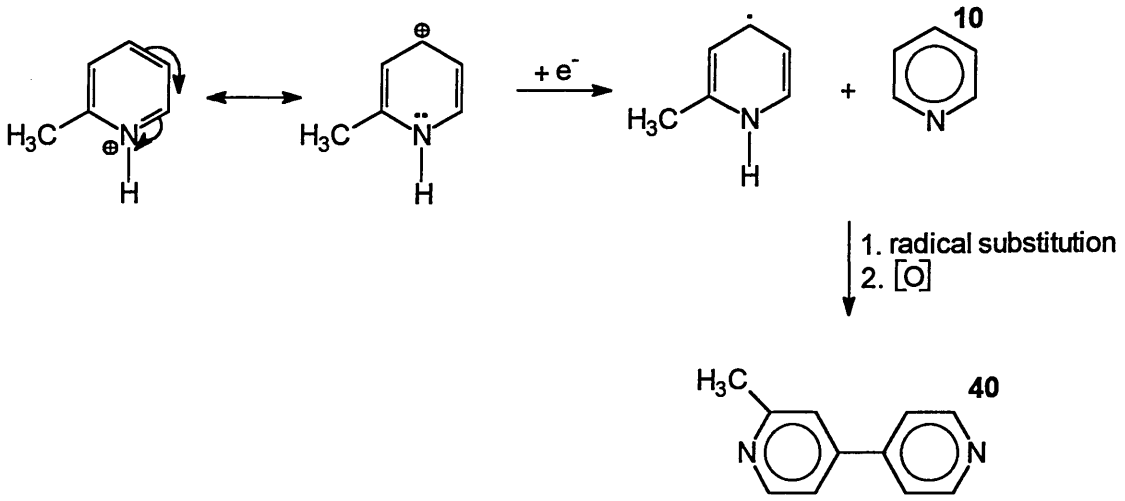
Components **40** and **28** were formed in both the copper(II)$_B$- and copper(I)-catalysed oxidation reactions and they were thought to arise as a result of the oxidation of related dimeric structures. For example, 2,2'-dimethyl-4,4'-bipyridine **26**, which was observed as an oxidation product in the copper(II)$_B$-catalysed oxidation reaction, would account for the formation of 2-methyl-4-(4-pyridyl)pyridine **40** via loss of a methyl group.

Scheme 15



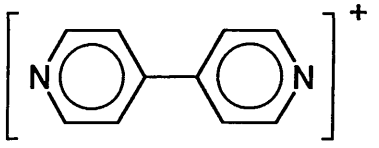
However, as observed earlier in the iron-catalysed oxidation of 2-methylpyridine, component **40** could have been formed via a radical substitution reaction occurring between the appropriate methylpyridyl radical and pyridine as shown in Scheme 15a.

Scheme 15a

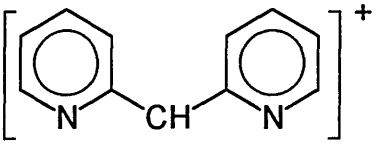


The product 2-(2-pyridylmethyl)pyridine **28** could have been formed via similar processes to those seen in Scheme 15 and 15a. If a mechanism similar to that shown in Scheme 15 took place, then the loss of a methyl group from 2-methyl-6-(2-pyridylmethyl)pyridine **24** would have occurred. Component **24** was not observed as an oxidation intermediate here but may have been formed and destroyed under the oxidising conditions to give **28**. If a mechanism similar to that shown in Scheme 15a took place involving radical reactions, then the radical substitution reaction would have been similar to that seen earlier in Scheme 10a.

Although components **28** and **40** possessed the same apparent molecular ion, their mass spectral fragmentation patterns were very different. The mass spectrum of 2-Methyl-4-(4-pyridyl)pyridine **40** exhibited a base peak at m/z 156, indicating the formation of the stable fragment ion shown below.



The mass spectrum of 2-(2-pyridylmethyl)pyridine **28** exhibited a base peak at *m/z* 169 indicating the formation of a different stable fragment ion, represented below.

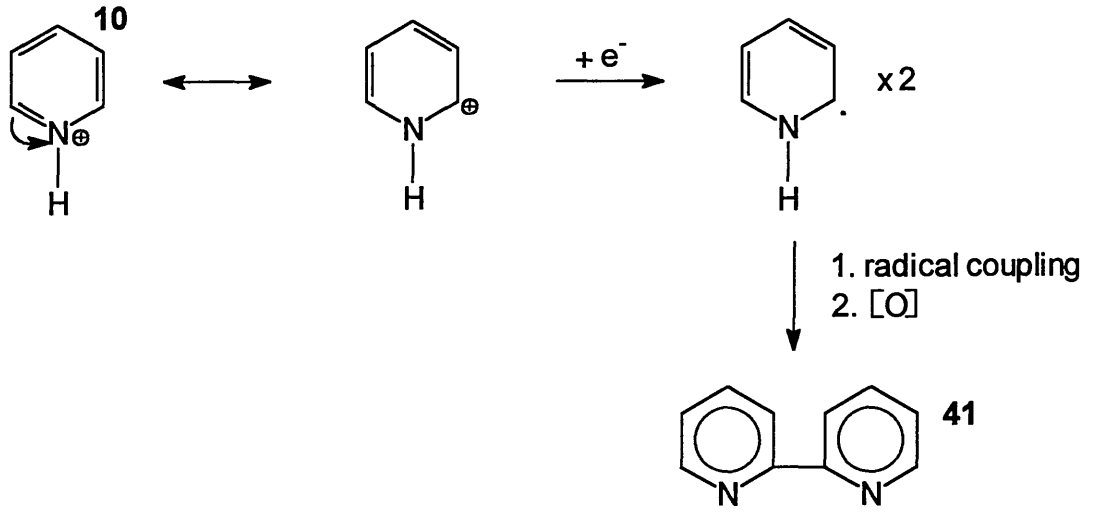


Both **28** and **40** were formed as oxidation intermediates during the initial stages of the reaction.

Two components **41** and **42** were formed during the oxidation reaction and both had the same apparent relative molecular mass of 156. Component **41** was only formed in the copper(II)$_B$-catalysed reaction. The structure of **41** was identified as 2,2'-bipyridine by comparison of mass spectral data and t_R with those of the standard material - Appendix 7; both exhibited a base peak at *m/z* 156. This structure could have been formed via the destructive oxidation of a dimer such as 2,2'-dimethyl-6,6'-bipyridine **27**. The latter is not observed as an oxidation intermediate in the copper catalysed reactions but, again, this is not evidence that it was not formed at an early stage.

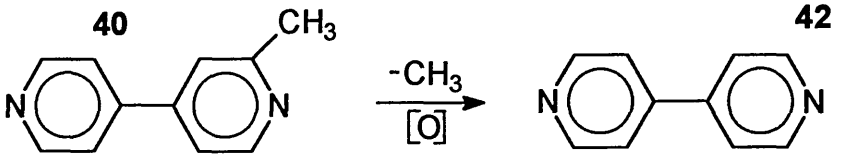
2,2'-Bipyridine could also have been formed via a radical coupling reaction occurring between two pyridyl radicals as shown in Scheme 16.

Scheme 16

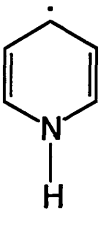


4,4'-Bipyridine **42** was formed in all three copper-catalysed oxidation reactions and this could have been formed from the continued destructive oxidation of **40** by loss of a further methyl group.

Scheme 16a



Component **42** could also have been formed via a radical coupling reaction taking place between pyridyl radicals, as shown above in Scheme 16. However, a coupling reaction between the radical indicated below would have been required in order to form 4,4'-bipyridine.



Components **29** and **30** were also observed as oxidation intermediates in all three copper catalysed autoclave oxidation reactions. 2-Hydroxymethyl-6-methylpyridine **29** and 6-methylpyridine-2-carboxaldehyde **30** were also formed in the iron catalysed oxidation of 2-methylpyridine. The mechanism of their formation is likely to be the same, arising from the oxidation of 2-methyl-6-(2-pyridylmethyl)pyridine **24** - Scheme 11. However, in all three copper catalysed reactions, component **24** was not observed as an intermediate.

Components **31**, **33**, and **8** all have the same relative molecular mass of 109. Component **31** was identified as 2-hydroxymethylpyridine and was found in both copper(II)-catalysed reactions. The other two components were thought to be related isomeric hydroxy(methyl)pyridines as they possessed similar mass spectral fragmentation patterns. 4-Hydroxy-2-methylpyridine **33** and 2-hydroxy-6-methylpyridine **8** were also observed in the iron-catalysed oxidation reactions, probably arising from hydroxyl radical substitution at the pyridine ring of 2-methylpyridine - Scheme 12.

Components **9**, **10**, and **23** were observed in all three copper-catalysed reactions and also in some of the iron catalysed reactions discussed earlier. Pyridine-2-carboxaldehyde **9** is an expected oxidation product due to the expected ease of oxidation of the methyl group attached to the pyridine ring. The formation of pyridine **10** has probably occurred as a result of the decarboxylation of pyridine-2-carboxylic acid, another expected oxidation product. Acetic acid **23** is a common product under the WAO conditions imposed during the autoclave oxidation.

2.3.2.2. 3-Methylpyridine

The autoclave oxidation of 3-methylpyridine was carried out in the presence of three copper-containing catalysts and the reaction mixtures were analysed using GC-MS techniques and temperature programme 2. The autoclave oxidation reactions involving copper(II)$_A$ were analysed using instrument 1 and the other two copper catalysed reactions were analysed using instrument 2. Those observations that were made are summarised in Table 8, and Figure 8 represents a possible pathway for the formation of those oxidation products indicated in the table below.

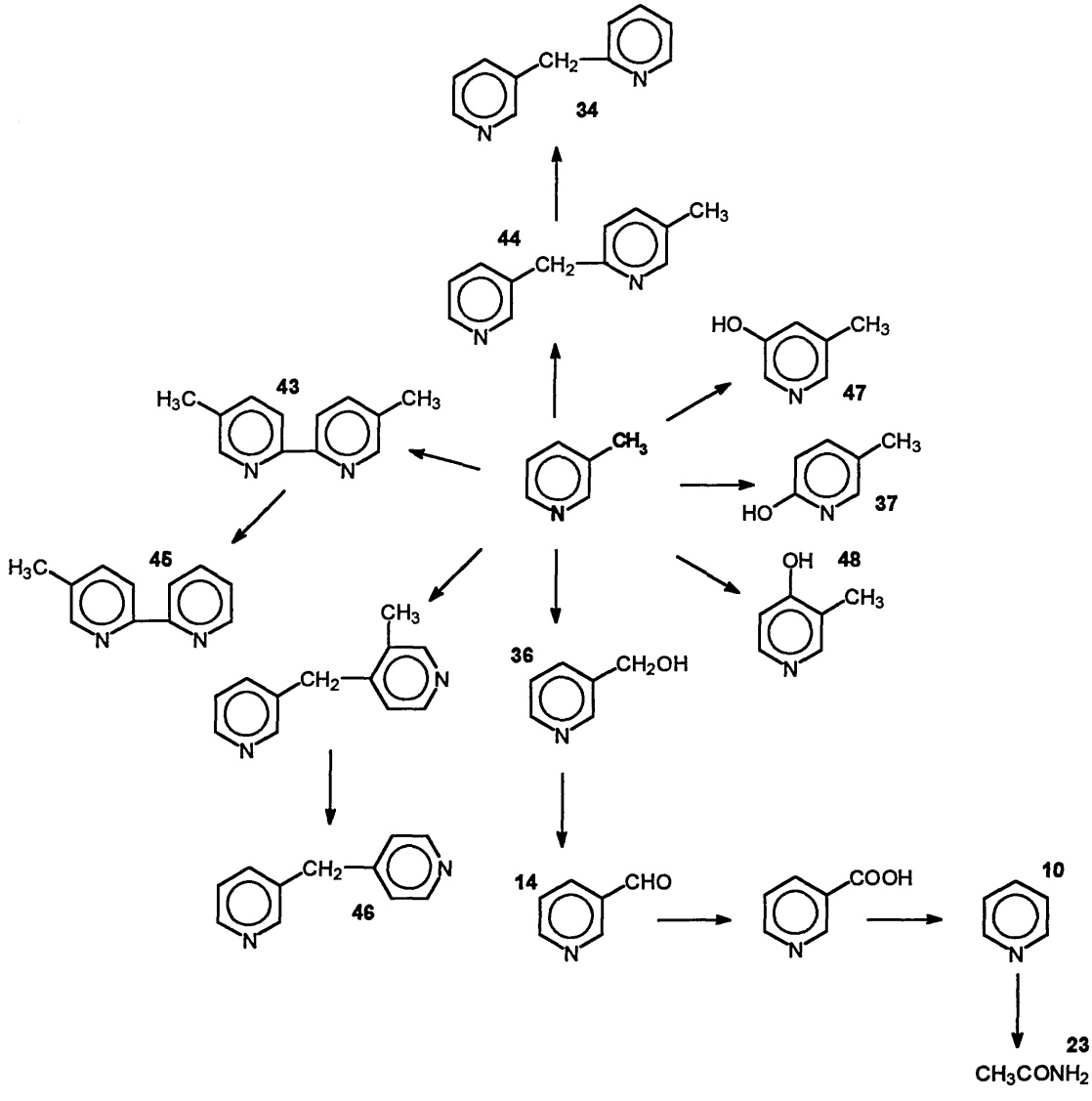
Table 8 Oxidation products arising from the copper catalysed autoclave oxidation of 3-methylpyridine

Component	t_R			RMM	Proposed structure
	Cu(II)$_A$	Cu(II)$_B$	Cu(I)		
43*	-	23.50	-	184	5,5'-dimethyl-2,2'-bipyridine
44*	-	29.25	-	184	5-methyl-2-(3-pyridylmethyl)pyridine
45*	-	21.09	-	170	5-methyl-2-(2-pyridyl) pyridine
34*	-	22.51	-	170	2-(3-pyridylmethyl) pyridine
46*	-	23.10	-	170	4-(3-pyridylmethyl) pyridine
36	-	17.38	-	109	3-hydroxymethylpyridine

47*	19.56	-	-	109	3-hydroxy-5-methylpyridine
37*	-	20.54	18.07	109	2-hydroxy-5-methylpyridine
48*	-	21.07	-	109	4-hydroxy-3-methylpyridine
14	11.24	10.27	9.36	107	pyridine-3-carboxaldehyde
10	-	3.41	3.18	79	pyridine
11	-	11.24	-	59	acetamide

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

Figure 8

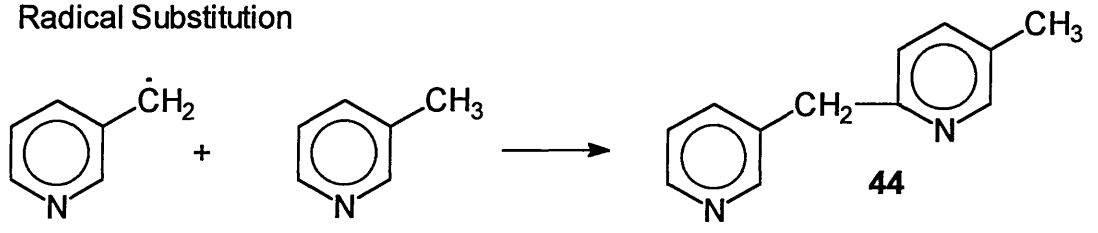


Compared with the uncatalysed and iron-catalysed oxidation reaction, a much greater variety of oxidation products was observed for the copper catalysed oxidation of 3-methylpyridine. Components **43**, and **44** both represent the presence of saturated dimeric structures which were first observed at the beginning of the process at T_1, and they were also observed as oxidation products at T_4. None of these structures were observed in any of the other autoclave oxidation reactions studied involving 3-methylpyridine as the substrate. Both of these components exhibit very different mass spectra.

Component **44** is thought to occur as a result of radical substitution reaction occurring at the pyridine ring of the parent substrate - Scheme 17.

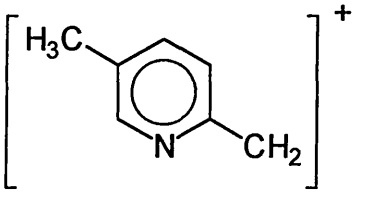
Scheme 17

Radical Substitution

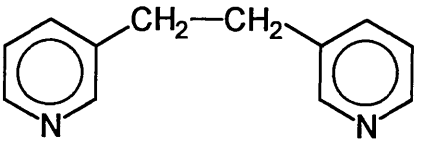


44

Component **44** was identified as 5-methyl-2-(3-pyridyl)pyridine (Appendix 8) since its mass spectrum exhibited a base peak at *m/z* 106, indicating the formation of the stable fragment below.

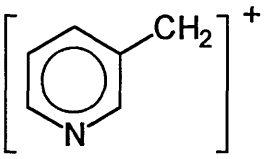


An alternative structure which would also be expected to give rise to a fragment ion at m/z 106 is 1,2-bis-(3-pyridyl)ethane - Appendix 8.



1,2-bis-(3-pyridyl)ethane

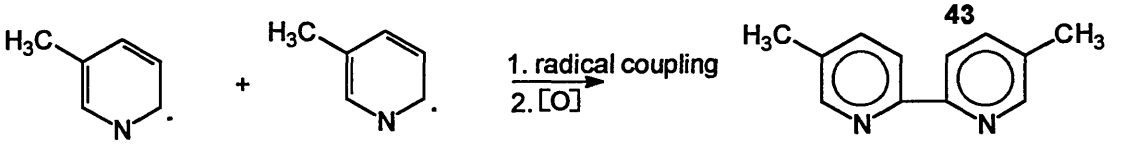
However, the authentic substance gives rise to a stable fragment ion at *m/z* 92 and the structure of this ion is shown below.



Therefore the probable structure of component **44** is as indicated in Table 8.

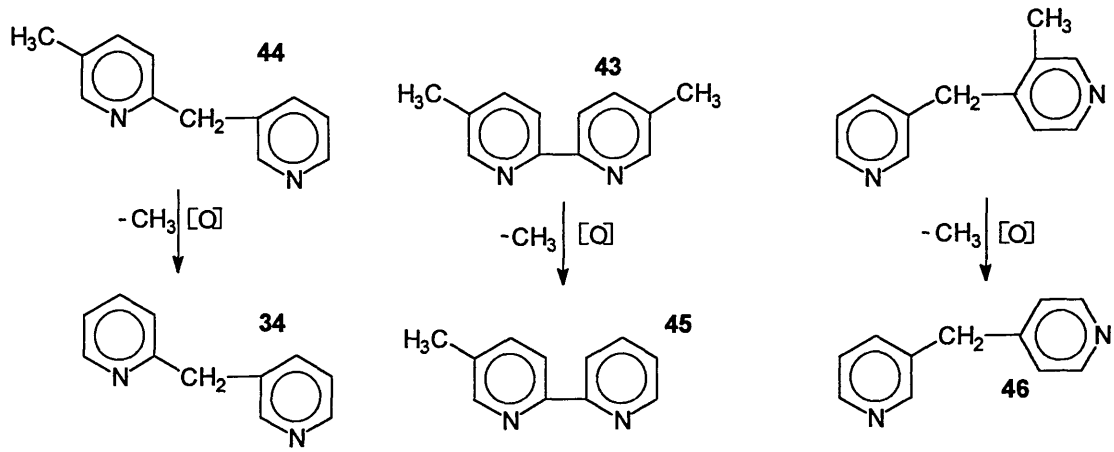
Component **43** is also thought to be formed by a radical reaction, but instead of radical substitution taking place, radical coupling could be responsible for this product. The formation of methylpyridyl radicals required for radical coupling reactions is very similar to the mechanism displayed earlier in Scheme 9. On the formation of such radicals, the production of 5,5'-dimethyl-2,2'-bipyridine **43** is possible - Scheme 18.

Scheme 18



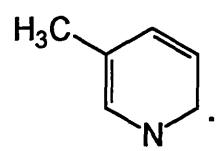
Components **45**, **46**, and **34** are possibly formed as a result of the oxidation of the saturated dimeric structures such as component **43** observed above in Scheme 18. Loss of a methyl group has occurred to generate the structures indicated below in Scheme 19, and all of these components exhibit the same apparent molecular ion at *m/z* 170 - Appendix 9.

Scheme 19



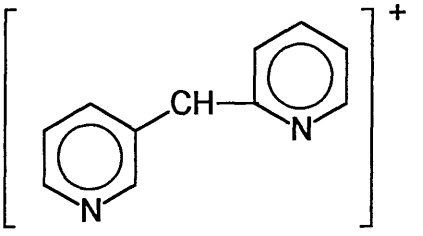
Although the precursor to component **46**, 3-methyl-4-(3-pyridylmethyl)pyridine, was not observed as an oxidation product, this is not conclusive evidence that it had not been formed at some stage during the oxidation reaction. Under those oxidising conditions adopted, the oxidation of such a structure may have occurred quickly to give component **46**.

Components **34**, **45**, and **46** may also have been formed via radical reactions. Components **34**, and **46** will have been formed by a mechanism similar to that seen in Scheme 13a. Component **45** will have required the formation of the radical shown below which could then itself undergo a radical substitution reaction with pyridine, as this is an observed oxidation product.



Components **45** and **46** both possessed similar mass spectra in that the only stable fragment ion observed was in the region of the apparent molecular ion at *m/z* 170. However, component **34** had a mass spectrum which contained a

stable fragment at m/z 169 indicating the formation of the stable fragment shown below.



All of the oxidation products discussed so far have only been observed in the oxidation of 3-methylpyridine where copper(II)$_B$ was used as the catalyst. However, the oxidation reactions involving the other two catalytic systems did generate other oxidation products. Various components which all have the same relative molecular mass of 109 were observed. Component **36** was identified as 3-hydroxymethylpyridine by comparison with the authentic substance, as both contained a stable fragment ion at *m/z* 108. The other structures were thought to be formed as a result of hydroxyl radical substitution occurring at the pyridine ring of the parent substrate, as indicated in Scheme 14, to form 3-hydroxy-5-methylpyridine **47**, 2-hydroxy-5-methylpyridine **37**, and 4-hydroxy-3-methylpyridine **48**. Components **47**, **37**, and **48** all possessed similar mass spectra which exhibited apparent molecular ions at *m/z* 109 and a stable fragment ion at *m/z* 80.

An oxidation product common to all oxidation reactions was pyridine-3-carboxaldehyde **14**, an expected oxidation product under these conditions. Pyridine **10** was formed in two of the catalysed oxidation reactions, copper(II)$_B$ and copper(I), probably as a result of decarboxylation of pyridine-3-carboxylic acid, similar to that observation made earlier for the autoclave oxidation of 2-methylpyridine (2.2.1. (b)). For the copper(II)$_B$-catalysed reaction, acetamide **11** was formed indicating that ring destruction may have taken place.

2.3.2.3. 4-Methylpyridine

The autoclave oxidation of 4-methylpyridine was carried out in the presence of just two of the copper containing catalysts, copper(II)$_A$and copper(II)$_B$. The oxidation products were investigated using GC-MS techniques and temperature programme 2. The autoclave oxidation reaction catalysed by copper(II)$_A$ was analysed using instrument 1 and the copper(II)$_B$ catalysed reaction was analysed using instrument 2. The observations made are summarised in Table 9, and Figure 9 represents a possible pathway for the formation of the oxidation products indicated in the table below.

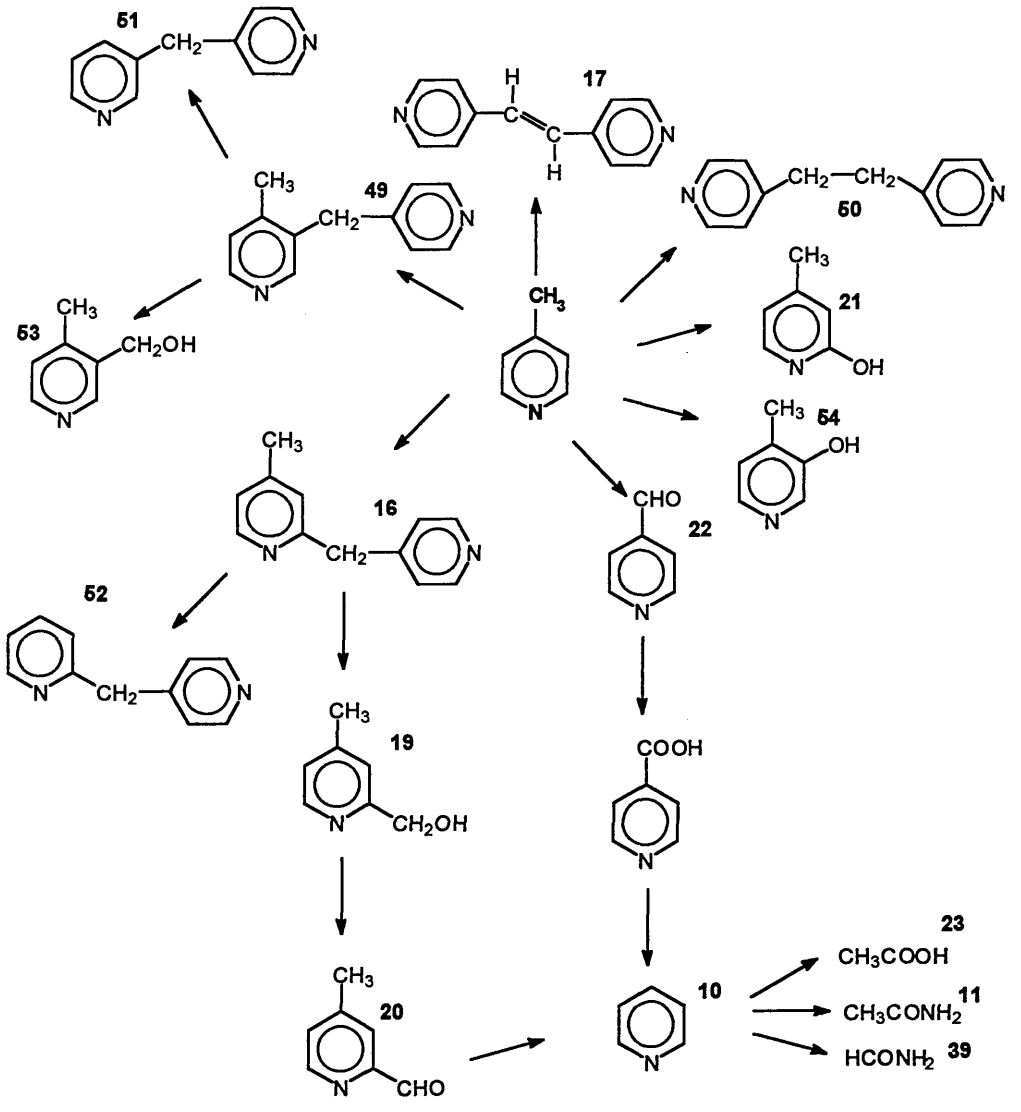
Table 9 Oxidation products arising from the copper catalysed autoclave oxidation of 4-methylpyridine

Component	t_R		RMM	Proposed structure
	Cu(II)$_A$	Cu(II)$_B$		
49*	-	21.27	184	4-methyl-3-(4-pyridylmethyl)pyridine
16*	23.10	22.20	184	4-methyl-2-(4-pyridylmethyl)pyridine
50	-	28.35	184	1,2-bis-(4-pyridyl)ethane
17	30.54	-	182	*trans*-1,2-bis-(4-pyridyl)ethene
51*	-	23.01	170	3-(4-pyridylmethyl) pyridine
52*	-	23.05	170	2-(4-pyridylmethyl) pyridine

19*	22.42	-	123	2-hydroxymethyl-4-methylpyridine
53	-	24.51	123	3-hydroxymethyl-4-methylpyridine
20*	12.28	12.08	121	4-methylpyridine-2-carboxaldehyde
21*	-	20.14	109	2-hydroxy-4-methylpyridine
54*	-	23.03	109	3-hydroxy-4-methylpyridine
22	10.54	10.06	107	pyridine-4-carboxaldehyde
10	4.90	3.18	79	pyridine
23	7.65	6.32	60	acetic acid
11	-	10.24	59	acetamide
39	7.44	-	45	formamide

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

Figure 9

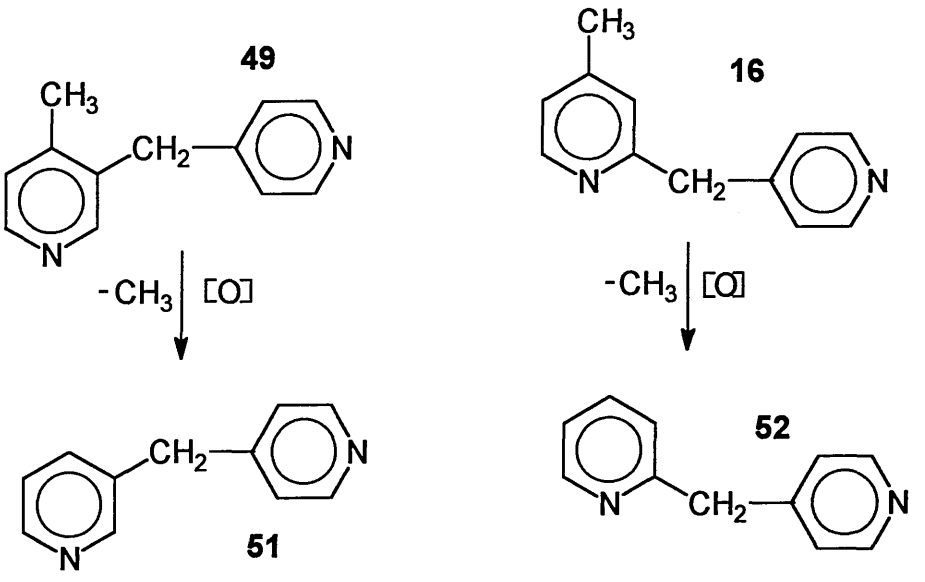


The copper(II)$_B$-catalysed autoclave oxidation of 4-methylpyridine generated a more extensive range of oxidation products than the copper(II)$_A$-catalysed reaction. Components **49**, **16**, and **50** were all identified as being dimeric in structure due to the fact that they all exhibited apparent molecular ions at *m/z* 184. Component **50** was identified as 1,2-bis-(4-pyridyl)ethane as, on comparison with the standard material, both exhibited base peaks at *m/z* 92 - Appendix 3 & 10. This structure will have been formed by a radical coupling reaction as seen earlier in Scheme 7. Component **16** was observed as an oxidation intermediate in both of the copper-catalysed reactions studied. It was

also observed as a product in the uncatalysed and iron-catalysed autoclave oxidation reaction of 4-methylpyridine. Its structure has therefore been suggested as being 4-methyl-2-(4-pyridylmethyl)pyridine and its formation would have occurred as a result of a reaction involving radical substitution as indicated in Scheme 7 also. Component **49** is thought to be another dimeric structure and due to the fact that **16** and **49** both have very similar mass spectra in that both exhibit stable fragment ions at *m/z* 106 and *m/z* 78, **49** is thought to be an isomer of **16**, for example, 4-methyl-3-(4-pyridylmethyl)pyridine, as shown in Scheme 7. All of the saturated dimeric structures were observed as oxidation intermediates as early as T_0, and they were still present at T_4 illustrating their stability under such conditions. In the copper(II)$_A$-catalysed reaction *trans*-1,2-bis-(4-pyridyl)ethene **17** was observed at T_0 but it was oxidised under the autoclave conditions as it was not detected amongst the oxidation products at T_4.

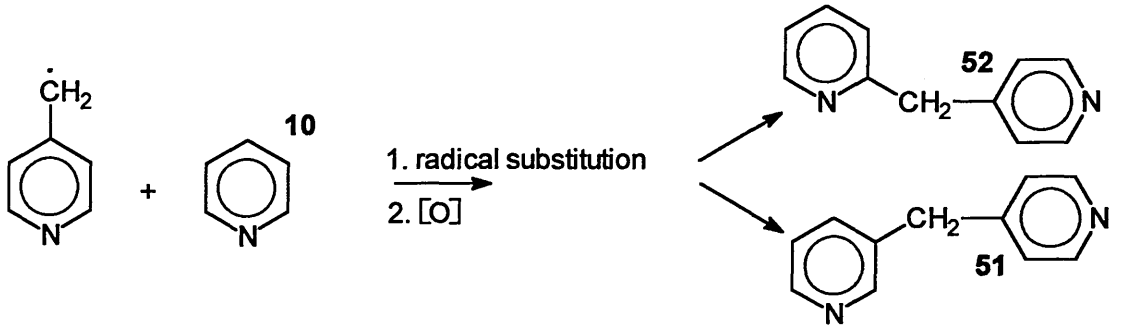
Components **51**, and **52** were both detected as products in the copper(II)$_B$-catalysed oxidation reaction of 4-methylpyridine. Both of these structures could have been formed by the destructive oxidation of dimeric structures such as components **16** and **49** formed in the copper-catalysed oxidation of this methylpyridine. The structures of **51** and **52** can be accounted for by considering the destruction of **16** and **49** resulting in loss of a methyl group in the following way.

Scheme 20



However, both components **51** and **52** could have been formed via a radical substitution reaction occurring between methylpyridyl radicals and pyridine as pyridine was observed as an oxidation product. The mechanism for this possible reaction is represented in Scheme 20a.

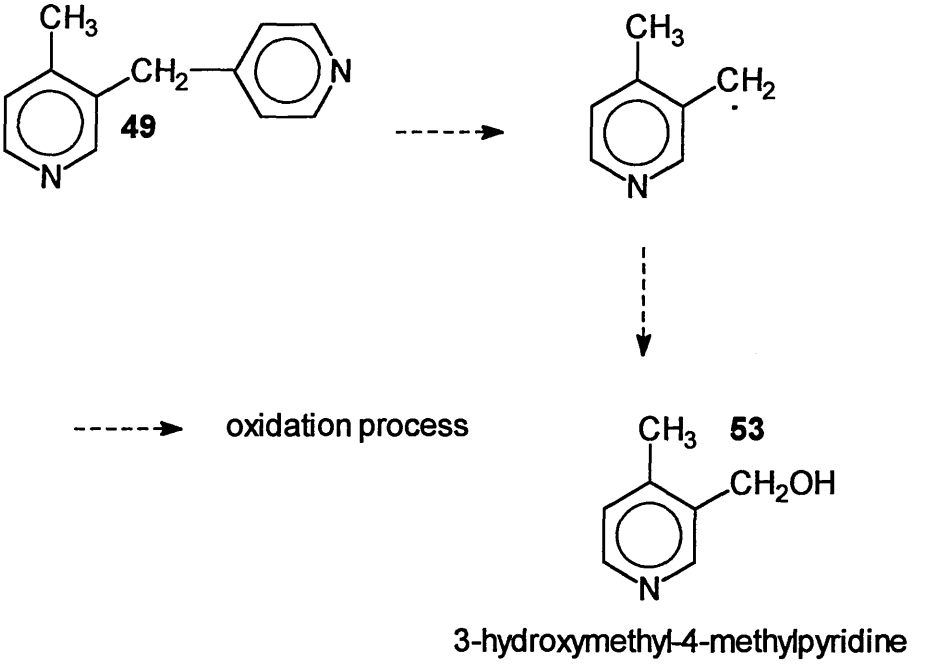
Scheme 20a



Components **19** and **20** were observed in earlier reactions involving the oxidation of 4-methylpyridine and their structures are thought to be 2-hydroxy-4-methylpyridine **19** and 4-methyl-2-carboxaldehyde **20** respectively, formed

as a result of the oxidation of dimeric structures such as **16**. Their formation was illustrated earlier in 2.3.1.3. The oxidation process involves 4-methyl-2-(4-methylpyridyl)pyridine **16** undergoing destruction resulting in loss of a methyl group and the resulting alkyl chain undergoes further oxidation to give component **19** followed by further oxidation to form **20**. These components were observed as oxidation products in both of the copper catalysed reactions being studied here. Component **53** had a similar mass spectrum to component **19** but it had a different t_R. Therefore this component could have arisen via the oxidation of component **49** as shown below in Scheme 21.

Scheme 21

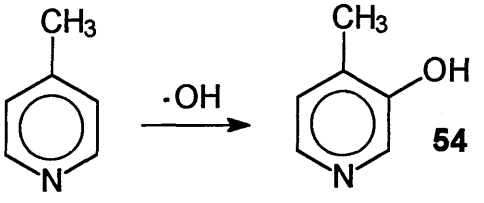


4-Methyl-3-(4-methylpyridyl)pyridine has undergone destructive oxidation involving loss of a pyridine ring and then the subsequent oxidation of the alkyl chain to give component **53**.

The copper(II)$_B$-catalysed oxidation reaction generated components 2-hydroxy-4-methylpyridine **21** and 3-hydroxy-4-methylpyridine **54** and their

formation was first observed at T_1. Both of the components have the same relative molecular mass of 109 and exhibited similar mass spectra in that both showed stable fragment ions at *m/z* 80. Component **21** had been observed earlier as an oxidation product in the iron(II)-catalysed oxidation reaction of 4-methylpyridine. It was thought to be an intermediate formed as a result of hydroxyl substitution occurring at the pyridine ring of the substrate, as shown in Scheme 8. Component **54** is thought to be an isomer of **21** and its mode of formation is suggested in Scheme 22 below.

Scheme 22



54

Pyridine-4-carboxaldehyde **22**, pyridine **10**, and acetic acid **23** were formed in both of the copper catalysed reactions. Acetamide **11** and formamide **39** were also observed in each of the reaction mixtures being studied, and their formation is possible evidence of ring destruction.

2.3.2.4. Summary

The catalysed autoclave oxidation of 2-, 3-, and 4-methylpyridine has produced an extensive array of oxidation products. Some of these compounds are common to both uncatalysed and catalysed oxidation reactions, whereas others are formed as a direct result of the presence of the catalysts. A general observation is that the presence of both the iron and the copper catalysts, in each of the reactions studied, generates an extensive array of oxidation products, in comparison with the uncatalysed reactions. The formation of

dimeric structures indicates that, again, free radical chemistry is occurring in all of the catalysed oxidation reactions, as does the formation of structures such as 2-hydroxy-4-methylpyridine **21**. This is also the case in the uncatalysed autoclave reactions carried out earlier. However, the formation of the appropriate pyridinecarboxaldehyde in each of the catalysed reactions is evidence that other types of oxidation reactions are taking place.

In contrast to the uncatalysed autoclave oxidation of 3-methylpyridine, the catalysed reactions appear to have proceeded much further in all of the reactions studied as a greater array of oxidation products is observed in all cases.

2.4. Comparisons between the Uncatalysed and Catalysed WAO of 2-, 3, and 4-Methylpyridines

Each of the autoclave oxidation reactions studied has been discussed and the oxidation products observed have been summarised and comparisons, where possible, have been made. The measurement of the COD values for each of the reaction mixtures before and after WAO is, however, a standard method for identifying the degree of oxidation that has taken place in any reaction. It is therefore interesting to compare those COD values obtained after oxidation has taken place in order to establish the effect of the catalyst adopted, in terms of destroying the organic content, and how each catalyst compares with each other. COD data was provided by Leigh Environmental who carried out each of the autoclave oxidation reactions.

Table 10 % COD reduction values for both the uncatalysed and catalysed autoclave oxidation reactions of 2-, 3-, and 4-methylpyridine

	2-Methylpyridine	**3-Methylpyridine**	**4-Methylpyridine**
No catalyst	25.6	0	37.5
$Fe(II)/H_2O_2$	28.6	40.5	25.8
$Fe(III)/H_2O_2$	-	-	-
Cu(II)	49.4	16.3	47.5
$Cu(II)/H_2O_2$	46.8	20.0	50.0
Cu(I)	43.0	6.0	

On comparing those results obtained for the oxidation of 2-, and 4-methylpyridine, the presence of the copper(II) containing catalysts achieved the best % COD reduction results. The data associated with 3-methylpyridine, however, did not bear any resemblance to the other two substrates in this respect. The presence of a catalyst did improve the autoclave oxidation of this methylpyridine, but here the iron containing catalyst appeared to be more efficient than the copper ones.

Unfortunately, no COD data are available for any of the $Fe(III)/H_2O_2$ catalysed autoclave reactions of each of the methylpyridines. However, from the results that are available, it would appear that in order to get an appreciable COD reduction for a simple mixture of 2-, 3-, and 4-methylpyridine, a mixture of iron(II) and copper(II) in the presence of hydrogen peroxide should be used. This compares well with the work reported by Chowdbury et al which established that under WAO conditions, a mixture of iron(II) and copper(II) in the presence of hydrogen peroxide produced an efficient catalytic system[13] for the oxidation of various organic substances.

2.5. Future work

The study so far has investigated each of the oxidation reactions using GC/MS techniques. However, it would appear that this analysis has not provided a full picture regarding the products of oxidation. Further investigation using LC/MS techniques, initially using the method developed for separation using HPLC (2.1.3.), would be appropriate to complete this study and identify the presence of involatile products formed in the oxidation process.

The WAO process is thought to proceed in a radical fashion with hydroxyl radicals initiating the process. Some of the products observed from the oxidation of 2-, 3-, and 4-methylpyridines support this theory. However, it may be of use to confirm this idea conclusively by allowing the autoclave oxidation reactions discussed to proceed in the presence of a radical trap (Chapter 3, section 3.5.6.). The effect of each of the catalytic systems has been considered with reference to COD values. This value represents the oxidisable organic content that remains after oxidation is complete. Quantitatively determining the amount of starting material i.e. the methylpyridines remaining after oxidation would also lend support to the investigation regarding the effectiveness, if any, of the oxidation process taking place (Chapter 3, section 3.3.).

2.6. References

1. Chowdbury A.K. & Ross L.W., Catalytic Wet Oxidation of Strong Waste Waters, *AIChE Symposium Series - Water 1975*, **71**, 46-58.
2. Oliver B.G. & Bothen K.D., Determination of Chlorobenzenes in Water by Capillary Gas Chromatography, *Analytical Chemistry*, 1980, **52**, 2066-2069.
3. Conditt M.K. & Sievers R.E., Microanalysis of Reaction Products in Sealed Tube Wet Air Oxidations by Capillary Gas Chromatography, *Analytical Chemistry*, 1984, **56**, 2620-2622.
4. Lao R.C., Thomas R.S., Bastien P., Halman R.A. & Lockwood J.A., Analysis of Organic Priority and Non-Priority Pollutants in Environmental Samples by GC/MS/Computer Systems, Analytical Techniques in Environmental Chemistry 2., edited by Albaiges J., pp 107-118.
5. Krupcik J., Leclercq P.A., Garaj J. & Simova A., Analysis of Alkylated Mixtures of Polychlorinated Biphenyls by Capillary Gas Chromatography-Mass Spectrometry, *J. Chromatography*, 1980, **191**, 207-220.
6. Talley C.P., High Speed Ion Exchange Chromatography of Several Monosubstituted Pyridine Isomers, *Analytical Chemistry*, 1971, **43**, 1512.
7. Baillod C.R., Faith B.M. & Masi O., Fate of Specific Pollutants during Wet Oxidation and Ozonation, *Environmental Progress*, 1982, **1**, 217-226.
8. Joule J.A., Mills K. & Smith G.F., Heterocyclic Chemistry, Chapman and Hall Publications, Third Edition, 1995.
9. Randall T.L. & Knopp P.V., Detoxification of Specific Organic Substances by Wet Oxidation, *Journal WPCF*, 1980, **52**, 2117-2130.
10. Walling C., Fenton's Reagent Revisited, *Acc. Chem. Res.*, 1975, **8**, 4, 125-131.
11. Barton D.H.R. & Doller D., The Selective Functionalisation of Saturated Hydrocarbons: Gif Chemistry, *Acc. Chem. Res.*, 1992, **25**, 504-512.

12. Barton D.H.R., Boivin J., Schwartzentruber K., Ozbalik N., Gaudin D. & Jankowski K., GC-MS Study of Gif-Oxidation System. GC-MS Contribution to Elucidation of Gif-Oxidation Mechanism on the Formation of Bipyridines and Coupled Pyridines, *Spectroscopy Letters*, 1987, **20**, 12, 963-981.

13. Chowdbury A.K. & Ross L.W., Catalytic Wet Oxidation of Strong Waste Waters, *AIChE Symposium Series - Water 1975*, **71**, 46-58.

14. Goldstein S., Meyerstein D. & Czapski G., The Fenton Reagents, *Free Radical Biology and Medicine*, 1993, **15**, 435-445.

Chapter 3

Fenton and Related-Catalysed Oxidation Reactions of Methylpyridines at Ambient Temperature and Atmospheric Pressure

Chapter 3 - Fenton and Related-Catalysed Oxidation Reactions of Methylpyridines at Ambient Temperature and Atmospheric Pressure

The oxidation of 2-, 3-, and 4-methylpyridines was carried out at room temperature and atmospheric pressure using various catalyst systems. The catalyst systems were all metal-containing and related to the Fenton system, and to those that had been used in the autoclave oxidation reactions detailed in Chapter 2. The experimental conditions used in each of the cases studied were related to those used for the hydroxylation of benzene using Fenton's reagent[1]. Ito et al established optimum conditions for the effective formation of phenol from benzene and the criteria established were adopted in this study.

3.1. Experimental

All of the oxidation reactions considered in this chapter were carried out under aqueous conditions. Each catalyst system was prepared by first taking the appropriate amount of the metal salt (3.1.1.) and dissolving it in dilute sulphuric acid (25 cm^3, 1 mol dm^{-3}). The appropriate methylpyridine (0.01 mol) was then added to the aqueous acidic solution and the reaction vessel was purged with nitrogen by use of a nitrogen balloon. Then with ice cooling where necessary, a hydrogen peroxide mixture was added dropwise. The hydrogen peroxide mixture contained hydrogen peroxide (0.1 mol, 6 or 30% w/v solution in water) together with dilute sulphuric acid (25 cm^3, 1 mol dm^{-3}) and the volume of this mixture was made up to 85 cm^3 by the addition of water. This was done since, initially, different concentrations of hydrogen peroxide in water, supplied by Aldrich, were used. The concentrations used included a 6% w/v solution and a 30% w/v solution of hydrogen peroxide in water. The aim was therefore to ensure that all reactions were carried out in the same volume so that results might be more comparable. Each of the oxidation reactions was allowed to

continue for a period of time which ranged from 30 minutes to 24 hours, and the appropriate time was recorded accordingly.

3.1.1. Catalysed Oxidation Reactions

Various catalyst systems have been used in the study discussed in this chapter. They included mixtures that have been suggested in the literature[2] and which proved to be effective under the autoclave conditions discussed in Chapter 2. Other catalytic systems that had also been suggested in the literature as having oxidising capabilities were also studied[3]. The catalyst systems that were used are indicated below:-

Iron(II) sulphate ($1x10^{-2}$ mol)/hydrogen peroxide

Iron(III) sulphate ($1x10^{-2}$ mol)/hydrogen peroxide

Copper(II) sulphate ($1x10^{-2}$ mol)/hydrogen peroxide

Iron (II) sulphate, copper(II) sulphate ($1x10^{-2}$ mol)/hydrogen peroxide

Titanium(III) chloride ($1x10^{-2}$ mol)/hydrogen peroxide

Vanadium(IV) sulphate ($1x10^{-2}$ mol)/hydrogen peroxide

Iron(II) sulphate ($1x10^{-2}$ mol)/ ammonium persulphate

The oxidation of each of the methylpyridines was studied using each of these catalysts. The results, together with information from the literature, led to the investigation of other oxidation reactions. This included carrying out the Fenton catalysed oxidation reactions of 2-, 3-, and 4-methylpyridines in the presence of TEMPO, a radical trap, and EDTA, a complexing agent, respectively. The oxidation of each of the methylpyridines was also carried out using ozone as the oxidising system. The results of these latter reactions will be discussed, at the end of this chapter, but sample preparation and analysis was the same for all catalysed oxidation reactions considered.

3.1.2. Sample Preparation

After the reaction time was complete, sample preparation involved altering the pH of the reaction mixture, where required, to neutral by the addition of sodium hydroxide (2 mol dm^{-3}). The insoluble metal salts that formed were filtered off and the remaining aqueous mixture was extracted with either dichloromethane or diethyl ether (4 x 100 cm^3). The organic layers were combined and dried using magnesium sulphate, and the extract was evaporated to approximately 2 cm^3 under reduced pressure. The dichloromethane/diethyl ether-insoluble 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.

3.1.3. Sample Analysis

The analysis of the oxidation products formed in all of the reactions considered in this chapter involved the use of both Gas Chromatography-Mass Spectrometry (GC-MS) and High Performance Liquid Chromatography (HPLC) techniques. The instruments and conditions that were used are identical to those found in Chapter 2, section 2.1.3.

3.1.4. Summary

All of the catalysed oxidation reactions considered in this chapter contain unchanged starting material at the end of each reaction, in different amounts. The amount remaining was determined quantitatively in some of the reactions considered, so that direct comparisons could be made between each of the catalysts used. Details concerning quantitative analysis procedures will appear, where appropriate, in this chapter.

From 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 sections that follow in this chapter.

It is also important to note, at this point, that different GC temperature programme ramps and different instruments were used to investigate these oxidation reactions, and hence aid the determination of the nature of the oxidation products formed in each case. Therefore, any differences noted in retention time values for the same compounds have to be considered with reference to the precise analytical conditions used in the analysis of each of the samples. Hence, more reliable comparisons can be made between the products of oxidation formed by each of the methylpyridines in the various reactions investigated.

3.2. The Catalysed Oxidation of 2-, 3-, and 4-Methylpyridines

3.2.1. Fenton's Reagent and Fenton-Related Reagents

3.2.1.1. 2-Methylpyridine

a) Analysis by GC-MS

The initial study involved the oxidation of 2-methylpyridine using Fenton's reagent as the catalyst. The oxidation reactions were carried out over time periods of 30 minutes, 2 hours and 24 hours, respectively, and the oxidation products observed in each reaction are summarised in Table 1 below. Figure 1

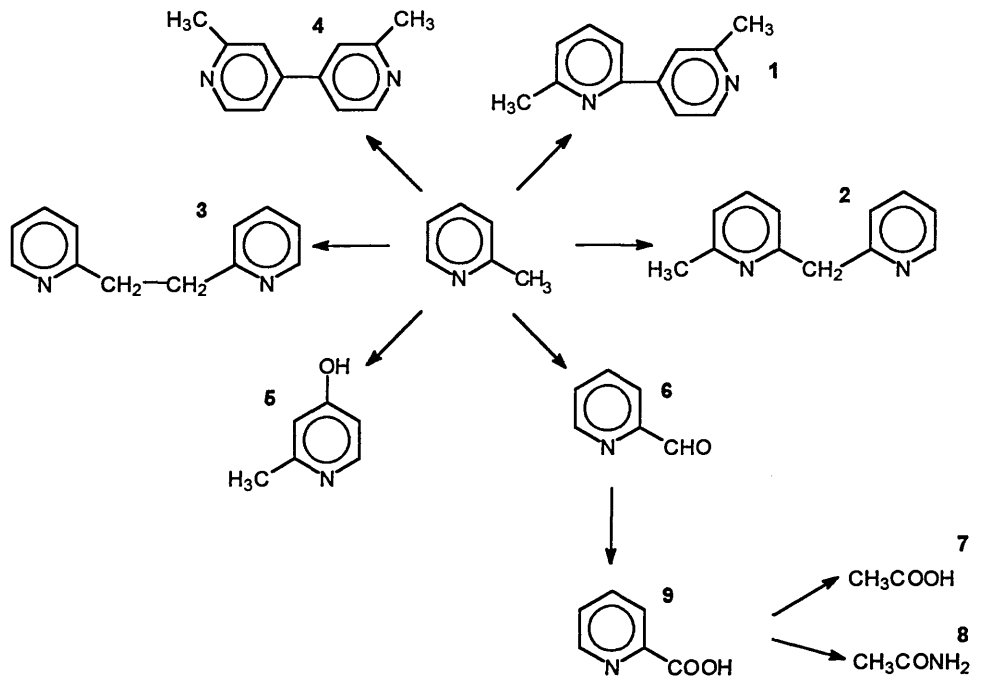
represents a possible pathway for their formation. For the 2 hour and 24 hour reactions, instrument 1 was used for the analysis; for the 2 hour reaction temperature programme 2 was adopted and for the 24 hour reaction temperature programme 1 was used. The 30 minute reaction was analysed using temperature programme 2 on instrument 2.

Table 1 - Oxidation products arising from the Fenton-catalysed oxidation of 2-methylpyridine

Component	t_R			RMM	Proposed Structure
	0.5hr	2hr	24hr		
1*	15.56	14.81	-	184	2,2'-dimethyl-2,4-bipyridine
2	-	16.13	-	184	2-methyl-6-(2-pyridylmethyl)pyridine
3	18.01	16.63	-	184	1,2-bis-(2-pyridyl)ethane
4*	18.35	17.07	-	184	2,2'-dimethyl-4,4'-bipyridine
5*	16.32	15.12	-	109	4-hydroxy-2-methylpyridine
6	6.52	-	-	107	pyridine-2-carboxaldehyde
7	5.27	5.76	11.41	60	acetic acid
8	-	-	15.54	59	acetamide

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

Figure 1



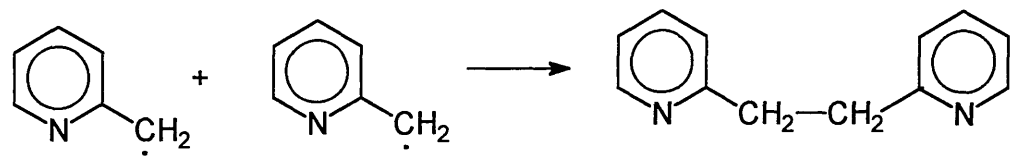
From the table it appears that allowing the reaction to continue for 24 hours takes the reaction almost to completion in that the only oxidation products observed were acetic acid and acetamide. Acetic acid is an expected oxidation product as attack on the acid by a hydroxyl radical •OH generates the radical $\bullet CH_2COOH$ which is then reduced back to the starting compound by the iron(II) present in the mixture[3].

Allowing the reaction to continue for only 30 minutes is sufficient time for the reaction to give an extensive range of oxidation products. This included several oxidation products that all exhibited an apparent molecular ion at *m/z* 184 and some of these structures were still observed after a 2 hour period. Their formation would presumably occur via a similar process to that occurring in the catalysed autoclave reactions considered in Chapter 2, as components **2**, **3** and **4** were all observed in the iron(III) catalysed autoclave oxidation of 2-methylpyridine.

Components **2** and **3** were identified as 2-methyl-6-(2-pyridylmethyl)pyridine and 1,2-bis-(2-pyridyl)ethane respectively by comparison with the authentic standards that had been previously prepared. Such structures will have been formed via radical reactions taking place which are represented in Scheme 1 below.

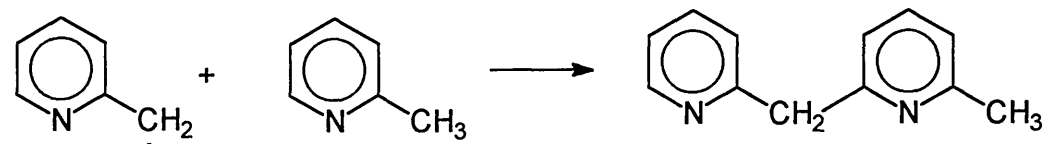
Scheme 1

Radical coupling



1,2-bis-(2-pyridyl)ethane **3**

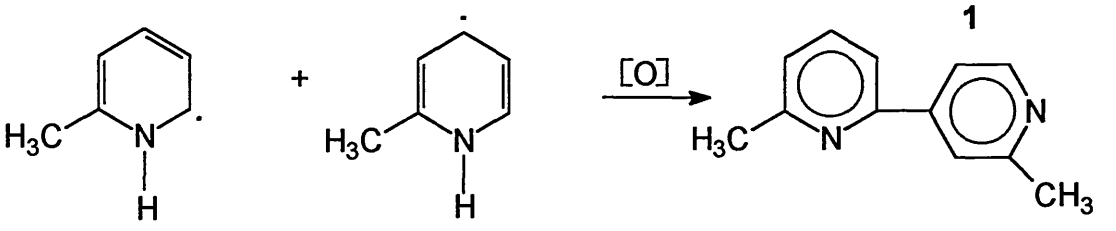
Radical substitution



2-methyl-6-(2-pyridylmethyl)pyridine **2**

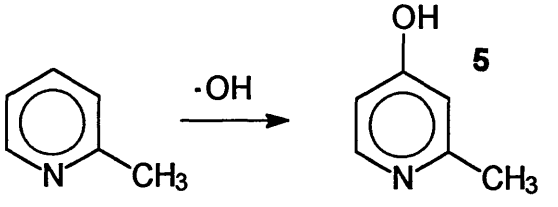
Components **1** and **4** will also have been formed via a radical process. The formation of 2,2'-dimethyl-4,4'-bipyridine **4** was represented in Scheme 9 in Chapter 2, where a radical coupling reaction was responsible for the formation of **4**. The formation of component **1** will have occurred in a similar way to this, except that the radical coupling reaction will have occurred between two different radicals as shown below.

Scheme 2



Component **5** was observed in both the 30 minute and 2 hour reactions. This component exhibited an apparent molecular ion at *m/z* 109 and it was also observed as an oxidation product in the iron- and copper-catalysed autoclave oxidation reactions. The formation of this component is evidence of the presence of hydroxyl radicals •OH as the structure of **5** indicates that this radical has undergone a substitution reaction at the pyridine ring of the substrate, 2-methylpyridine - Scheme 3.

Scheme 3



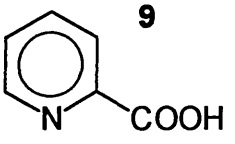
4-hydroxy-2-methyl pyridine

Components **6**, **7**, and **8** are expected oxidation products. Component **6** was identified as pyridine-2-carboxaldehyde which has formed as a result of the oxidation of the methyl group attached to the pyridine ring in 2-methylpyridine. Components **7** and **8** were identified as acetic acid and acetamide respectively. Their presence indicates that ring destruction has taken place and that the reaction is moving towards complete oxidation of the ring system.

b) Analysis by HPLC

The identification of involatile oxidation products that may have been formed in the Fenton catalysed oxidation of 2-methylpyridine requires the use of HPLC techniques. As in the autoclave oxidation reactions studied in Chapter 2, an expected oxidation product is pyridine-2-carboxylic acid. Therefore, analysis of the oxidation reaction that had been left for 24 hours was carried out to determine if the acid was present as an oxidation product.

The HPLC method that is outlined in Chapter 2, section 2.1.3. was used to analyse the 24 hour reaction and no sample preparation was required. The chromatogram obtained only contained two large peaks (t_R = 3.09 and 5.75 mins), the latter being identified as the acid, pyridine-2-carboxylic acid **9** by spiking the sample with a small amount of the standard - Appendix 11.



An extra peak was not observed in the chromatogram despite the addition of the standard, confirming that the peak at t_R=5.75 is due to the presence of pyridine-2-carboxylic acid being formed as an oxidation product. The identity of the other significant component (t_R = 3.09 mins) has not yet been determined.

The detection of pyridine-2-carboxylic acid as an oxidation product after a 24 hour reaction time period is in contrast with the autoclave oxidation reaction. It would seem that under the Fenton oxidation conditions at room temperature, the carboxylic acid is not undergoing the decarboxylation process observed in the autoclave, which leads to the formation of pyridine. It is significant that pyridine was not detected as an oxidation product under the Fenton conditions

and that a significant amount of the acid was detected at the end of the catalysed reaction.

3.2.1.2. 3-Methylpyridine

a) Analysis by GC-MS

The oxidation of 3-methylpyridine was carried out using Fenton's reagent as the catalytic system and the reaction was monitored over time periods of 2 and 24 hours, respectively. The oxidation reaction carried out for 24 hours was analysed using instrument 1 and temperature programme 1, whereas the 2 hour oxidation reaction was analysed using instrument 2 and temperature programme 2. The oxidation products observed have been assigned structures by comparison with either standard materials, or by consideration of mass spectral data and they are summarised in Table 2 below. Figure 2 represents a possible pathway for their formation.

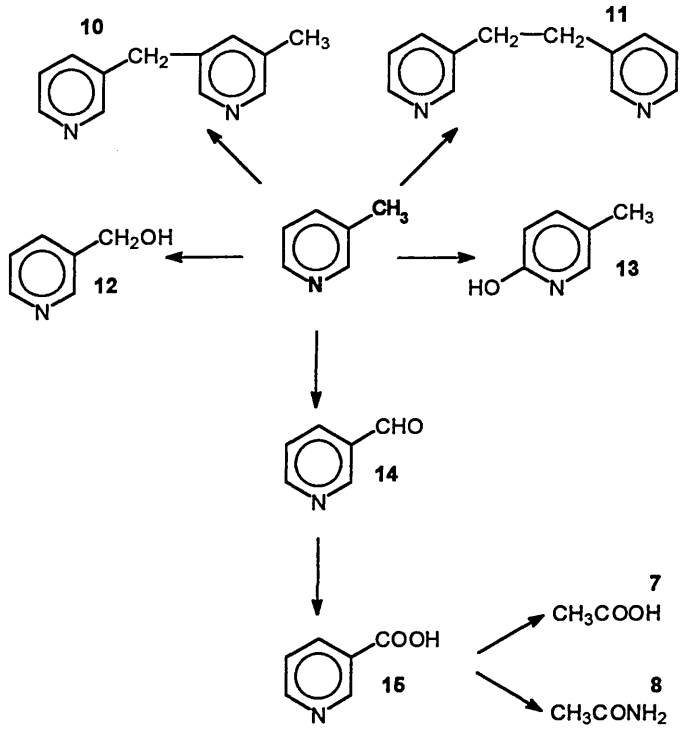
Table 2 - Oxidation products arising from the Fenton-catalysed oxidation of 3-methylpyridine

Component	t_R		RMM	Proposed Structure
	2hr	24 hr		
10*	19.43	27.48	184	3-methyl-5-(3-pyridylmethyl)pyridine
11	19.73	27.93	184	1,2-bis-(3-pyridyl)ethane
12*	14.43	20.58	109	3-hydroxymethylpyridine
13*	17.00	23.38	109	2-hydroxy-5-methylpyridine
14	8.91	14.80	107	pyridine-3-carboxaldehyde

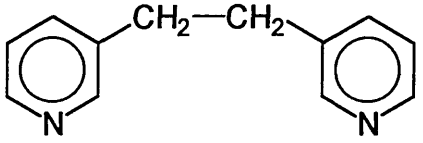
7	5.67	-	60	acetic acid
8	-	15.37	59	acetamide

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

Figure 2

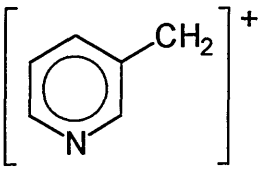


The first observation to be made from the Fenton catalysed oxidation of 3-methylpyridine is that allowing the oxidation to proceed for 24 hours does not significantly affect the range of oxidation products formed. Components **10** and **11** were observed in both reactions, exhibiting the same apparent molecular ion. Component **11** was identified by comparison with the standard as being 1,2-bis-(3-pyridyl)ethane,



1,2-bis-(3-pyridyl)ethane

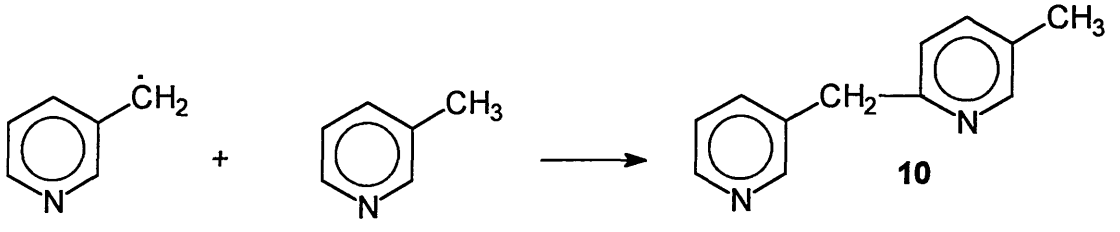
since the mass spectrum of **11** contained a stable fragment ion at *m/z* 92 shown below.



This compares with the standard material, and **11** is thought to be formed via a radical coupling reaction similar to that seen in Scheme 1, earlier in this chapter.

Component **10** also exhibited an apparent molecular ion at m/z 184 but this component possessed a different mass spectrum to that for component **11**, as here no stable fragment ion at *m/z* 92 was observed. The structure of this component was thought to arise as a result of a radical reaction also, but this time a radical substitution reaction is responsible for the formation of 3-methyl-5-(3-pyridylmethyl)pyridine **10**, as indicated in Scheme 4.

Scheme 4



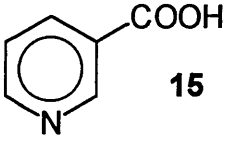
Components **12** and **13** both have a relative molecular mass of 109, but they have different mass spectra when compared with each other - Appendix 2 & 12. Component **12** was considered to be 3-hydroxymethylpyridine as its mass spectrum compared with that of the standard material, 2-hydroxymethylpyridine, both exhibiting a stable fragment ion at *m/z* 108 and

the molecular ion at *m/z* 109. Component **13**, however, was thought to be 2-hydroxy-5-methylpyridine, resulting from a substitution reaction occurring between the pyridine ring of 3-methylpyridine and a hydroxyl radical. The mass spectrum of this component contained a stable fragment ion at *m/z* 80 but, in this case, no stable fragment was observed at *m/z* 108. The molecular ion did, however, appear again at *m/z* 109. These components were also observed as oxidation products in the autoclave oxidation reactions of 3-methylpyridine discussed in Chapter 2.

Pyridine-3-carboxaldehyde **14** was formed in both of the reactions being considered here, forming as a result of oxidation of the methyl group in the parent substrate. Ring destruction products were also generated in the form of acetamide **8** and acetic acid **7**.

b) Analysis by HPLC

The identification of involatile oxidation products formed in the Fenton catalysed oxidation of 3-methylpyridine requires the use of HPLC techniques. The analysis was carried out using those conditions outlined in Chapter 2, section 2.1.3. and, as was the case for the oxidation of 2-methylpyridine using Fenton's reagent, pyridine-3-carboxylic acid **15** was detected as an oxidation product.



15

3.2.1.3. 4-Methylpyridine

a) Analysis by GC-MS

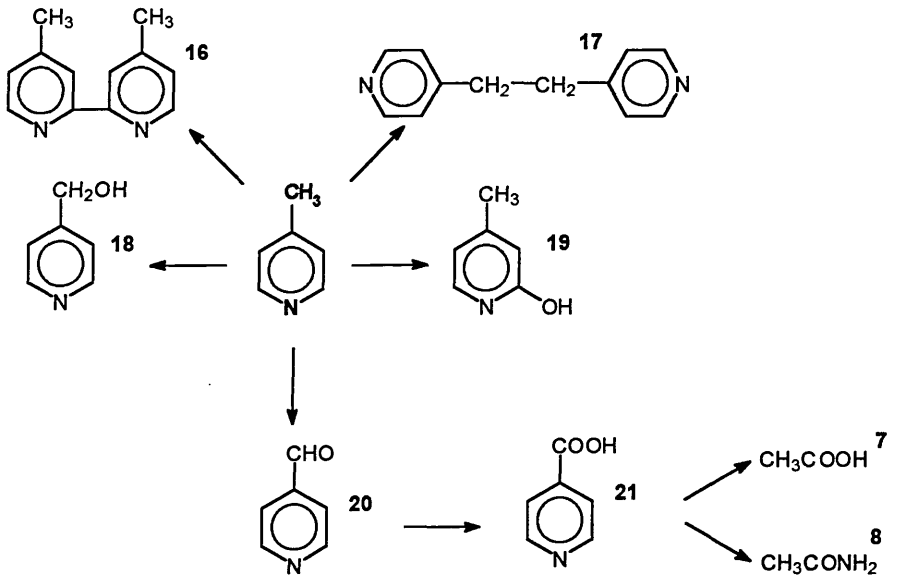
The Fenton-catalysed oxidation of 4-methylpyridine was carried out over two time periods of 2 and 24 hours, respectively. Both reactions were analysed using instrument 1, with the two hour reaction having been analysed using temperature programme 1 and the 24 hour reaction having been analysed using temperature programme 2. The oxidation products have been assigned structures by comparison with the authentic standard or by consideration of mass spectral data and they are summarised in Table 3 below. Figure 3 represents a possible pathway for their formation.

Table 3 - Oxidation products arising from the Fenton-catalysed oxidation of 4-methylpyridine

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
16	19.75	-	184	4,4'-dimethyl-2,2'-bipyridine
17	20.15	-	184	1,2-bis-(4-pyridyl)ethane
18*	14.70	16.73	109	4-hydroxymethylpyridine
19*	16.27	-	109	2-hydroxy-4-methylpyridine
20	8.29	-	107	pyridine-4-carboxaldehyde
7	5.72	11.27	60	acetic acid
8	9.68	15.37	59	acetamide

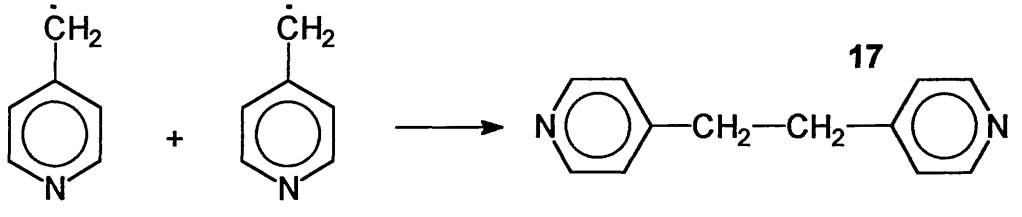
* indicates that proposed structure has not been proved by comparison with the authentic substance

Figure 3

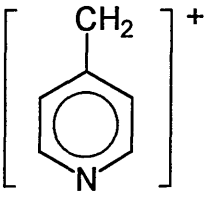


From the table it can be seen that allowing the oxidation of 4-methylpyridine to proceed for only a short time period (2 hours) produces a greater range of oxidation products than is observed at the end of a 24 hour period. This includes components **16** and **17** which are dimeric structures, thought to arise as a result of radical reactions taking place. The structures of both components were identified by comparison with the authentic standard material. Component **17** is thought to arise as a result of a radical coupling reaction to form 1,2-bis-(4-pyridyl)ethane as shown in Scheme 5.

Scheme 5



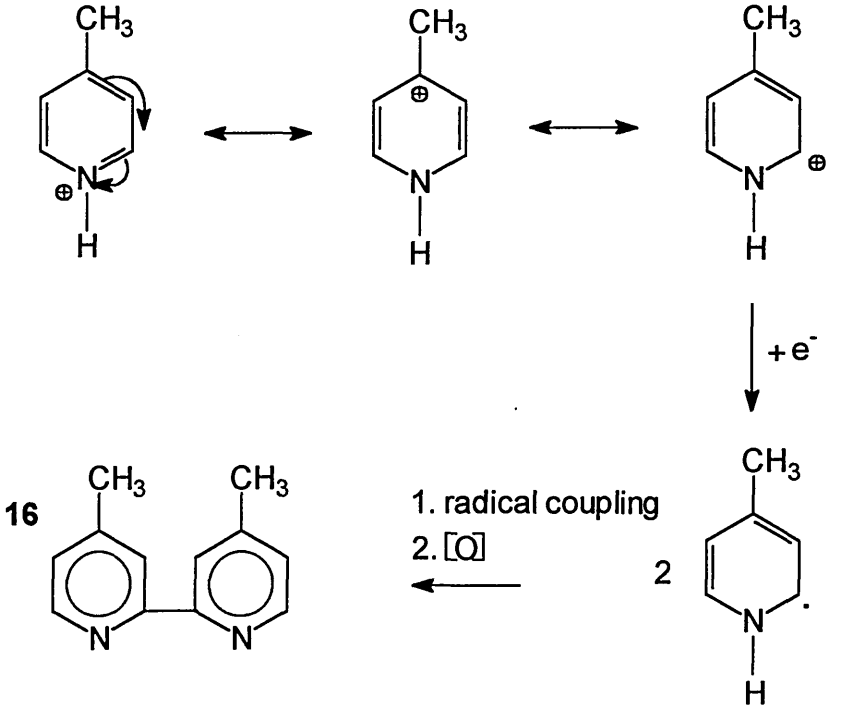
The mass spectrum for this component contained a stable fragment ion at *m/z* 92 due to the formation of the fragment ion indicated below,



and this compares with the standard material.

Component **16** is also thought to arise as a result of a radical coupling reaction but the coupling reaction occurs via radicals that are formed as shown in Scheme 6. The radicals that are generated then couple together to form 4,4'-dimethyl-6,6'-bipyridine **16** and the mass spectrum of this component compares with that of the standard material as both exhibit a base peak at *m/z* 184 and their retention times match also.

Scheme 6

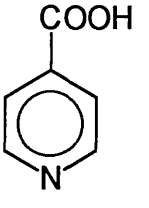


Components **18** and **19** both have the same relative molecular mass of 109 but both have different mass spectra when compared with each other, and therefore they have different structures. Component **18** has been identified as 4-hydroxymethylpyridine by comparison of the mass spectrum with that of 2-hydroxymethylpyridine. Although the comparison substance is not identical to component **18**, they are very similar and their mass spectra are alike in that both give rise to a base peak at *m/z* 108 and a stable fragment ion at *m/z* 80. Component **19** was thought to be 2-hydroxy-4-methylpyridine forming as a result of hydroxyl substitution occurring at the pyridine ring of the parent substrate, as shown in Scheme 8 in Chapter 2. This component was also observed as a product in the autoclave oxidation reactions involving 4-methylpyridine.

Components **20**, **7**, and **8** were identified as pyridine-4-carboxaldehyde, acetic acid, and acetamide, respectively, all of these being expected oxidation products.

b) Analysis by HPLC

The identification of any involatile oxidation products again requires the use of HPLC techniques. Using the experimental procedure outlined in Chapter 2, section 2.1.3. for analysis by HPLC, the 24 hour Fenton catalysed oxidation of 4-methylpyridine was analysed. Pyridine-4-carboxylic acid **21** was detected as an oxidation product as was the case for the Fenton catalysed oxidation of 2-, and 3-methylpyridines.



21

The subsequent decarboxylation of the acid is not expected under the conditions of room temperature and atmospheric pressure used in this study. Pyridine was not observed in the GC/MS study of this system.

3.2.1.4. Summary

The oxidation of each of the methylpyridines using Fenton's reagent generates an extensive array of oxidation products. The structure of these products resembles those seen earlier in Chapter 2, which arose from the autoclave oxidation reactions. Since the structures of the products are very similar to those seen in Chapter 2, it would seem that the mechanisms for their formation must be similar i.e. there is some form of free radical chemistry occurring in the reactions where Fenton's reagent is used to oxidise each of the methylpyridines. This assumption is based largely on the formation of a range of dimeric structures in each of the reactions studied here. The Fenton-catalysed oxidation reactions do appear to be time dependent. This is apparent especially in the oxidation of 2-, and 4-methylpyridines, as allowing the reaction to proceed overnight produces a greater degree of destructive oxidation as fewer oxidation products are observed.

Other Fenton-like systems were considered in the oxidation of each of the methylpyridines e.g. a mixture of iron(III) and hydrogen peroxide, copper(II) and hydrogen peroxide, and a mixture of iron(II), copper(II) and hydrogen peroxide. All of these oxidising systems generated an extensive range of oxidation products very similar to those described above. However, in order to draw any comparisons between each of them, quantitative analysis was carried out using the decrease in concentration of the appropriate methylpyridine during each of the oxidation reactions as an indication of the effectiveness of the system used.

3.3. Quantitative Analysis of the Fenton-Catalysed and Related Oxidation Reactions of 2-, 3-, and 4-Methylpyridine

Quantitative analysis was carried out using GC/MS techniques. The initial part of the study involved establishing if the GC/MS system responded to changes in concentration of 2-, 3-, and 4-methylpyridine in a linear fashion. To do this calibration graphs were plotted by use of appropriate standards. In the preparation of the standards, each of the methylpyridines was supplied by Aldrich, diethyl ether used for extraction was supplied by Prolabo and the water used was distilled.

3.3.1. 2-Methylpyridine - Preparation and Analysis of Standards

Two stock solutions were prepared

Stock Solution A - 1 cm^3 of 2-methylpyridine in 100 cm^3 of water

Stock Solution B - 0.4 cm^3 of 3-methylpyridine in 100 cm^3 of water

where stock solution B was the internal standard used.

The standards were then prepared by taking set quantities of each of the stock solutions, A and B, and adding them to water to give 10 cm^3 aliquots. The volumes of solution A and B used are found in the table below.

Table 4

Stock A/cm3	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 of the standards was prepared in duplicate and extracted with 2 x 5 cm^3 of diethyl ether. The organic layers were combined and dried using magnesium sulphate and each of the extracts were analysed by GC/MS.

GC/MS Analysis

The conditions for analysis that were used here are detailed in Chapter 2, section 2.1.3. with instrument 1 being used for the analysis. The temperature programme adopted involved a ramp of 70°C to 90°C @ 2°C/min.

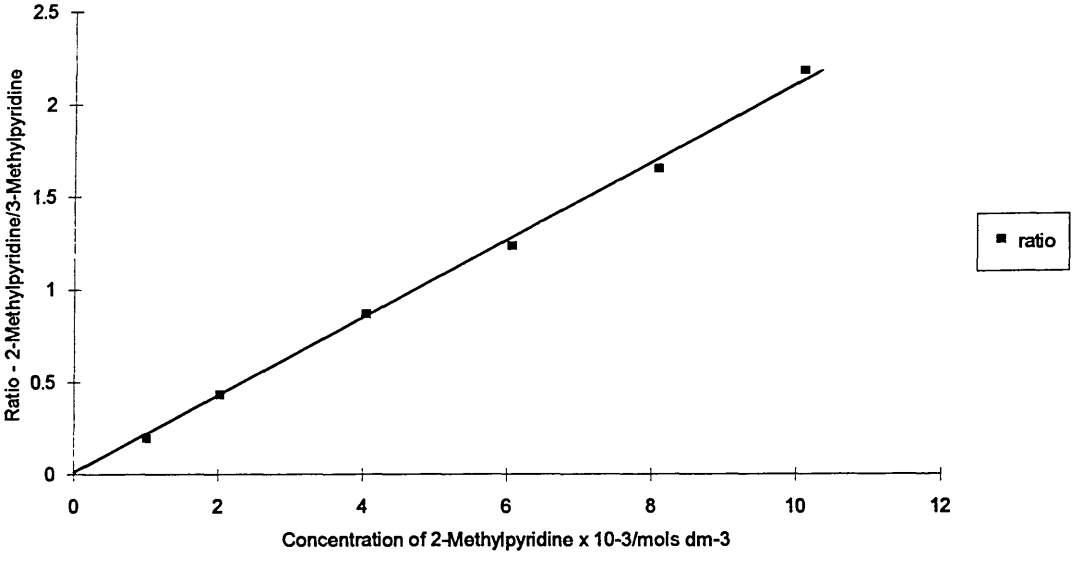
Results

Table 5

Conc. of 2-methylpyridine x 10^{-3} /mol dm^3 - (A)	Ratio - 2-methylpyridine(A) /3-methylpyridine (B)	% RSD
1.01	0.196	7.0
2.03	0.435	12.0
4.06	0.869	7.8
6.08	1.236	4.7
8.11	1.655	3.6
10.13	2.183	8.8

The values are represented graphically below and the graph is found to be a straight line with a correlation coefficient of 0.9987

Figure 4



This shows that the GC/MS system does respond linearly to changes in the concentration of 2-methylpyridine.

3.3.2. 3-Methylpyridine - Preparation and Analysis of Standards

The preparation and analysis of standards for 3-methylpyridine was carried out in exactly the same way as for those in 3.3.1. above, except that here the internal standard (stock solution B) used was 2-methylpyridine.

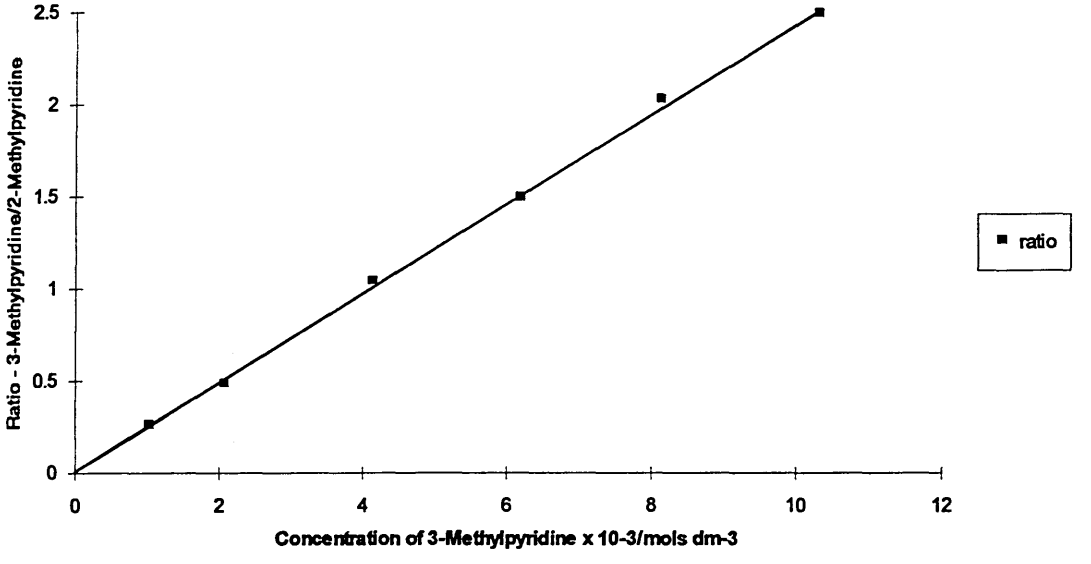
Results

Table 6

Conc. of 3-methylpyridine x 10^{-3} /mol dm^3 - (A)	Ratio - 3-methylpyridine (A) /2-methylpyridine (B)	% RSD
1.03	0.266	4.4
2.06	0.490	5.8
4.12	1.044	4.3
6.17	1.498	5.4
8.11	2.033	3.4
10.30	2.499	1.2

The values are represented graphically below and the graph is found to be a straight line with a correlation coefficient of 0.9995

Figure 5



This shows that the GC/MS system does respond linearly to changes in concentration of 3-methylpyridine

3.3.3. 4-Methylpyridine - Preparation and Analysis of Standards

The preparation and analysis of standards was carried out again in exactly the same way as for those in 3.3.1. above, and again the internal standard (stock solution B) used was 2-methylpyridine.

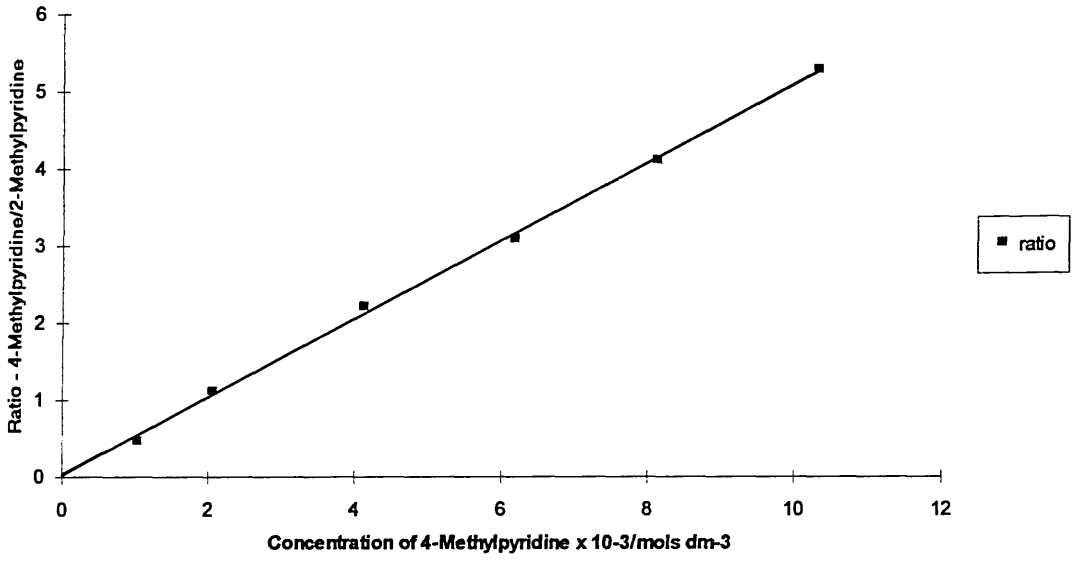
Results

Table 7

Conc. of 4-methylpyridine x 10^{-3} /mol dm^3 - (A)	**Ratio - 4-methylpyridine (A) /2-methylpyridine (B)**	**% RSD**
1.03	0.473	6.3
2.06	1.123	4.6
4.12	2.222	9.6
6.17	3.101	10.6
8.11	4.120	7.1
10.30	5.295	4.6

The values are represented graphically below and the graph is a straight line with a correlation coefficient of 0.9993.

Figure 6



This shows that the GC/MS system responds linearly to changes in the concentration of 4-methylpyridine.

3.3.4. Quantitative Analysis of the Fenton-Catalysed and Related Oxidation Reactions of 2-, 3-, and 4-Methylpyridines - Experimental

The oxidation reactions were carried out exactly as outlined in 3.1. earlier in this chapter. 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 10 cm^3 aliquot was neutralised by the addition of sodium hydroxide (2 mol dm^{-3}), extracted with 2 x 5 cm^3 of diethyl ether, and dried using magnesium sulphate. Each of the samples was then analysed five times using GC/MS techniques and the GC conditions used for the analysis of the standards in 3.3.1. above were adopted.

3.3.5. Results

The tables below list each of the different Fenton and related catalytic systems that were considered for the oxidation of 2-, 3-, and 4-methylpyridines over two different time periods. The tables include the ratio values observed between the remaining methylpyridine and the appropriate internal standard used, that had both been extracted using diethyl ether (2 x 5 cm^3). The associated methylpyridine concentration values, indicating the amount of each of the methylpyridines remaining after the oxidation reaction was complete, were then determined from the appropriate calibration graph. These values are expressed as a percentage of the initial concentration in each of the tables below.

Table 8 - 2-Methylpyridine

Catalyst	**Ratio Values**	**% RSD**	**Concentration of 2-Methylpyridine x 10^{-3}/ mol dm^{-3}**	**2-Methylpyridine Remaining (%)**
$Fe(II)/H_2O_2$				
30 minutes -	1.018	2.1	4.85	49.6
24 hours -	0.0556	5.1	0.33	3.3
$Fe(II)/Cu(II)/H_2O_2$				
30 minutes	1.479	1.7	7.02	71.8
24 hours	0.162	4.2	0.83	8.5
$Cu(II)/H_2O_2$				
30 minutes	1.264	3.1	6.01	61.5
24 hours	1.449	5.8	6.88	70.3
$Fe(III)/H_2O_2$				
30 minutes	1.350	3.5	6.44	66.0
24 hours	0.0988	4.9	0.53	5.4

Table 9 - 3-Methylpyridine

Catalyst	Ratio Values	% RSD	Concentration of 3-Methylpyridine x 10^{-3}/ mol dm^{-3}	3-Methylpyridine Remaining (%)
$Fe(II)/H_2O_2$				
30 minutes -	1.528	3.1	6.21	63.5
24 hours -	0.675	3.0	2.72	27.8
$Fe(II)/Cu(II)/H_2O_2$				
30 minutes	1.929	5.1	7.85	80.3
24 hours	0.985	4.0	3.99	40.8
$Cu(II)/H_2O_2$				
30 minutes	>2.375	5.1	>9.68	>99.0
24 hours	1.661	2.0	6.76	69.1
$Fe(III)/H_2O_2$				
30 minutes	>2.375	2.4	>9.68	>99.0
24 hours	-	-	<0.1	<1.0

Table 10 - 4-Methylpyridine

Catalyst	Ratio Values	% RSD	Concentration of 4-Methylpyridine x 10^{-3}/mol dm^{-3}	4-Methylpyridine Remaining (%)
$Fe(II)/H_2O_2$				
30 minutes -	1.396	1.3	2.70	27.6
24 hours -	-	-	< 0.1	< 1.0
$Fe(II)/Cu(II)/H_2O$				
2	1.302	1.6	2.51	25.7
30 minutes	-	-	< 0.1	< 1.0
24 hours				
$Cu(II)/H_2O_2$				
30 minutes	2.066	1.9	4.01	41.0
24 hours	1.742	3.1	3.37	34.5
$Fe(III)/H_2O_2$				
30 minutes	1.629	3.9	3.15	32.2
24 hours	0.0799	7.3	0.11	1.2

3.3.6. Summary

From the results in Tables 8, 9, and 10, it appears that under the oxidising conditions indicated 4-methylpyridine is the most easily oxidised, with the Fenton system and the iron(II)/copper(II)/hydrogen peroxide mixture being the most effective. As is expected, 3-methylpyridine is the least reactive of all the methylpyridines discussed here. However, the iron(III)/hydrogen peroxide mixture seems to be an efficient catalyst when used to oxidise this substrate as using this catalyst gives rise to the destruction of more than 99% of the initial concentration of the 3-methylpyridine over a 24 hour period.

The oxidation of 2-methylpyridine was found to be efficient for all of the oxidising systems over a 24 hour period, except for the copper(II)/hydrogen peroxide catalyst which did not produce a degree of destruction of more than 90% of the initial 2-methylpyridine concentration over this time period. The copper(II)/hydrogen peroxide catalyst system was also found to be the least efficient catalyst when used to oxidise both 3-, and 4-methylpyridines.

It seems, from the oxidation of 2-, 3-, and 4-methylpyridines, that both iron(II) and iron(III), in the presence of hydrogen peroxide, are efficient catalysts. However, copper(II) has been shown to be less effective and in the presence of the Fenton catalyst, no improvement in the performance of the new catalyst (iron(II)/copper(II)/hydrogen peroxide) formed is obvious under the conditions used in this study.

The performance of each of the catalysts investigated here could be established further by investigating the kinetics associated with each system. A preliminary study was therefore carried out which involved a consideration of the kinetics associated with Fenton's reagent using 2-methylpyridine as the

substrate. An understanding of the kinetics is an important way of optimising a system as further information is gained regarding the mechanism of the process.

3.4. A Kinetic Study of the Fenton-Catalysed Oxidation of 2-Methylpyridine

The course of oxidation of 2-, 3-, and 4-methylpyridines using Fenton's reagent as a catalyst has been discussed. This investigation has involved the analysis of oxidation products formed in the process in order to provide an insight into the mechanism of oxidation occurring under such conditions. From the literature, a limited range of kinetic studies has revealed that the wet air oxidation (WAO) of organics is found to be first order with respect to the substrate concentration[4]-[6].

Therefore, the study of the Fenton-catalysed oxidation reaction of methylpyridines has been extended to include a kinetic study, to establish if first order kinetics are being followed under the Fenton conditions used in the present study. An understanding of the kinetics of such reactions is important since it may provide a means of optimising the process. The rate-limiting factors in a reaction can be determined and hence more detailed mechanistic conclusions reached. Since Fenton's reagent was also considered as a catalyst in the WAO of each of the methylpyridines, it would seem appropriate that the kinetics associated with the use of this catalyst are investigated. Establishing the kinetic order for this reaction may provide information of significance with regard to the mechanism of the reaction, and ultimately lead to an improvement in the rate of the Fenton-catalysed oxidation under WAO conditions

3.4.1. Experimental - Determination of the Rate Constant of the Fenton-Catalysed Oxidation of 2-Methylpyridine

In the initial study, the rate of the reaction was followed under pseudo first order conditions where the hydrogen peroxide and the metal salt were present in excess as follows.

A two fold excess of iron(II) sulphate (0.02 mol) and a ten fold excess of hydrogen peroxide (0.1 mol) were used in the Fenton catalysed oxidation reaction which was followed over a 2 hour period (approx.). Several reactions were carried out, in order to determine the rate of the oxidation reaction, and this involved using different initial quantities of 2-methylpyridine in the range 0.01 mol, 0.0097 mol, and 0.0086 mol of 2-methylpyridine. The observed rate constant for the Fenton-catalysed oxidation of 2-methylpyridine should remain constant irrespective of the initial concentration of the substrate if the correct rate law equation is established.

Each of the oxidation reactions was carried out in a thermostat bath held at 25°C. The appropriate amount of 2-methylpyridine was dissolved in a mixture of dilute sulphuric acid (25 cm^3, 1 mol dm^{-3}) and iron(II) sulphate (0.02 mol) and stirred by means of an overhead stirrer. The reaction mixture was suspended in the bath and allowed to reach 25°C. A hydrogen peroxide mixture was prepared which contained 0.1 mol of hydrogen peroxide (30% w/v solution in water), dilute sulphuric acid (25 cm^3, 1 mol dm^{-3}), and water (47 cm^3), and this was also suspended in the bath and allowed to reach the operating temperature of 25°C. After both mixtures had reached the constant temperature, the hydrogen peroxide mixture was added to the solution containing the 2-methylpyridine. The system was then immediately purged with nitrogen using a balloon, and the temperature of the reaction mixture quickly

rose to approximately 35°C, but the heat was dissipated relatively quickly by the bath and the reaction mixture returned to a temperature of 25°C after approximately 7 minutes. The reaction was monitored by following the fate of 2-methylpyridine, quantitatively, using GC/MS techniques.

3.4.1.1. Sample Preparation

At regular time intervals during the oxidation reaction, 1 cm^3 samples of each of the reaction mixtures were taken and spiked with 1 cm^3 of an internal standard stock solution, and made up to 10 cm^3 aliquots with water. The 10 cm^3 aliquot was then extracted, after neutralisation with dilute sodium hydroxide (2 mol dm^{-3}), with of diethyl ether (2 x 5 cm^3) and the extracts were dried using magnesium sulphate. Each of the samples was then analysed using GC/MS techniques.

3.4.1.2. Sample Analysis

The analysis of each of the samples, taken from all of the oxidation reactions considered, involved using those GC conditions outlined in Chapter 3, section 3.3.1. and each of the samples was analysed 5 times.

3.4.1.3. Results

All of the results relate to the concentration of 2-methylpyridine remaining, after set time intervals, and these values were established from the use of the calibration graph that appeared in Chapter 3, section 3.3.1.

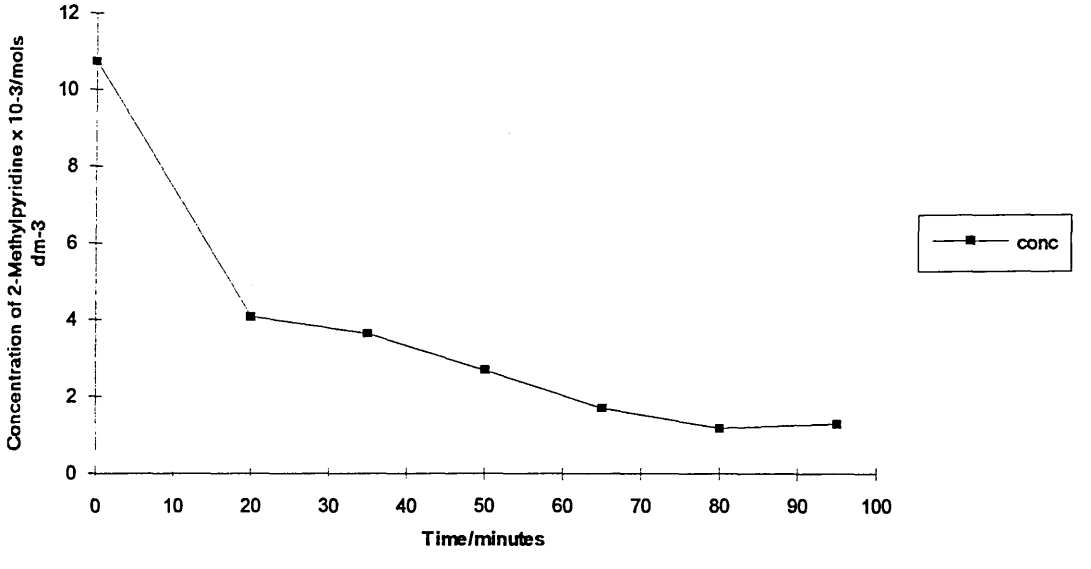
3.4.1.3.1. Experiment 1 - Oxidation of 2-Methylpyridine (0.01 mol) using Fenton's Reagent at 25°C over the First 2 Hour Period

Table 1

Conc. of 2-methylpyridine x 10^{-3} /mols dm^{-3}	Time/minutes	% RSD	2-Methylpyridine Remaining (%)
10.75	0	5.7	100.0
4.08	20	4.5	40.0
3.63	35	9.3	33.8
2.69	50	6.6	25.0
1.70	65	11.7	15.8
1.18	80	15.7	11.0
1.30	95	11.7	12.1

This table is represented graphically in Figure 1 below.

Figure 1



The graph in Figure 1 shows a very sharp initial decrease in the concentration of 2-methylpyridine over the first 20 minutes followed by a much slower decrease in the concentration value over the remaining time of the reaction. The slight observed increase in the 2-methylpyridine concentration between the 80^{th} and 95^{th} minute cannot be classed as a real increase as a 10% error is allowed about each value. The concentration value obtained after 95 minutes falls within the error band of the preceding value obtained after 80 minutes. Therefore, it is assumed that the concentration of 2-methylpyridine does not change over this final time period i.e. the reaction has reached virtual completion.

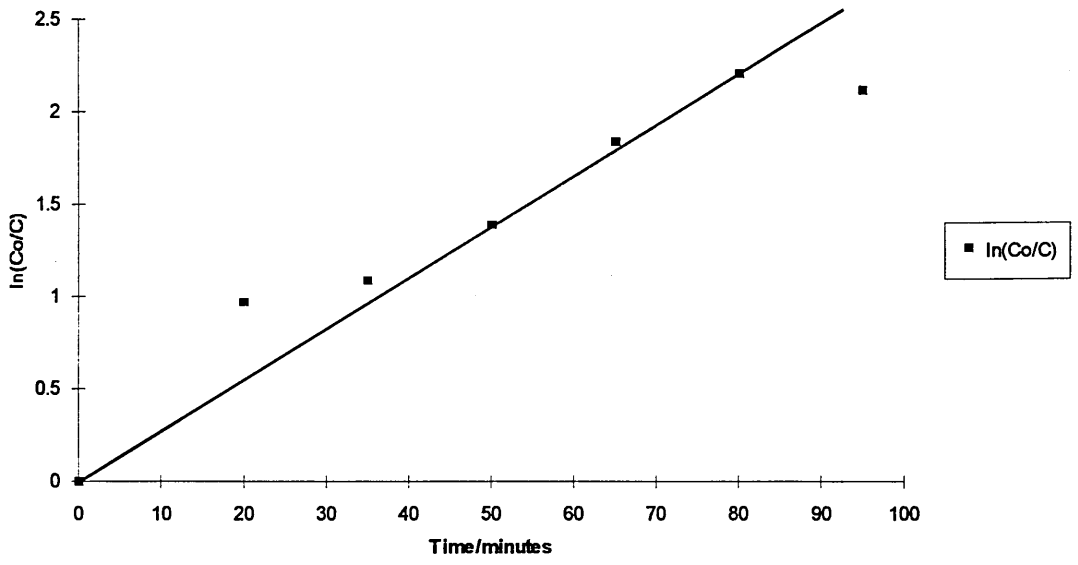
The rate constant for this reaction was then determined by plotting a graph of $\ln(C_O/C)$ against time, where C_O is the initial concentration of 2-methylpyridine used in the oxidation reaction and C is the concentration of the methylpyridine remaining after a set time. The values used to plot this graph can be found in Table 2.

Table 2

$\ln(C_O/C)$	Time/minutes
0	0
0.97	20
1.09	35
1.39	50
1.84	65
2.21	80
2.12	95

This table of data is represented graphically in Figure 2.

Figure 2



The graph shown in Figure 2 gives an approximate straight line through the origin, allowing for the complexity of the mixture and experimental error, Therefore, it can be seen that the oxidation of 2-methylpyridine using Fenton's reagent as the catalyst is following a first order trend(7). Hence the rate of the reaction can be said to be proportional to the concentration of 2-methylpyridine to the first power.

$$\text{Rate} \propto [\text{2-methylpyridine}]^1$$

The rate constant, k, for this oxidation reaction can be determined from the gradient of the graph. The value for k in this case was found to be $0.0281 min^{-1}$.

The validity of this value was investigated by repeating the Fenton catalysed oxidation of 2-methylpyridine and keeping the concentration of all the reagents constant and in excess, except for the concentration of 2-methylpyridine. The same value for k should be obtained in each case.

Hence, two more reactions were carried out where different initial concentrations of 2-methylpyridine were used, as discussed earlier in section 3.4.1.

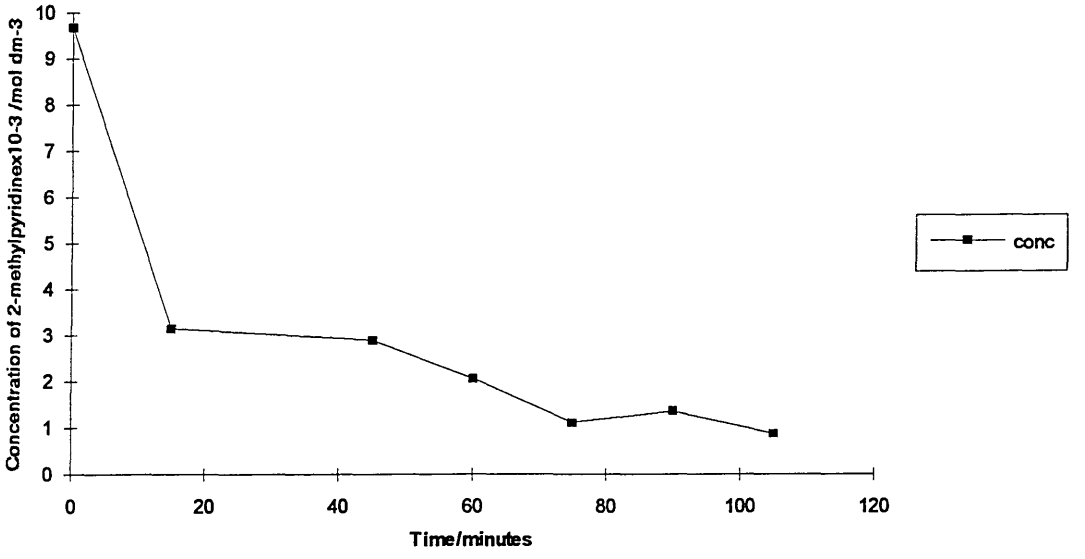
3.4.1.3.2. Experiment 2 - Oxidation of 2-Methylpyridine (0.00968 mol) using Fenton's Reagent at 25°C over the First 2 Hour Period

Table 3

Conc. of 2-methylpyridine x 10^{-3} /mol dm^{-3}	**Time/minutes**	**% RSD**	**2-Methylpyridine Remaining (%)**
9.68	0	5.7	100
3.15	15	6.3	32.5
2.90	45	5.5	30.0
2.07	60	1.7	21.4
1.12	75	6.5	11.6
1.36	90	6.2	14.0
0.88	105	2.7	9.1

The data in this table are represented graphically in Figure 3 below.

Figure 3



The shape of this curve is very similar to that seen above in 3.4.1.3.1. as both contain the initial fall in the concentration of 2-methylpyridine. This is then followed by a more gradual decrease in concentration of the substrate over the remaining time of the reaction.

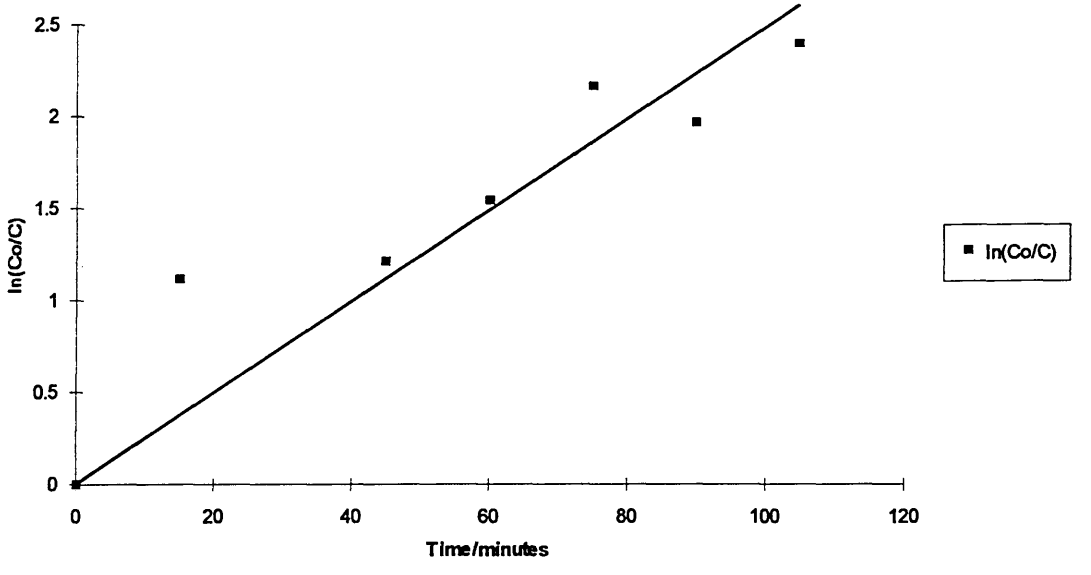
The rate constant for this reaction was calculated by determining the gradient of a plot of the $\ln(C_O/C)$ against time, as in 3.4.1.3.1. above. The values used to plot this graph can be found in Table 4.

Table 4

$\ln(C_o/C)$	Time/minutes
0	0
1.12	15
1.21	45
1.54	60
2.16	75
1.96	90
2.39	105

The data in this table are represented graphically in Figure 4.

Figure 4



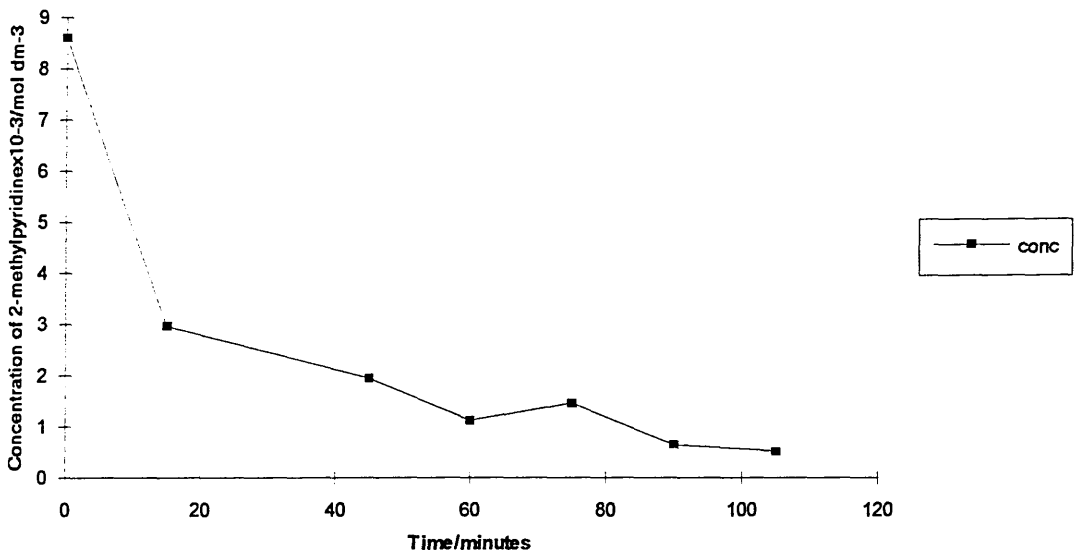
The graph shown in Figure 4 gives an approximate straight line through the origin, again allowing for the complexity of the mixture and experimental error. The oxidation reaction is still following first order kinetics and therefore the gradient of the graph corresponds to the rate constant for this reaction. The value for k was found to be 0.0250 min^{-1}.

3.4.1.3.3. Experiment 3 - Oxidation of 2-Methylpyridine (0.00860 mol) using Fenton's Reagent at 25°C over the First 2 Hour Period

Table 5

Conc. of 2-methylpyridine x 10^{-3} /mol dm^{-3}	Time/minutes	% RSD	2-Methylpyridine Remaining (%)
8.60	0	5.7	100
2.97	15	3.1	34.5
1.94	45	6.0	22.6
1.13	60	4.6	13.1
1.46	75	3.0	17.0
0.65	90	4.0	7.5
0.52	105	4.8	6.0

The data in this table are represented graphically in Figure 5.



The shape of this graph is very similar to those graphs seen in Experiment 1 (3.4.1.3.1.) and Experiment 2 (3.4.1.3.2.) above. Therefore, in order to

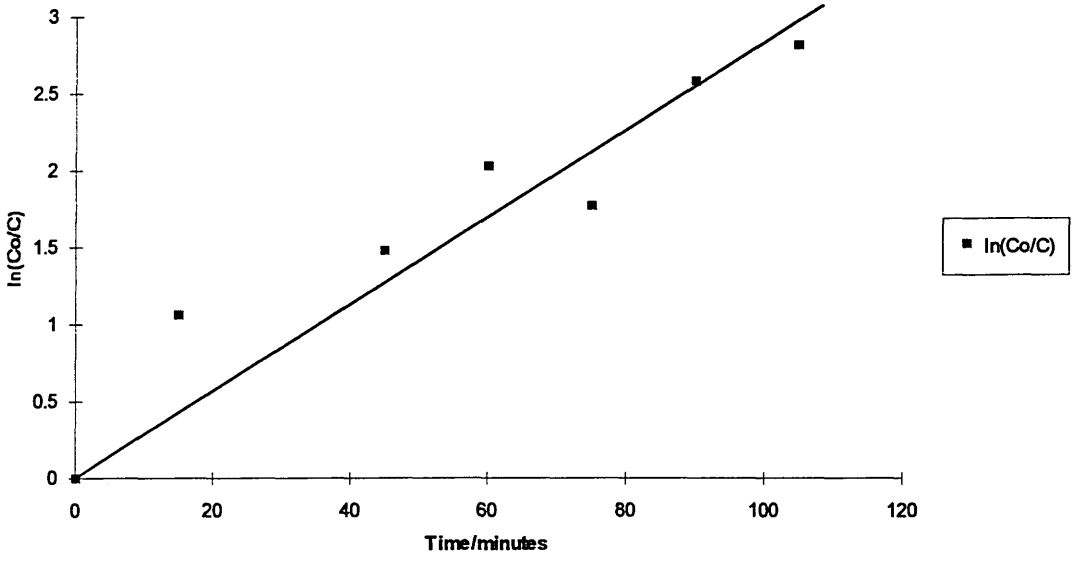
determine the rate constant for this reaction, a plot of $\ln(C_O/C)$ is again required. The data used to plot this graph can be found in Table 6.

Table 6

$\ln(C_O/C)$	Time/minutes
0	0
1.06	15
1.48	45
2.03	60
1.77	75
2.58	90
2.81	105

These data are represented graphically in Figure 6 below.

Figure 6



This graph is following an approximate straight line, allowing for experimental error. Therefore the oxidation reaction is still following first order kinetics and

therefore the gradient of the graph corresponds to the rate of the rate constant for this reaction. The value for k was found to be 0.0286 min^{-1}.

3.4.1.3.4. Discussion

The three experiments above have dealt with the Fenton catalysed oxidation of 2-methylpyridine. The data generated form each experiment were used to determine the rate constant for this reaction. The rate constants calculated from each experiment are listed below:-

Experiment 1 - k = 0.0281 min^{-1}

Experiment 2 - k = 0.0250 min^{-1}

Experiment 3 - k = 0.0286 min^{-1}

Therefore the pseudo first order rate constant value for the Fenton-catalysed oxidation of 2-methylpyridine was taken to be the average of these values and is therefore found to be 0.0272 min^{-1}. Thus, under the conditions used, the rate determining step involves one molecule of 2-methylpyridine.

These experiments provided a rate constant value for the Fenton-catalysed oxidation of 2-methylpyridine. However, on considering Figures 1, 3, and 5, a constant observation was made from each plot concerning the initial fall in the concentration of 2-methylpyridine against time. Over the first 15-20 minutes of the reaction the 2-methylpyridine concentration falls by approximately half. However, over the remaining time of the reaction, the fall in concentration is more gradual. Hence, a study of the first 15-20 minutes of the Fenton-catalysed oxidation of 2-methylpyridine was required to provide some information as to the course of the oxidation reaction over this time period. The details of this study are highlighted in Experiment 4.

3.4.1.3.5. Experiment 4 - Oxidation of 2-Methylpyridine (0.01 mol) using Fenton's Reagent at 25°C over the First 30 Minute Period

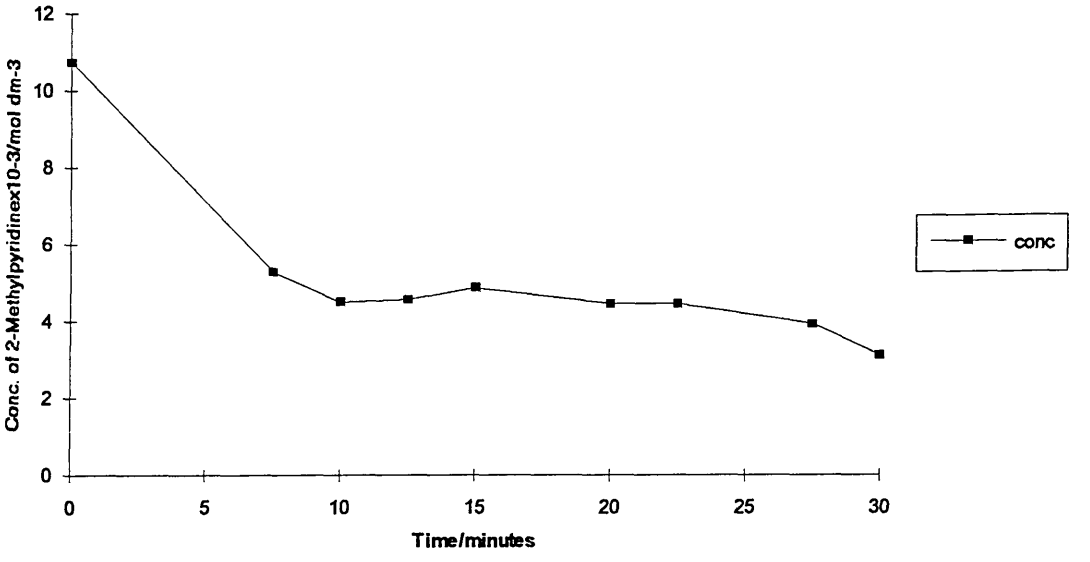
This experiment was carried out by taking samples of the reaction mixture over shorter time intervals than those in experiments 1-3 above. This experiment used identical conditions to those used previously (section 3.4.1.) only here samples of the reaction mixture were taken at 2.5 minute intervals after 7.5 minutes had elapsed. The samples were prepared for analysis, and GC/MS conditions used were the same as indicated earlier in section 3.4.1.1. and 3.4.1.2. respectively. The results from this experiment can be found in Table 7 below.

Table 7

Conc. of 2-methylpyridine x 10^{-3} /mol dm^{-3}	**Time/minutes**	**% RSD**	**2-Methylpyridine Remaining (%)**
10.75	0	5.7	100
5.29	7.5	5.6	49.2
4.51	10	9.0	42.0
4.57	12.5	7.2	42.5
4.87	15	3.3	45.3
4.45	20	9.8	41.4
4.46	22.5	5.1	41.5
3.93	27.5	6.0	36.6
3.11	30	4.4	28.9

These data are represented graphically below

Figure 7



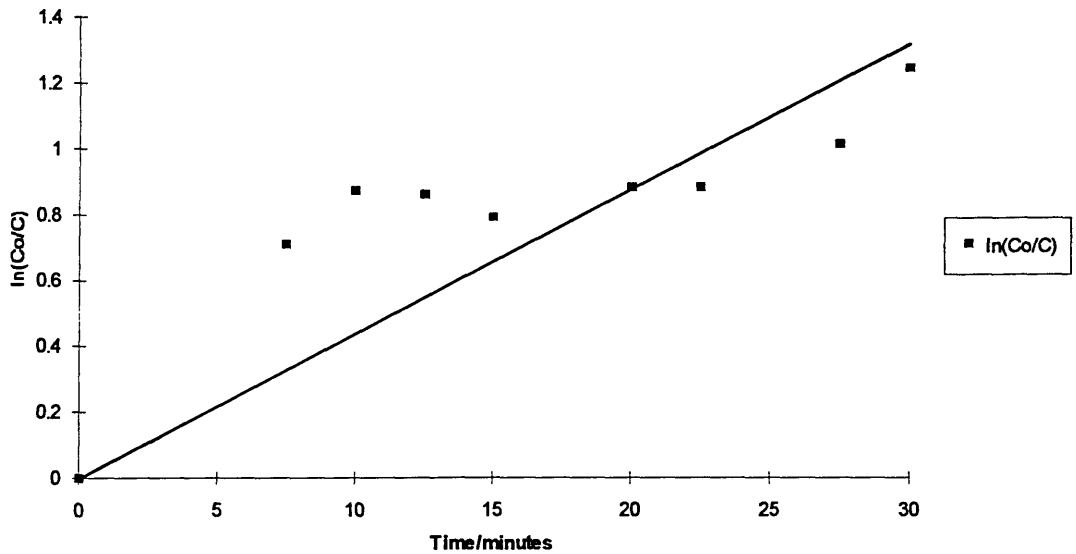
The shape of this graph is very similar to those seen earlier in 3.4.1.3.1., 3.4.1.3.2., and 3.4.1.3.3. in that the sharp initial decrease in the concentration of 2-methylpyridine is still apparent even though the first sample was taken after 7.5 minutes. It would seem that the Fenton catalysed oxidation of 2-methylpyridine is half way to completion even after the first 7.5 minutes. A plot of $\ln(C_O/C)$ was also carried out here and the data used to plot this graph can be found in Table 8.

Table 8

$\ln(C_o/C)$	Time/minutes
0	0
0.71	7.5
0.87	10
0.86	12.5
0.79	15
0.88	20
0.88	22.5
1.01	27.5
1.24	30

These data are represented graphically in Figure 8 below.

Figure 8



The observations made here prove that the initial stage (7 minutes) of the Fenton catalysed oxidation is very rapid and that the initial rise in temperature, over this time period, is probably aiding the rate of this oxidation. This would indicate that the Fenton-catalysed oxidation reactions are temperature

dependent[8]. A rise in temperature of the reaction mixture would be expected to increase the rate of the Fenton-catalysed oxidation of 2-methylpyridine.

3.4.1.3.6. Summary

Thus, to summarise, the above kinetic study has shown a first order rate dependence of the oxidation of 2-methylpyridine on the concentration of the heterocyclic substrate. In future studies, it will be necessary to establish the rate dependence of the reaction on the concentration of each of the other reagents used i.e. iron(II) and hydrogen peroxide. Only then will a fuller picture of the rate determining step become clear.

3.5. Other Oxidising Systems

The oxidation reactions of each of the methylpyridines in this chapter has involved the use of both iron- and copper-containing catalysts. This is analogous to the autoclave oxidation reactions studied in Chapter 2 that involved the use of similar catalytic systems. However, there are several metal ions that are capable of interacting with hydrogen peroxide to produce a reagent that is capable of oxidising an organic system[3]. They include vanadium (IV) and (V) and titanium (III) and all of these metal ions appear to form hydroxyl radicals in the presence of hydrogen peroxide.

The literature[3] also suggests other oxidising systems that involve radical chemistry. It has been postulated that the oxidising species in each of the metal ion/hydrogen peroxide catalysed oxidation reactions considered so far is the hydroxyl radical •OH. The action of a metal ion M^{n+} on hydrogen peroxide gives rise to the •OH radical by loss of an electron from the metal ion. However, instead of using hydrogen peroxide as the source of oxygen, the use

of ammonium persulphate was suggested as in the presence of a metal ion such as iron(II), the following reaction is thought to occur:-

$$Fe^{2+} + S_2O_8^{2-} \rightarrow Fe^{3+} + SO_4^{2-} + \bullet SO_4^{-} \qquad (1)$$

The sulphate radical anion $\bullet SO_4^{-}$ is supposed to initiate reactions in a very similar fashion to the hydroxyl radical •OH. It was therefore of interest to compare those observations made from reactions involving ammonium persulphate with those from a typical Fenton system.

Hence, the oxidation of 2-, 3-, and 4-methylpyridines was carried out using a mixture of vanadium (IV) sulphate and hydrogen peroxide, a mixture of titanium(III) chloride and hydrogen peroxide, and a mixture of iron(II) and ammonium persulphate, in amounts that were indicated earlier in 3.1.1. The experimental procedure for each of these oxidation reactions is outlined in 3.1. and the GC/MS conditions are discussed in Chapter 2, section 2.1.3.

3.5.1. Oxidation Reactions involving the use of Vanadium(IV)

3.5.1.1. 2-Methylpyridine

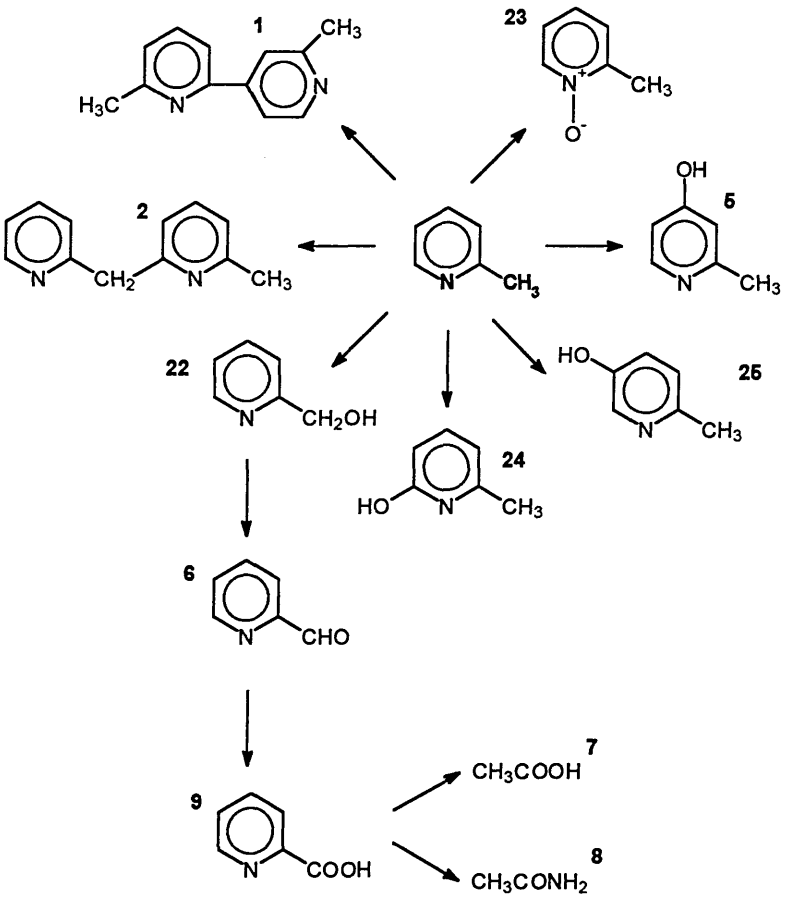
The vanadium(IV) catalysed oxidation of 2-methylpyridine was carried out over time periods of 2 and 24 hours. Both reaction mixtures were analysed using instrument 1 and temperature programme 2. The oxidation products detected have been assigned structures by comparison with the authentic standard or by consideration of mass spectral data, and they are summarised in Table 11 below. Figure 7 represents a possible pathway for their formation.

Table 11 - Oxidation products arising from the vanadium(IV)-catalysed oxidation of 2-methylpyridine

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
1*	14.70	14.73	184	2,2'-dimethyl-2,4-bipyridine
2	16.03	-	184	2-methyl-6-(2-pyridylmethyl)pyridine
22	10.68	-	109	2-hydroxymethylpyridine
23	13.78	-	109	2-methylpyridine-N-oxide
5*	15.05	15.25	109	4-hydroxy-2-methylpyridine
24	-	16.05	109	2-hydroxy-6-methylpyridine
25*	-	16.34	109	5-hydroxy-2-methylpyridine
6	6.98	7.02	107	pyridine-2-carboxaldehyde
7	5.65	5.80	60	acetic acid
8	9.47	9.87	59	acetamide

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

Figure 7



The range of oxidation products formed is very similar to that formed in the Fenton-catalysed oxidation of 2-methylpyridine. Thus it is probable that the same mechanism of formation is occurring under both conditions i.e. some form of radical chemistry is taking place, probably as a result of the formation of hydroxyl radicals as the literature suggests[3]. The oxidation process does not appear to be as efficient as the Fenton-catalysed reaction since, even after leaving the reaction for a 24 hour period, dimeric structures together with a range of hydroxy(methyl)pyridines are still observed.

Quantitative analysis was also carried out on this oxidation reaction using the experimental procedure outlined in 3.3. earlier in this chapter. The results from the analysis are indicated below. The ratio values observed between 2-

methylpyridine and the internal standard were used to determine the concentration of 2-methylpyridine remaining in each reaction by use of the appropriate calibration graph:-

Table 12

Catalyst	**Ratio Values**	**% RSD**	**Concentration of 2-Methylpyridine x 10^{-3}/mol dm^{-3}**	**2-Methylpyridine Remaining (%)**
V(IV)/H_2O_2				
30 minutes	0.919	1.3	4.39	44.9
24 hours	0.698	2.6	3.35	34.3

It would appear that the Vanadium(IV) catalysed oxidation reaction destroys approximately half of the 2-methylpyridine over the first 30 minutes of the reaction and that at this stage the reaction has almost reached completion. Over the remaining 23.5 hours, the concentration of 2-methylpyridine remaining only falls from 4.39 x 10^{-3} to 3.35 x 10^{-3} mol dm^{-3}.

3.5.1.2. 3-Methylpyridine

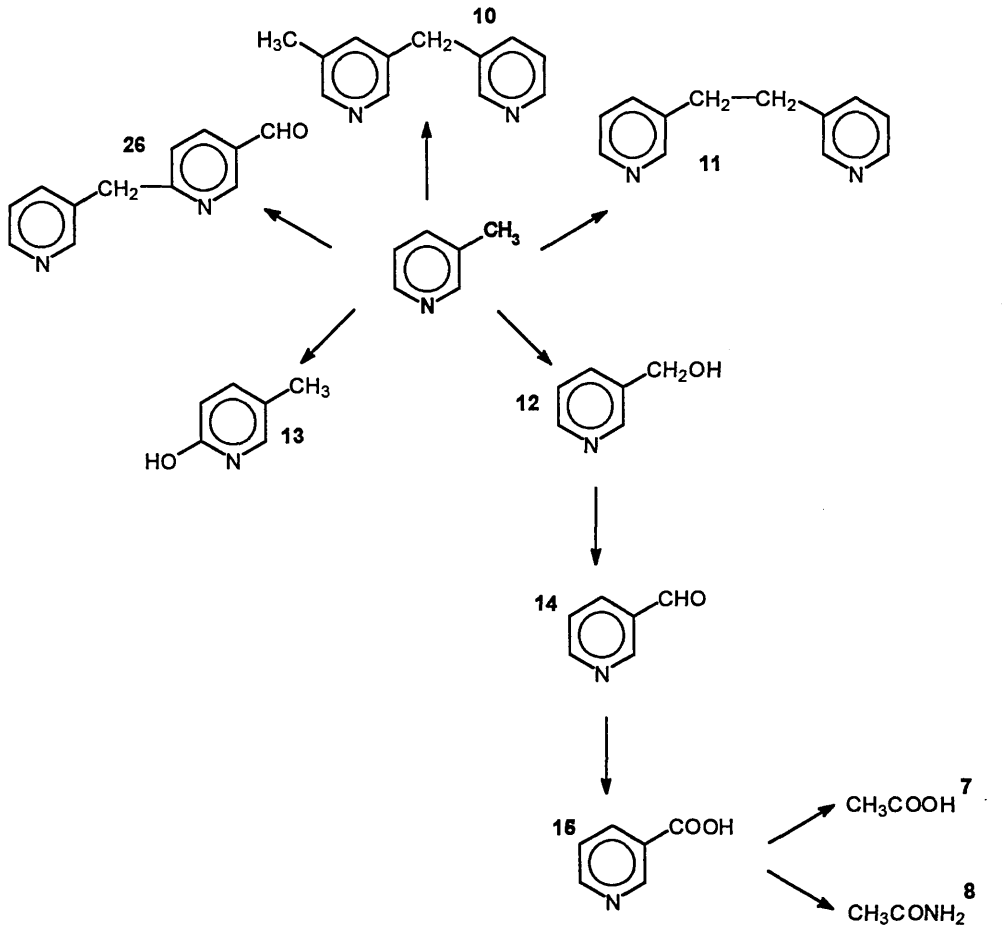
The oxidation of 3-methylpyridine was also carried out using vanadium(IV) in the presence of hydrogen peroxide over time periods of 2 and 24 hours. Both reactions were analysed using instrument 1 and temperature programme 2 and the oxidation products formed were assigned structures which are summarised in Table 13 below. Figure 8 represents a possible pathway for their formation.

Table 13 - Oxidation products arising from the vanadium(IV)-catalysed oxidation of 3-methylpyridine

Component	t_R 2hr	t_R 24hr	RMM	Proposed Structure
26*	-	21.82	198	5-(3-pyridylmethyl)pyridine-2-carboxaldehyde
10*	19.45	19.38	184	3-methyl-5-(3-pyridylmethyl)pyridine
11	-	19.57	184	1,2-bis-(3-pyridyl)ethane
12	14.36	14.27	109	3-hydroxymethylpyridine
13*	-	17.07	109	3-hydroxy-5-methylpyridine
14	9.00	8.87	107	pyridine-3-carboxaldehyde
7	5.56	5.48	60	acetic acid
8	-	9.58	59	acetamide

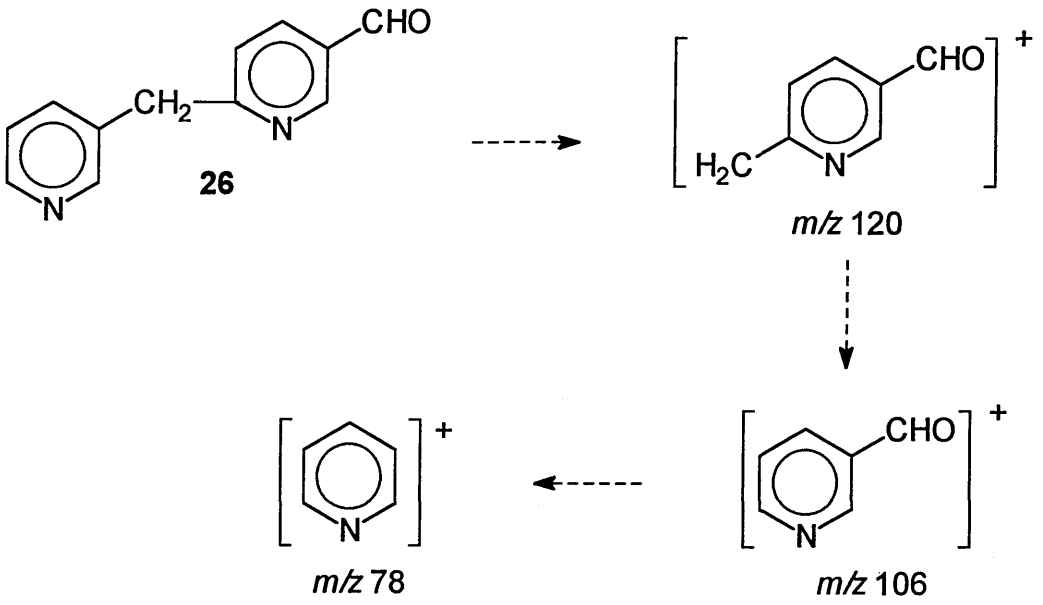
* indicates that the proposed structure has not been proved by comparison with the authentic substance

Figure 8

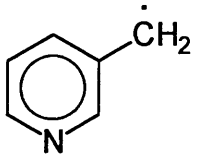


The range of oxidation products again resembles that seen earlier in the Fenton-catalysed oxidation of 3-methylpyridine. This would seem to indicate that they have been formed via the same mechanism, involving the intermediacy of hydroxyl radicals. However, an interesting observation was made in the formation of component **26** which was not detected in the Fenton-catalysed oxidation of 3-methylpyridine discussed earlier. This component is considered to be 6-(3-pyridylmethyl)pyridine-3-carboxaldehyde, on the basis of the mass spectral fragmentation pattern which exhibits stable fragment ions at *m/z* 120, 106, 92, and 78. This could imply that the molecule has fragmented according to the pathway indicated in Scheme 7.

Scheme 7



Component **26** could have formed as a result of radical substitution reaction occurring at the pyridine ring of pyridine-3-carboxaldehyde **14**, also identified as an oxidation product. The radical required to undergo the substitution reaction is indicated below.



The oxidation of 3-methylpyridine, using vanadium(IV), does not appear to be as efficient as the 2-methylpyridine oxidation using the same catalyst, as is expected. The range of oxidation products becomes more extensive when the oxidation of 3-methylpyridine is left for a longer time period.

Quantitative analysis was also carried out on both of the above reactions using the method outlined in 3.3. The results of this analysis are detailed in Table 14 below where the ratio values observed between 3-methylpyridine and the

internal standard were used to determine the concentration of 3-methylpyridine remaining. This was done by use of the appropriate calibration graph:-

Table 14

Catalyst	Ratio Values	% RSD	Concentration of 3-Methylpyridine x 10^{-3}/mol dm^{-3}	3-Methylpyridine Remaining (%)
V(IV)/H_2O_2				
30 minutes -	1.510	2.8	6.14	62.8
24 hours -	1.436	2.8	5.84	59.7

The vanadium(IV) catalysed oxidation reaction destroys approximately one third of the 3-methylpyridine initially present over the first thirty minutes of the reaction. However, it appears that at this stage the reaction has almost reached completion as over the remaining time of the oxidation process the concentration of 3-methylpyridine only falls from 6.14 x 10^{-3} to 5.84 x 10^{-3} mol dm^{-3}.

3.5.1.3. 4-Methylpyridine

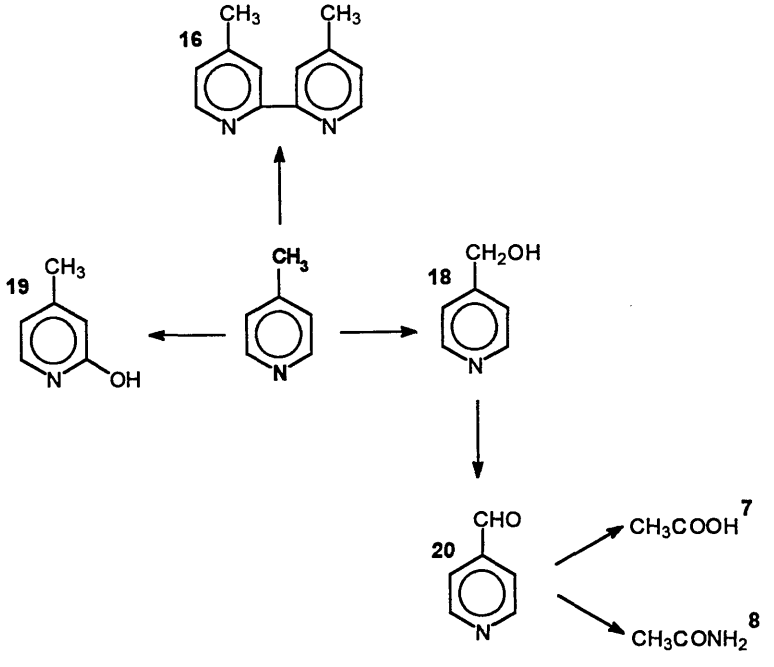
The oxidation of 4-methylpyridine was carried out using vanadium(IV) and again the reaction was studied over time periods of 2 and 24 hours. The reaction mixtures were analysed using GC/MS techniques involving instrument 1 and temperature programme 2. The oxidation products observed were assigned structures by comparison with the authentic substance or by consideration of mass spectral data, and they are summarised in Table 15 below. Figure 9 represents a possible pathway for their formation.

Table 15 - Oxidation products arising from the vanadium(IV)-catalysed oxidation of 4-methylpyridine

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
16	19.64	-	184	4,4'-dimethyl-2,2'-bipyridine
18	14.58	-	109	4-hydroxymethylpyridine
19*	16.34	16.30	109	2-hydroxy-4-methylpyridine
20	8.23	8.22	107	pyridine-4-carboxaldehyde
7	-	5.50	60	acetic acid
8	9.48	9.48	59	acetamide

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

Figure 9



The range of oxidation products formed is, again, very similar to that formed in the Fenton-catalysed oxidation of 4-methylpyridine. The evidence for radical chemistry occurring when vanadium(IV) is present as a catalyst is provided by the formation of dimeric structures and hydroxy(methyl)pyridine components. The extent of oxidation of 4-methylpyridine seemed to have proceeded further over a 24 hour period than for 3-methylpyridine in that no dimeric structures were observed. This was confirmed by quantitative data on the amount of 4-methylpyridine remaining at various stages.

Quantitative analysis was carried out on this reaction mixture using the method outlined in 3.3. above. The results obtained are detailed below in Table 16, where the ratio values observed between 4-methylpyridine and the internal standard were used to determine the remaining 4-methylpyridine concentration values by use of the appropriate calibration graph:-

Table 16

Catalyst	**Ratio Values**	**% RSD**	**Concentration of 4-Methylpyridine x 10^{-3}/mol dm^{-3}**	**4-Methylpyridine Remaining (%)**
V(IV)/H_2O_2				
30 minutes	1.245	4.0	2.40	24.5
24 hours	1.016	3.0	1.95	19.9

The values indicated in this table show that the vanadium(IV)-catalysed oxidation of 4-methylpyridine is more efficient than the oxidation of both 2-, and 3-methylpyridine using the same catalyst. However, on a similar note, the reaction appears to have reached completion after 30 minutes as leaving the reaction for a further 23.5 hours only results in the concentration of 4-methylpyridine falling from 2.40 x 10^{-3} to 1.95 x 10^{-3} mol dm^{-3}.

3.5.2. Oxidation Reactions involving the use of Titanium(III)

The oxidation of 2-, 3-, and 4-methylpyridines was carried using titanium(III) in the presence of hydrogen peroxide All of the reactions considered here were analysed using GC-MS techniques which involved the use of instrument 1 and temperature programme 2. The oxidation of 2-methylpyridine was considered first and this was carried out over time periods of 2 and 24 hours. The oxidation of the two other methylpyridines was investigated over a 24 hour period only.

The oxidation of 2-methylpyridine over a 24 hour period generated a mixture of oxidation products that included pyridine-2-carboxaldehyde **6**, 2-hydroxymethylpyridine **22**, and acetic acid **7**. No oxidation products were observed from the analysis of the 2 hour oxidation reaction. This is in contrast with all of the observations that have been made so far in connection with the catalysed oxidation of 2-methylpyridine. The oxidation of 3-methylpyridine over 24 hours generated only 2-hydroxy-5-methylpyridine **13** and the oxidation of 4-methylpyridine generated no oxidation products over the same time period. Thus, the titanium(III)/hydrogen peroxide system would seem to be an inefficient catalyst system for the oxidation of alkylpyridines. This was confirmed by quantitative data on the amount of methylpyridine remaining at the various stages of the reaction.

Quantitative analysis was carried out on each of the titanium(III)/hydrogen peroxide catalysed oxidation reactions involving 2-, 3-, and 4-methylpyridine as the substrate. The results are detailed below in Table 17, where the ratio values were used to determine the remaining methylpyridine concentration by use of the appropriate calibration graphs:-

Table 17

Catalyst - $Ti(III)/H_2O_2$	Ratio Values	% RSD	Concentration Values x 10^{-3}/mol dm^{-3}	Methylpyridine Remaining (%)
2-Methylpyridine				
30 minutes	1.725	3.6	8.21	83.9
24 hours	1.660	4.5	7.90	80.8
3-Methylpyridine				
30 minutes	>2.375	2.4	>9.68	>99.0
24 hours	1.834	2.4	7.47	76.4
4-Methylpyridine				
30 minutes	1.931	3.8	3.75	38.3
24 hours	1.966	3.2	3.81	38.9

From this table it appears that 4-methylpyridine is destroyed in the presence of a titanium(III)/hydrogen peroxide catalyst mixture, but allowing the oxidation reaction to proceed for the 24 hour period does not give rise to any further destruction of the methylpyridine. Also, on comparison of this data with all the other quantitative values obtained previously for the catalysed oxidation of 4-methylpyridine, the values obtained here for the titanium(III)-catalysed oxidation indicate that this catalyst is not as efficient at destroying the 4-methylpyridine. The oxidation of both 2-, and 3-methylpyridine is not efficient either, when using a titanium(III)/hydrogen peroxide mixture, as not even half of the initial concentration of the methylpyridines is destroyed in the oxidation reaction.

The analysis of the 4-methylpyridine reaction mixture did not identify the presence of any oxidation products. Although, from quantitative analysis, 4-methylpyridine appears to have undergone oxidation, the products formed, presumably the appropriate carboxylic acid, may not have been volatile enough for analysis using GC/MS techniques.

3.5.3. Oxidation Reactions involving the use of Ammonium Persulphate

The oxidation of 2-, and 4-methylpyridine was carried out using iron(II) sulphate in the presence of a ten-fold excess of ammonium persulphate. All of the reactions considered here were analysed using GC/MS techniques which involved the use of instrument 2 and temperature programme 2. The oxidation of these methylpyridines was considered over a 24 hour period only.

The analysis of the oxidation products generated from the oxidation of 2-methylpyridine revealed only pyridine-2-carboxaldehyde **6** and a significant amount of unchanged 2-methylpyridine. The oxidation of 4-methylpyridine under the same conditions generated no oxidation products that could be identified by GC/MS techniques.

Although no quantitative analysis was carried out here, it appears that using this catalyst system to oxidise both 2-, and 4-methylpyridine is inefficient as few oxidation products were observed. When a typical Fenton-catalyst was used for the oxidation of each of these methylpyridines, ring destruction products were observed after a 24 hour period and the relative amounts of these to unchanged starting material indicated that the reaction had proceeded significantly. This was not the case where ammonium persulphate was used instead of hydrogen peroxide. However, it may not be correct to assume that the oxidation of each of the methylpyridines will never be successful using such a system. The problem could be related to the relative amounts of each of the reagents used in the oxidation reaction, and further study may be necessary.

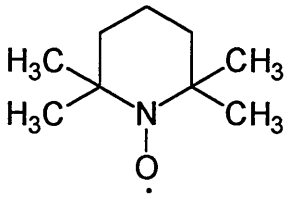
Chowdbury et al established in their work that certain concentrations of iron(II) are required, in relation to the concentration of hydrogen peroxide used, in

order to form free radicals at an effective rate[2]. A similar scenario could therefore be possible in the oxidation reactions using ammonium persulphate. Although the Fenton's reagent used in the reactions discussed in this chapter has been shown to be effective at the concentrations adopted, a different concentration of reagents may be required in order to initiate an effective oxidation reaction when iron(II) and ammonium persulphate are used as the catalyst. The reason for the inefficiency of this oxidation process may, however, be related to other factors and they are discussed in the summary below (3.5.4.).

3.5.4. Summary

There appear to be fundamental differences between the titanium(III)/hydrogen peroxide, and iron(II)/ammonium persulphate oxidising mixtures and other Fenton and related catalysed oxidation reactions. Sawyer et al[9] have suggested that the oxidising species generated by Fenton's reagent is not the hydroxyl radical •OH. The dominant reactant is said to be a complex involving the metal and therefore, in the systems discussed in this Thesis, this complex could be of the type $L_nFe^{II}OOH(BH^+)$. In the reactions studied in this Thesis, some of the methylpyridine can behave as a ligand (L_n) and the presence of acid will protonate some of the methylpyridine which can then behave as a base (BH^+). If this is the case, then the differences which appear evident between titanium(III) and other Fenton and related catalysed reactions maybe due to the formation of different types of complex. This argument may also be used to explain the different efficiencies that are evident from the quantitative analyses carried out on all of the catalysed oxidation reactions considered in this chapter.

In order to contribute to the debate associated with the oxidising species responsible for the destruction of each of the methylpyridines, an investigation was carried out which involved the oxidation of 2-, 3-, and 4-methylpyridines in the presence of a complexing agent and a radical trap. The Fenton catalysed oxidation of 2-, 3-, and 4-methylpyridines was carried out first in the presence of ethylenediaminetetraacetic acid (EDTA), a complexing agent . The presence of EDTA will ensure that the iron(II) present is complexed[10] and comparisons can therefore be made between the oxidation products that are formed with the complexing agent present and those formed in its absence. The Fenton catalysed oxidation of 2-, 3-, and 4-methylpyridines was then carried out in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), a radical trap.



TEMPO

Radicals, formed directly or indirectly from Fenton's reagent, will hopefully be trapped in the presence of this compound.

3.5.5. Catalysed Oxidation of 2-, 3-, and 4-Methylpyridines using Fenton's Reagent in the presence of EDTA

The oxidation reactions were carried out using the same experimental procedure as that indicated in 3.1. The EDTA (0.01 mol) was added initially to the reaction mixture before the hydrogen peroxide solution and the appropriate methylpyridine. The oxidation reaction was investigated over time periods of 2 and 24 hours, respectively, and the oxidation products detected have been assigned structures by comparison with the authentic standard or by

consideration of mass spectral data. The observations made have been summarised in the tables shown below.

Table 18 - Oxidation products arising from the Fenton-catalysed oxidation of 2-methylpyridine in the presence of EDTA

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
27*	19.15	-	170	2-methyl-6-(2-pyridyl)pyridine
24	15.58	16.13	109	2-hydroxy-6-methylpyridine
25*	-	17.15	109	5-hydroxy-2-methylpyridine
22	10.44	11.03	109	2-hydroxymethylpyridine
6	6.32	6.40	107	pyridine-2-carboxaldehyde
7	5.13	7.19	60	acetic acid
8	9.25	9.31	59	acetamide

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

Table 19 - Oxidation products arising as a result of the Fenton-catalysed oxidation of 3-methylpyridine in the presence of EDTA

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
28	21.25	24.15	184	3,3'-dimethyl-4,4'-bipyridine
11	21.43	24.43	184	1,2-bis-(3-pyridyl)ethane
29*	-	21.27	184	5-methyl-2-(3-pyridylmethyl) pyridine

30*	-	23.49	123	2-hydroxymethyl-5-methylpyridine
12*	15.01	16.03	109	3-hydroxymethylpyridine
13*	-	20.02	109	2-hydroxy-5-methylpyridine
14	8.35	8.51	107	pyridine-3-carboxaldehyde
7	5.10	5.13	60	acetic acid

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

Table 20 - Oxidation products arising from the Fenton-catalysed oxidation of 4-methylpyridine in the presence of EDTA

Component	t_R		RMM	Proposed Structure
	2hr	24hr		
31*	21.17	-	123	2-hydroxymethyl-4-methylpyridine
18	15.27	16.36	109	4-hydroxymethylpyridine
19*	-	18.52	109	2-hydroxy-4-methylpyridine
20	7.51	8.14	109	pyridine-4-carboxaldehyde
7	4.59	-	60	acetic acid

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

From the tables above it is apparent that there are similarities between the oxidation products formed here and those seen earlier in the Fenton-catalysed oxidation reaction in the absence of EDTA. The effect of complexing the iron only seems to be slowing down the oxidation process as a significant array of oxidation products are still observed after a 24 hour period for the oxidation

reactions involving 2-, and 4-methylpyridines. This is in contrast to those Fenton catalysed oxidation reactions carried out in the absence of EDTA. Since there does not appear to be any effect on the mechanism of destruction of each of the methylpyridines with EDTA present, it would seem that the presence of complexed iron(II) in a Fenton mixture is a possible scenario. The involvement of radical chemistry is still evident, however, as indicated by the formation of dimeric structures in the oxidation reaction involving 2- and 3-methylpyridine, and of hydroxy(methyl)pyridines in the oxidation of all of the substrates.

Quantitative analysis was carried out on the Fenton-catalysed oxidation of each of the methylpyridines in the presence of EDTA, over time periods of 30 minutes and 24 hours. The results obtained are detailed below in Table 21, where the ratio values were used to determine the remaining concentration of each of the methylpyridines by use of the appropriate calibration graph:-

Table 21

Catalyst - Fe(II)/H_2O_2/EDTA	**Ratio Values**	**% RSD**	**Concentration Values x 10^{-3}/mol dm^{-3}**	**Methylpyridine Remaining (%)**
2-Methylpyridine				
30 minutes -	0.981	1.7	4.70	48.1
24 hours -	0.938	2.7	4.49	45.9
3-Methylpyridine				
30 minutes -	1.545	2.1	6.28	64.2
24 hours -	1.314	4.0	5.33	54.5
4-Methylpyridine				
30 minutes -	1.031	4.3	1.98	20.2
24 hours -	1.071	3.2	2.06	21.1

The presence of EDTA appears to bring the Fenton catalysed oxidation reaction to completion, in all of the cases studied, over the initial 30 minute period. Also, these results compare with those seen earlier in section 3.3.4. where the catalysed oxidation of 4-methylpyridine was seen to be the most efficient and the catalysed oxidation of 3-methylpyridine the least, when Fenton's reagent was used as the catalyst.

3.5.6. Catalysed Oxidation of 2-, 3-, and 4-Methylpyridines using Fenton's Reagent in the Presence of TEMPO

The oxidation of 2-, 3-, and 4-methylpyridine was carried out in the presence of TEMPO and the oxidation of 2-methylpyridine was considered over time periods of 2 and 24 hours, respectively. The remaining methylpyridines were oxidised over a 24 hour period only. These oxidation reactions were carried out in the same way but on a smaller scale than the previous Fenton catalysed oxidation reactions discussed earlier in section 3.1.

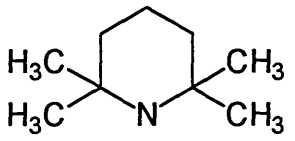
3.5.6.1. Experimental

Each of the methylpyridines (0.001 mol) was added to a mixture containing iron(II) sulphate (0.001 mol), TEMPO (0.0011 mol), and dilute sulphuric acid (2.5 cm^3, 1 mol dm^{-3}). A hydrogen peroxide mixture was then added, with stirring and ice bath cooling where necessary, under a nitrogen atmosphere. This mixture contained hydrogen peroxide (0.01 mol, 30% w/v solution in water), dilute sulphuric acid (2.5 cm^3, 1 mol dm^{-3}) and water (4 cm^3). Sample preparation and analysis using GC/MS techniques were identical to those methods used in 3.1.2. earlier in this chapter and Chapter 2, section 2.1.3. respectively, except that for sample preparation, the extraction was carried out

into diethyl ether (4 x 10 cm^3). For GC/MS analysis, instrument 2 and temperature programme 2 were used.

3.5.6.2. Results

The products of oxidation of 2-methylpyridine over the two time periods (2 hours and 24 hours) were analysed and, on comparison with those oxidation products detected in the Fenton-catalysed oxidation in the absence of TEMPO (3.2.1.1.) over a 2 hour period, a significant difference was observed. The oxidation reaction in the absence of TEMPO generated a range of oxidation products that included dimeric structures and hydroxy(methyl)pyridines which are all thought to arise via a free radical pathway. These structures are not detected in the oxidation reaction in which TEMPO has been introduced; instead a range of oxidation products is observed that have either apparent molecular ions of *m/z* 140 or mass spectra that contain stable fragment ions at *m/z* 140. The partial structure which has a relative molecular mass of 140 is shown below.



TEMPO fragment

Hence, the components which contain a fragment ion at *m/z* 140 are thought to be structures where the TEMPO has combined with a radical species. It is important to note at this stage that the GC trace for those reactions, where TEMPO has been introduced, were very complex due to the presence of what are believed to be the TEMPO adducts. There was, however, evidence of ring destruction both in the presence and absence of TEMPO over a 24 hour period

which suggests that the process of oxidative ring destruction is possibly non-radical in nature.

A similar picture was observed in the Fenton-catalysed oxidation of 3-, and 4-methylpyridines. The oxidation of 3-methylpyridine in the absence of TEMPO over a 24 hour period generated a range of oxidation products which have been discussed earlier in 3.2.1.2. Such products were not observed when TEMPO had been introduced into the reaction mixture. The only oxidation products that could be identified and compared with the previous reaction were pyridine-3-carboxaldehyde **14** and 3-hydroxymethylpyridine **12**.

The oxidation of 4-methylpyridine over a 24 hour period in the absence of TEMPO gave rise to a mixture of oxidation products that did not include dimeric structures. Thus, it was not surprising to find that such compounds were also not present when the reaction was repeated in the presence of a radical trap such as TEMPO. The oxidation products that were detected included 4-hydroxymethylpyridine **18** and acetic acid **7**, together with what again appear to be TEMPO adducts. This would again appear to suggest that the formation of products **18** and **7** could possibly be occurring via a non radical route.

3.5.6.3. Summary

The Fenton-catalysed oxidation of 2-, 3-, and 4-methylpyridines in the presence of a radical trap has generated some interesting points. The oxidation of 2-methylpyridine over a 2 hour period has been shown to form an interesting range of oxidation products thought to have been formed via radical reactions. This did not occur when TEMPO was present in the reaction

mixture, which would seem to suggest that the presence of the radical trap was interfering with the usual radical-based oxidation process occurring.

The oxidation of 3-methylpyridine also provided interesting observations in that over a 24 hour period an extensive range of oxidation products is observed, some of which are thought to have been formed via radical reactions. The presence of TEMPO interfered with the formation of these products. The oxidation of 4-methylpyridine does not provide us with such a clear contrast in observations since the oxidation of 4-methylpyridine over a 24 hour period under Fenton conditions is very efficient and a significant degree of oxidation takes place. However, the observations made in the above study lend support to the proposal that free radical routes are significant in Fenton oxidation reactions of the methylpyridines, but also that non-radical pathways, analogous to Gif chemistry involving high oxidation state iron complexes, may be involved[11].

3.5.7. Oxidation of 2-, 3-, and 4-Methylpyridine using Ozone

The use of ozone as an oxidising agent was discussed earlier in Chapter 1, section 1.4, where it was suggested that ozone was a source of hydroxyl radicals under certain conditions[12]. Andreozzi et al[13] investigated the ozonation of pyridine and the products of ozonation indicated the likely involvement of hydroxyl radical chemistry - Chapter 1, Scheme 10. Hence, in the present study ozonation of the methylpyridines was carried out in order to investigate and compare the products formed with those formed in the metal-ion catalysed oxidation reactions considered earlier in this chapter.

3.5.7.1. Experimental

The ozonation procedure involved dissolving the methylpyridines (0.016 mol) in water (100 cm^3) and then allowing ozone, generated by a B.O.C. Mark II Ozoniser, to bubble continuously through the reaction mixture for 3.5 hours. The workup of the reaction mixture involved extracting the products into dichloromethane (4 x 25 cm^3) and the combined extracts were dried using magnesium sulphate. The dichloromethane was evaporated to 1 cm^3 on a rotary evaporator prior to analysis by GC/MS. The aqueous phase was prepared for analysis by removing the excess water and extracting the residue with methanol.

Analysis of both the organic and aqueous extracts was carried out using GC/MS techniques as indicated in Chapter 2, section 2.1.3. For the analysis of the oxidation products formed in the ozonation reaction, instrument 1 and temperature programme 1 were used.

3.5.7.2. Results

The observations made in the ozonation of 2-methylpyridine indicated that a significant amount of unchanged substrate was still present at the end of the reaction. Two of the major oxidation products were pyridine-2-carboxaldehyde **6** and 2-picoline-N-oxide **32**. The only other oxidation product observed by analysis using GC/MS techniques was acetamide **8**. Similar observations were made from the analysis of the ozonation reactions involving 3- and 4-methylpyridines, respectively. The latter also gave rise to acetic acid as an oxidation product.

3.5.7.3. Summary

The pH of the reaction mixture was found to be ≈ 4-5 and therefore, from the literature[12] it is expected that the ozone will attack the organic compounds directly without the involvement of hydroxyl radicals - Chapter 1, Scheme 11. Since there appeared to be no evidence of radical chemistry occurring from those oxidation products observed, it would seem that the pH of the reaction has dictated the mechanism occurring. The formation of both the appropriate carboxaldehyde and N-oxide, observed as ozonation products, is expected to occur in a non-radical fashion. Since the formation of dimeric structures and hydroxy(methyl)pyridines did not occur in the ozonation reactions, this would suggest the absence of radicals, and hence supports the suggestion that the observed products have been formed via a non-radical route. The formation of acetamide and in the ozonation of 4-methylpyridine, acetic acid, would therefore suggest that the formation of ring destruction products does also not involve free-radical chemistry. Other oxidation products may have been formed in the ozonation of 2-, 3-, and 4-methylpyridine but they were not volatile enough to detected by GC methods.

Those observations made support the view that some of the oxidation products formed in the reactions studied earlier in this chapter are derived in a non-radical fashion, whereas others are formed as a result of the involvement of free radical intermediates.

3.6. Future Work

The metal ion-catalysed oxidation of 2-, 3-, and 4-methylpyridines has generated an extensive array of oxidation products which appear to suggest that two reaction pathways are taking place. One of the pathways indicates a non-radical route whereas the other indicates a free radical pathway. Attempts to investigate this have been carried out by allowing the Fenton-catalysed oxidation reaction to take place in the presence of a radical trap (TEMPO) and a complexing agent (EDTA). The oxidation reactions in the presence of EDTA have been followed in a quantitative manner (3.5.5.). Therefore, following the oxidation reactions in the presence of TEMPO, also in a quantitative manner, will enable comparisons between the efficiencies in both the presence and absence of a radical trap.

The oxidation of each of the methylpyridines using ozone was carried out at an acidic pH and the oxidation products observed have been reported (3.5.7.). However, at an alkaline pH the formation of hydroxyl radicals is supposed to be initiated. Thus, the ozonation of each of the methylpyridines at an alkaline pH will be interesting as comparisons can then be made between the oxidation products formed and those observed earlier ((3.5.7.2.). This investigation will hopefully lend support to the idea that the formation of some oxidation products, in particular the dimeric structures observed, are formed via the intermediacy of radicals.

All of the oxidation products observed so far from the oxidation of each of the methylpyridines, except for the appropriate carboxylic acid, have been identified using GC/MS techniques. Analysis of the product mixtures by HPLC, in particular LC/MS, may aid in the identification of other oxidation products. In particular, analysis of the oxidation reactions carried out using the

titanium(III)/hydrogen peroxide catalyst and the iron(II)/ammonium persulphate catalyst will provide more insight into the mechanism of oxidation. The oxidation processes taking place using these catalysts are still unclear. Quantitative analysis has been carried out on the titanium(III)-catalysed process, but not on the iron(II)/persulphate system and such quantitative information will hopefully aid the understanding of the processes taking place. It is possible that the conditions under which these two oxidation reactions were conducted are unsuitable for these types of catalyst to be effective.

The kinetic study carried out in this chapter has shown that the Fenton-catalysed oxidation of 2-methylpyridine is a pseudo first order process and the rate constant for this process has been determined. By using this information, it is possible to extend the study further by investigating the effect that variation of the concentration of each of the reagents used i.e. iron(II) sulphate, hydrogen peroxide and sulphuric acid has on the rate constant. By considering their effects, it will be possible to extend the understanding of the rate limiting steps in the overall Fenton process. An investigation of the kinetics associated with each of the catalysts discussed in this chapter would also be of interest, as comparisons of the rate of each of reaction would provide a more effective way of comparing the effectiveness of each of the processes.

3.7. References

1. Ito S., Mitarai A., Hikino K., Hirama M. & Sasaki K., Deactivation Reaction in the Hydroxylation of Benzene with Fenton's Reagent, *J. Org. Chem.*, 1992, 57, 6937-6941.
2. Chowdbury A.K. & Ross L.W., Catalytic Wet Oxidation of Strong Waste Waters, *AIChE Symposium Series - Water 1975*, **71**, 46-58.
3. Catalytic Oxidations with Hydrogen Peroxide, edited by Strukul G., Kluwer Academic Publishers, 1992, chapter 4, pp 97-151.
4. Joglekar H.S., Samant S.D. & Joshi J.B., Kinetics of Wet Air Oxidation of Phenol and Substituted Phenols, *Water Research*, 1991, **25**, 135-145.
5. Li L., Chen P. & Gloyna E.F., Generalised Kinetic Model for Wet Oxidation of Organic Compounds, *J. AIChE.*, 1991, **37**, 1687-1697.
6. Mishara V.S., Joshi J.B. & Mahajani V.V., Kinetics of Wet Air Oxidation of Diethanolamine and Morpholine, *Water Research*, 1994, **28**, 1601-1608.
7. Barrow G.M., Physical Chemistry, M^{c}Graw-Hill International Editions, chapter 18, pp 691.
8. Mohanty N.R. & Wei I.W., Oxidation of 2,4-Dinitrotoluene using Fenton's Reagent: Reaction Mechanisms and Their Practical Applications, *Hazardous Waste and Hazardous Materials*, 1993, **10**, 171-183.
9. Sawyer D.T., Kang C., Liobet A. & Redman C., Fenton Reagents (1:1 $Fe^{II}L_X$/HOOH) React via $[L_XFe^{II}OOH(BH^+)]$ (1) as Hydroxylases (RH→ROH), not as Generators of Free Hydroxyl Radicals (HO•), *J. Am. Chem. Soc.*, 1993, **115**, 5817-5818.
10. Koppenol W.H., The Reaction of Ferrous EDTA with Hydrogen Peroxide: Evidence against Hydroxyl Radical Formation, *J. Free Radicals in Biology and Medicine*, 1985, **1**, 281-285.
11. Barton D.H.R. & Doller D., The Selective Functionalisation of Saturated Hydrocarbons: Gif Chemistry, *Acc. Chem. Res.*, 1992, **25**, 504-512.

12. Ledon H., Why not Ozone?, pp 603-610, in Dioxygen Activation and Homogeneous Catalytic Oxidation, edited by Simandi L.I., Elsevier Science Publishers, 1991.

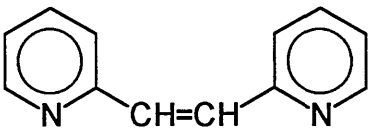
13. Andreozzi R., Insola A., Caprio V. & D'Amore M.G., Ozonation of Pyridine in Aqueous Solution: Mechanistic and Kinetic Aspects, *Water Research*, 1991, **25**, 655-659.

Chapter 4

Synthesis of a Range of Saturated Reference Dimeric Structures

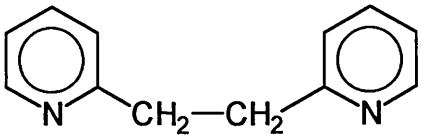
Chapter 4 - Synthesis of a Range of Standard Reference Dimeric Structures

The study discussed in this chapter has targeted the synthesis of a variety of dimeric structures which were formed as oxidation products during the oxidation of 2-, 3-, and 4-methylpyridines. Typical structures that have been indicated as possible products in earlier chapters include the following:-



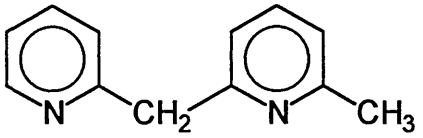
cis/trans 1,2-bis-(2-pyridyl)ethene **1**

Dipyridylethene - **A**



1,2-bis-(2-pyridyl)ethane **4**

Dipyridylethane - **B**



2-methyl-6-(2-pyridylmethyl)pyridine **7**

Dipyridylmethane - **C**

The structures indicated above are all possible oxidation products formed from the oxidation of 2-methylpyridine under certain conditions. However, the general structures **A**, **B**, and **C** are possible oxidation products formed from the oxidation of all of the three methylpyridines considered, again under certain conditions. Therefore attempts were made to synthesise the above structures and their isomers to use as reference compounds for identification purposes.

4.1. Dipyridylethenes - **A**

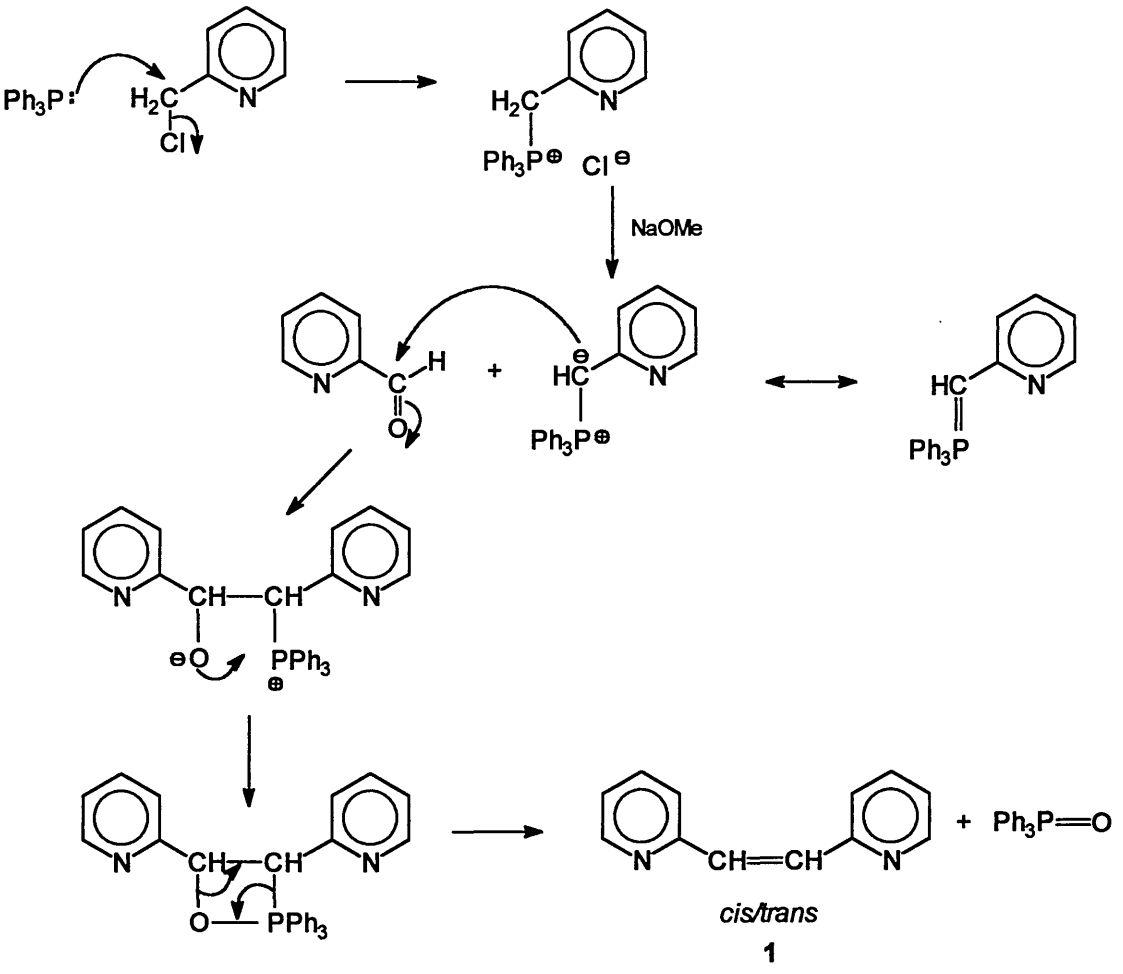
Dipyridylethenes in both the *cis* and *trans* forms were observed in the autoclave oxidation reactions of 2-, and 4-methylpyridine, both in the presence

and absence of catalysts. The appropriate dipyridylethenes were prepared, where required, to provide standard reference compounds, and also such structures were found to provide a starting material for the dipyridylethane isomers **B** that were also observed as oxidation products discussed in the earlier chapters.

4.1.1. Synthesis of *cis/trans* 1,2-bis-(2-pyridyl)ethene **1**

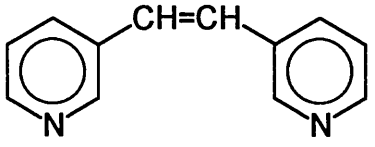
This compound was prepared via a Wittig reaction[1a] in which the alkyl halide, 2-chloromethylpyridine, was allowed to react with triphenylphosphine to give the appropriate phosphonium salt. The phosphonium salt can then interact with a suitable strong base such as n-butyllithium or sodium methoxide to give an ylide and the ylide that forms reacts rapidly with aldehydes and ketones to form the associated alkene and triphenylphosphine oxide - Scheme 1.

Scheme 1

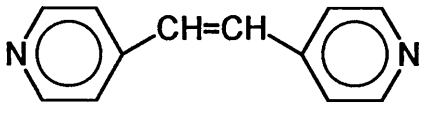


4.1.2. Discussion

All three possible symmetrical isomeric dipyridylethylene structures were prepared by this method, and the products of the reactions were analysed using GC/MS techniques which indicated the formation of both the *cis* and *trans* isomers in every case.



cis/trans 1,2-bis-(3-pyridyl)ethene **2**



cis/trans 1,2-bis-(4-pyridyl)ethene **3**

The three dipyridylethene isomers prepared are known compounds [1b] and their retention time (t_R) and mass spectra were compared with those of oxidation products generated, which also exhibited apparent molecular ions at *m/z* 182. The dipyridylethylenes prepared here were also of use as precursors to the dipyridylethane structures which are also known compounds and were observed as oxidation products throughout the study of the catalysed oxidation of 2-, 3-, and 4-methylpyridines.

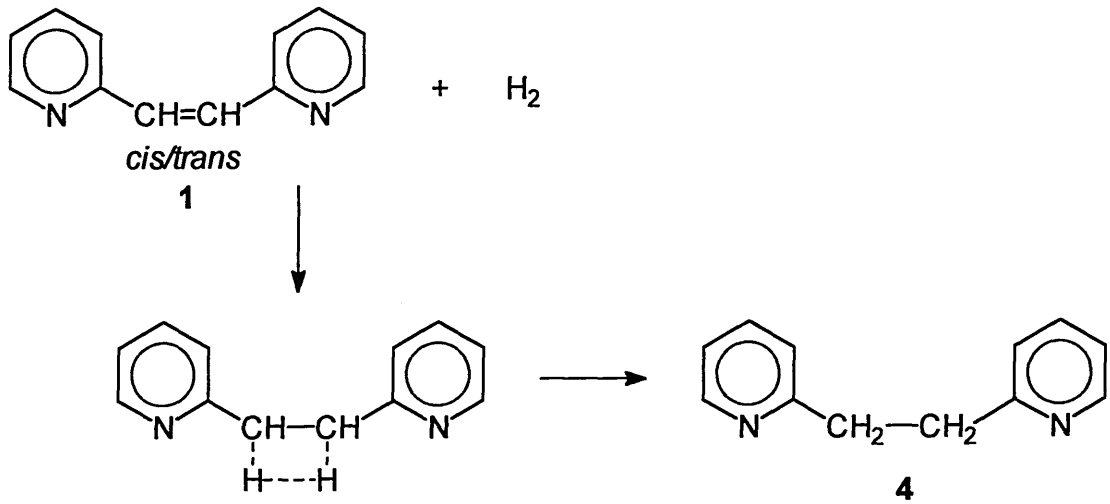
4.2. Dipyridylethanes **B**

Dipyridylethane structures **B** were observed as oxidation products in the catalysed autoclave oxidation of 2-methylpyridine and the Fenton-catalysed and other catalysed oxidation reactions of all three methylpyridines. Such structures were therefore prepared, as standard reference compounds, to use to compare with those oxidation products formed in the reactions discussed in earlier chapters.

4.2.1. Synthesis of 1,2-bis-(2-pyridyl)ethane **4**

This compound was prepared via the hydrogenation of the appropriate unsaturated dipyridylethene structure, *cis/trans* 1,2-bis-(2-pyridyl)ethene **1**, using hydrogen in the presence of an appropriate catalyst such as platinum(IV) oxide.

Scheme 2



cyclic four-membered transition state

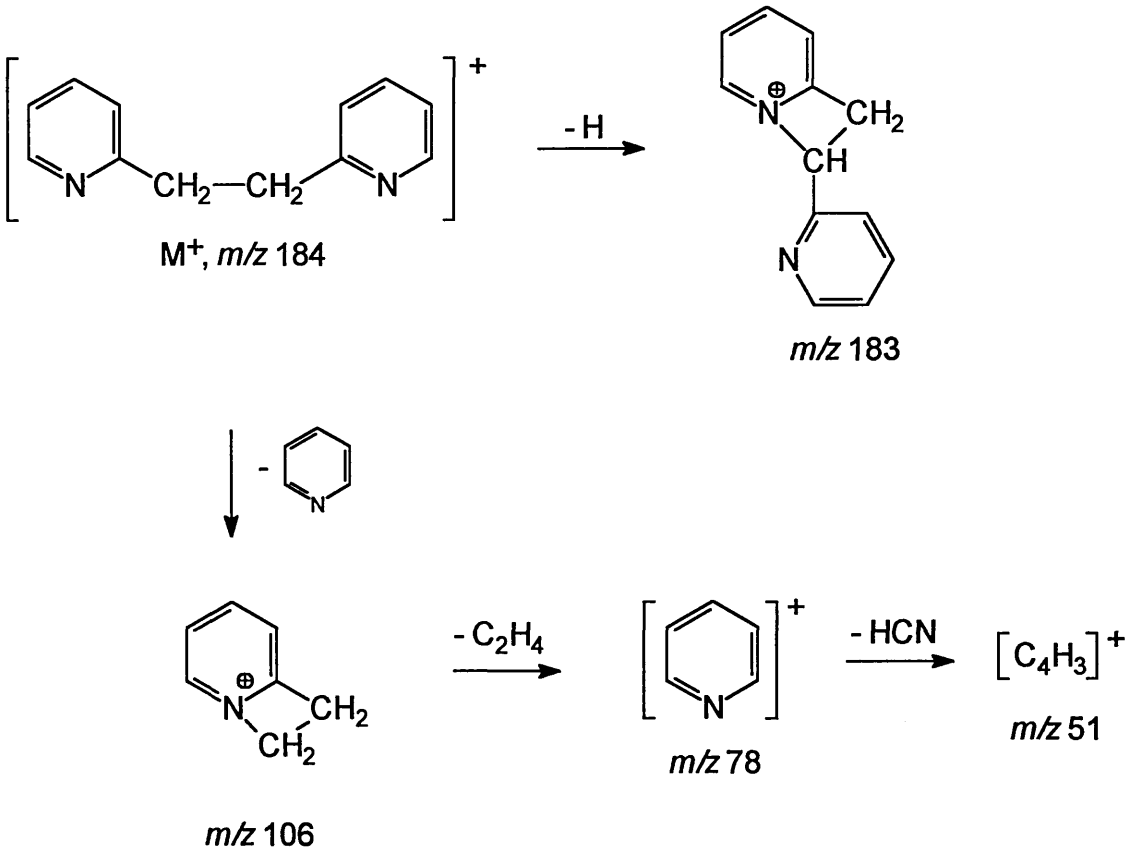
This mechanism involving a four-membered transition state has a very high energy but such a process is possible in the presence of a metal catalyst with the actual process taking place at the surface of the catalyst[1a].

4.2.2. Discussion

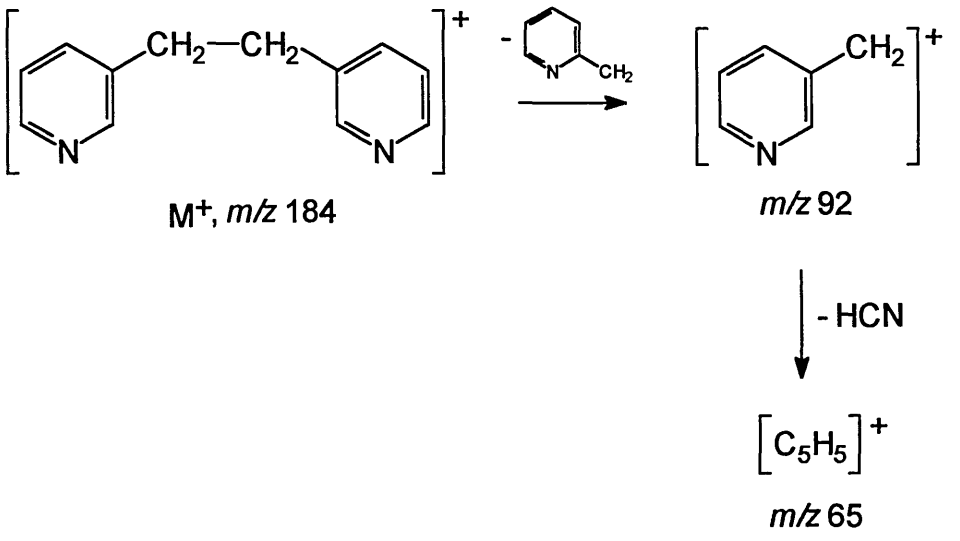
All three possible symmetrical isomeric dipyridylethane compounds, that could have been formed in the oxidation reactions studied, were prepared as standard reference compounds. They were all analysed by GC/MS to provide a "fingerprint" which could be compared with those oxidation products formed in our studies.

The three symmetrical dipyridylethane isomers are known compounds. The mass spectral fragmentation pathways exhibited by a series of dipyridylalkanes have been investigated by Osbourne[2]. The presence of the alkyl bridge between the pyridyl rings is supposed to lower the molecular stability of the compound towards electron bombardment. In his studies, Osbourne

interpreted the fragmentation of each of the isomers of interest in our study. For 1,2-bis-(2-pyridyl)ethane, the following fragmentation pathway is observed, where the fragment ion at *m/z* 106 is found to be the base peak.

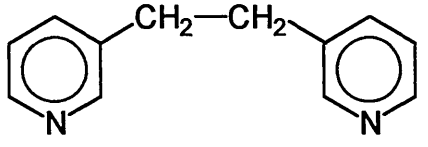


A very different behaviour was observed in the mass spectrum of 1,2-bis-(3-pyridyl)ethane and 1,2-bis-(4-pyridyl)ethane. For both of these, the fragmentation followed the pathway shown below.

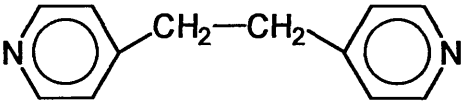


For these two structures, a base peak was found at *m/z* 92. Therefore, there are obvious differences in the fragmentation pathways between 1,2-bis-(2-pyridyl)ethane and the other two isomers prepared and discussed above.

Both 1,2-bis-(3-pyridyl)ethane and 1,2-bis-(4-pyridyl)ethane were also prepared by the same method used for the preparation of the 2-isomer. Analysis by GC/MS, using the same conditions, confirmed their structures. This was done by consideration of the mass spectra using the above information(2).



1,2-bis-(3-pyridyl)ethane **5**



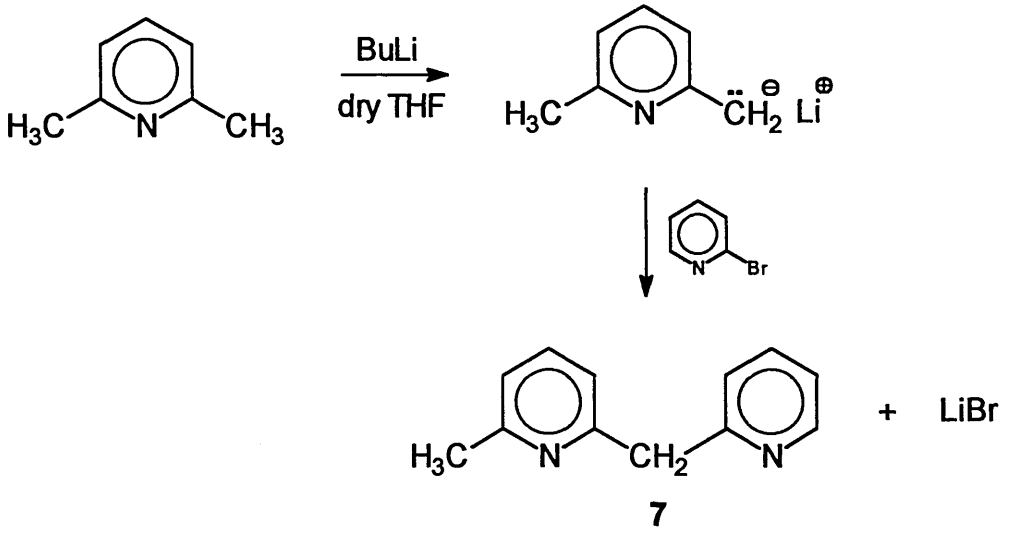
1,2-bis-(4-pyridyl)ethane **6**

4.3.1. Preparation of 2-methyl-6-(2-pyridylmethyl)pyridine **7**

4.3.1.1. Method 1

This method involved reacting 2,6-lutidine with n-butyllithium. The n-butyllithium removed one of the protons from one of the methyl groups attached to the pyridine ring. The anion that resulted was then allowed to react with 2-bromopyridine, via nucleophilic displacement, in an attempt to form the dipyridylmethane, 2-methyl-6(2-pyridylmethyl)pyridine **7**, as shown in Scheme 3 below.

Scheme 3



7

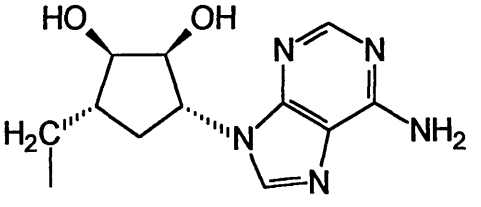
This method was successful for the preparation of 2-methyl-6-(2-pyridylmethyl)pyridine, whose presence in the reaction mixture was confirmed by GC/MS analysis. However, attempts to isolate and purify the compound failed due to the complexity of the mixture. The data produced here generated sufficient mass spectral evidence and retention time values for identification purposes. However, attempts continued to prepare a pure form of this

component so that a full structural characterisation could be carried out. Details of these attempts follow in this chapter.

4.3.1.2. Method 2

In this approach, the synthesis of the appropriate pyridylmethylcobaloxime complex was carried out. Such cobaloxime complexes are simple models of adenosylcobalamin, the active form of vitamin B_{12} which is essential for human health(3).

Adenosylcobalamin or Coenzyme B_{12}, contains a cobalt atom covalently bonded to carbon in the adensoyl moiety shown below.



In nature, reactions taking place involving the Coenzyme B_{12} generate the methylene radical of deoxyadenosine and a cobalt(II) species. Therefore two assumptions are made regarding the Coenzyme B_{12}:-

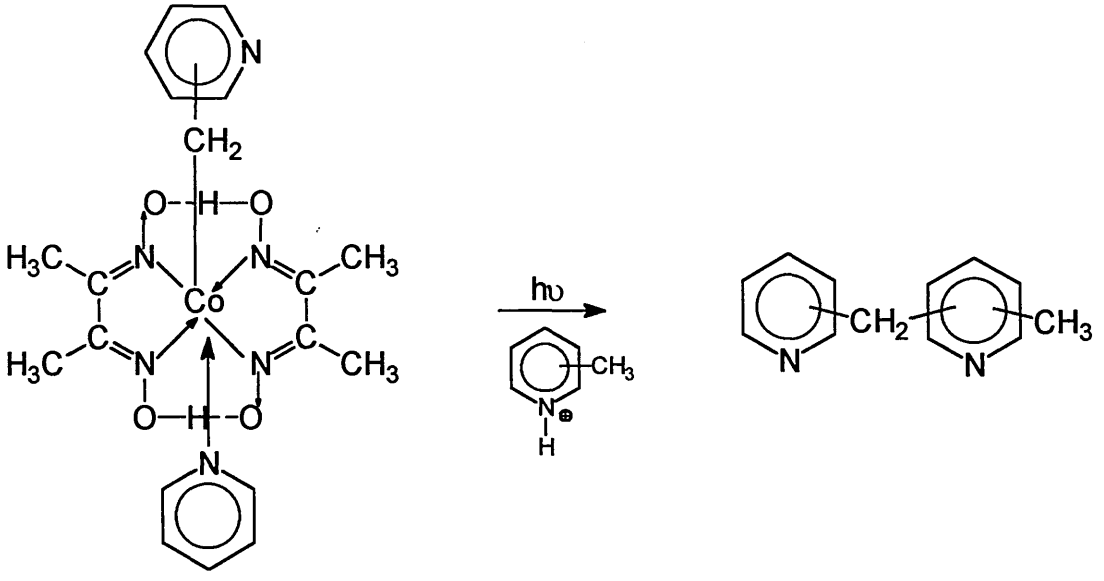
i) cobalt forms weak covalent bonds to carbon which nevertheless lead to relatively stable organocobalt compounds

ii) homolysis (using heat or light) of these organocobalt molecules provides a rich source of carbon radicals.

Alkylcobaloximes are found to behave in a similar way to the Coenzyme B_{12}. Alkylcobaloximes are known to undergo photolysis on irradiation with visible light to form alkyl radicals which can be subsequently trapped(4). Therefore, in our study, it was anticipated that a pyridylmethyl radical might be formed from

the photolysis of a pyridylmethylcobaloxime complex and subsequently trapped by a protonated methylpyridine, present in the reaction mixture, to give the desired dipyridylmethanes. This is illustrated below in Scheme 4.

Scheme 4



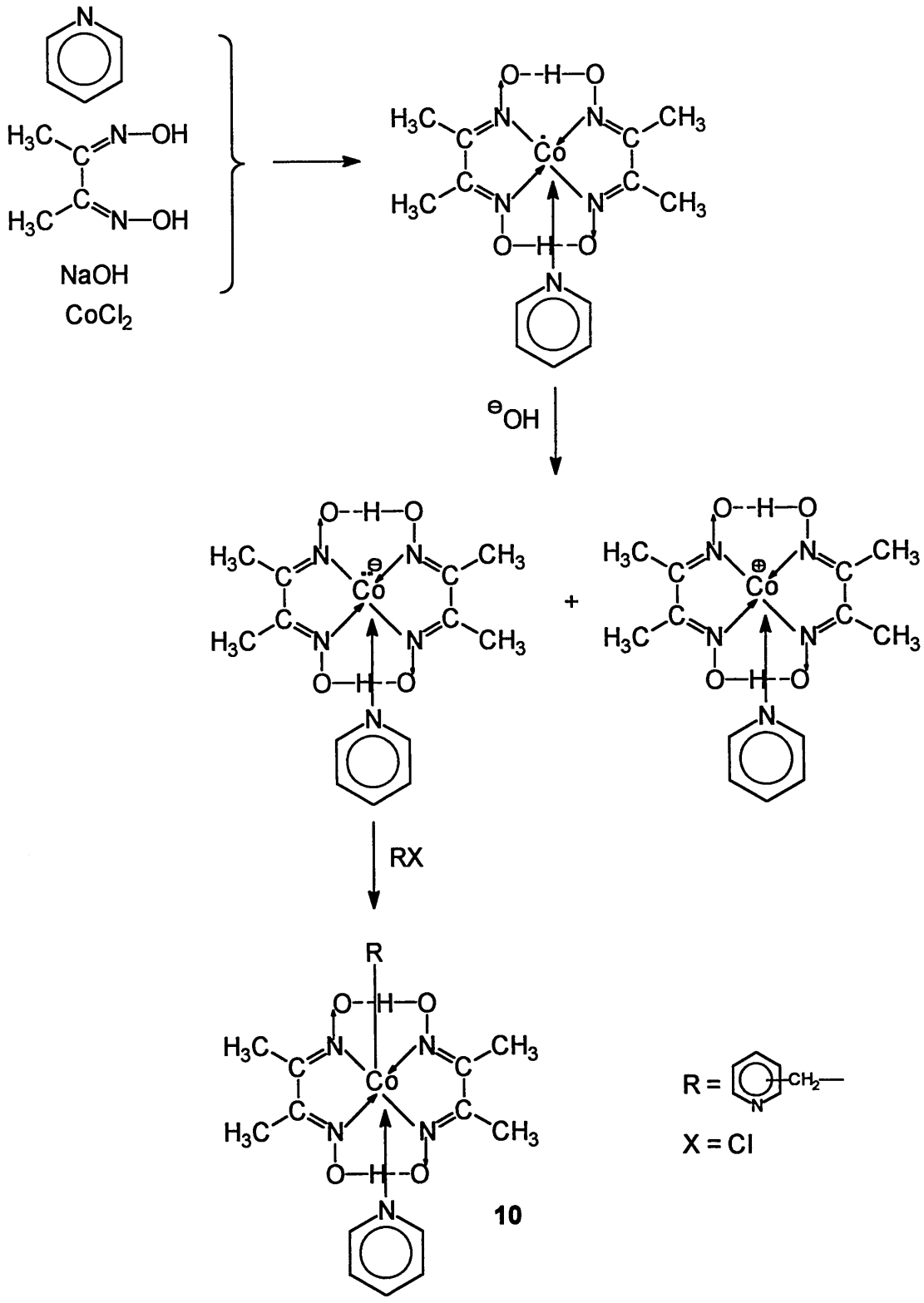
9

In the pyridylmethylcobaloxime complex **9** indicated above, a stable transition metal-carbon bond can be found and such structures can be formed by following the general method discussed below[5].

4.3.1.2.1. Preparation of Pyridylmethylcobaloxime complexes

Pyridylmethylcobaloxime complexes are prepared by adding dimethylglyoxime, cobalt(II) chloride, and pyridine together in the presence of a base such as sodium hydroxide. On the formation of the cobalt(I) species, the appropriate chloromethylpyridine was added to form the cobalt(III) cobaloxime, as indicated in the Scheme 5 below.

Scheme 5

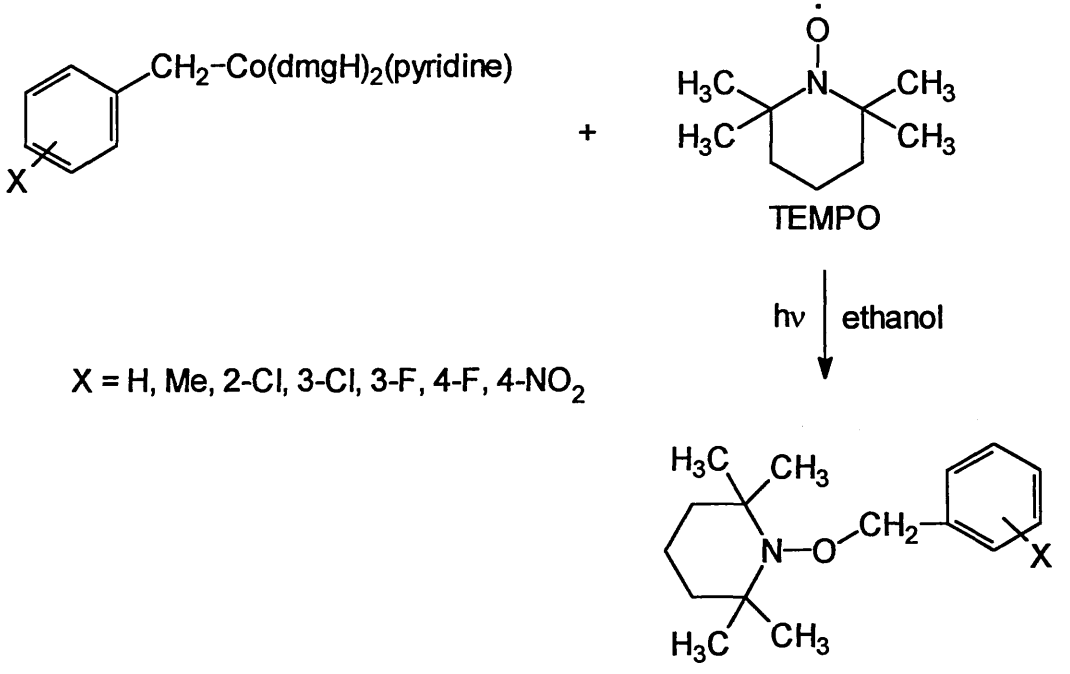


The synthesis of the 2-pyridylmethylcobaloxime complex was achieved using this method. Difficulties were encountered, however, on preparing the other two isomeric compounds.

4.3.1.2.2. Generation and Trapping of Radicals

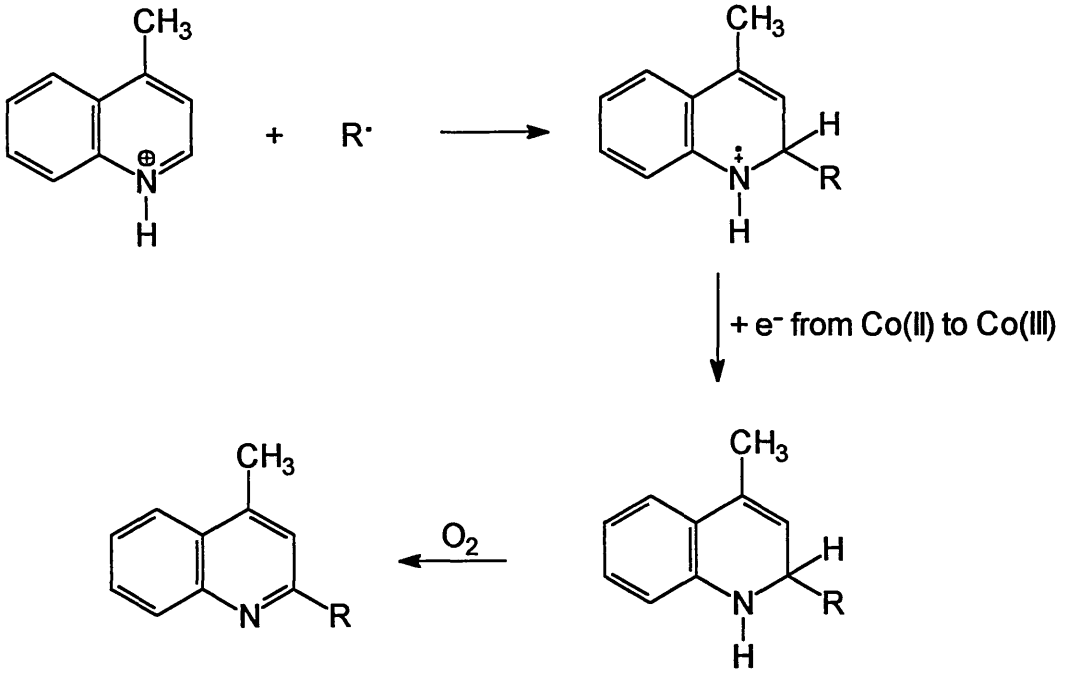
Brown et al[4] discussed in their work the formation of radicals via the photolysis of the appropriate cobaloxime. They demonstrated the formation of the radicals by trapping them with a radical trap such as TEMPO.

Scheme 6



In their work they also discussed other means of trapping the radical other than with TEMPO. Protonated heteroaromatic compounds have been reported as being good traps of alkyl and benzyl radicals[4].

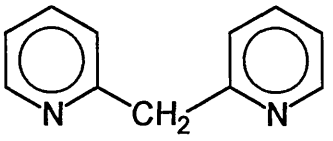
Scheme 7

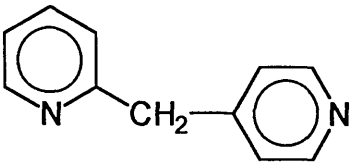


Other workers have also demonstrated the ease of generating radicals by this approach(6), (7) and thus this route was applied to the formation of dipyridylmethane structures.

4.3.1.2.3. Discussion

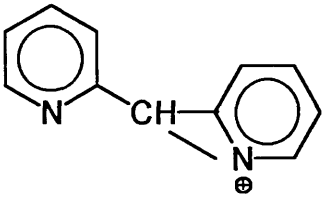
The synthesis of 2-pyridylmethylcobaloxime was successful but analysis of the products of the photolysis of 2-pyridylmethylcobaloxime in the presence of protonated 2-methylpyridine did not reveal the presence of the desired compound 2-methyl-6-(2-pyridylmethyl)pyridine **7**. However, a dipyridylmethane product was thought to have been formed which could have had a structure similar to either **12** or **13** shown below.





2-(2-pyridylmethyl)pyridine **12** 4-(2-pyridylmethyl)pyridine **13**

Such a structure was thought to have been formed, since the mass spectrum of this component contained an apparent molecular ion at *m/z* 170 and a base peak at *m/z* 169. This data suggests that a dipyridylmethane structure has been formed, as the stable fragment ion at *m/z* 169 could be due to the fragment ion shown below.



The formation of a compound such as **12** or **13** would imply that the cobaloxime complex is falling apart upon photolysis and subsequently the pyridine ligand is undergoing protonation under the conditions imposed. It is this that then traps the radicals generated instead of the protonated 2-methylpyridine present. Pyridine was also observed upon GC/MS analysis of the reaction mixture.

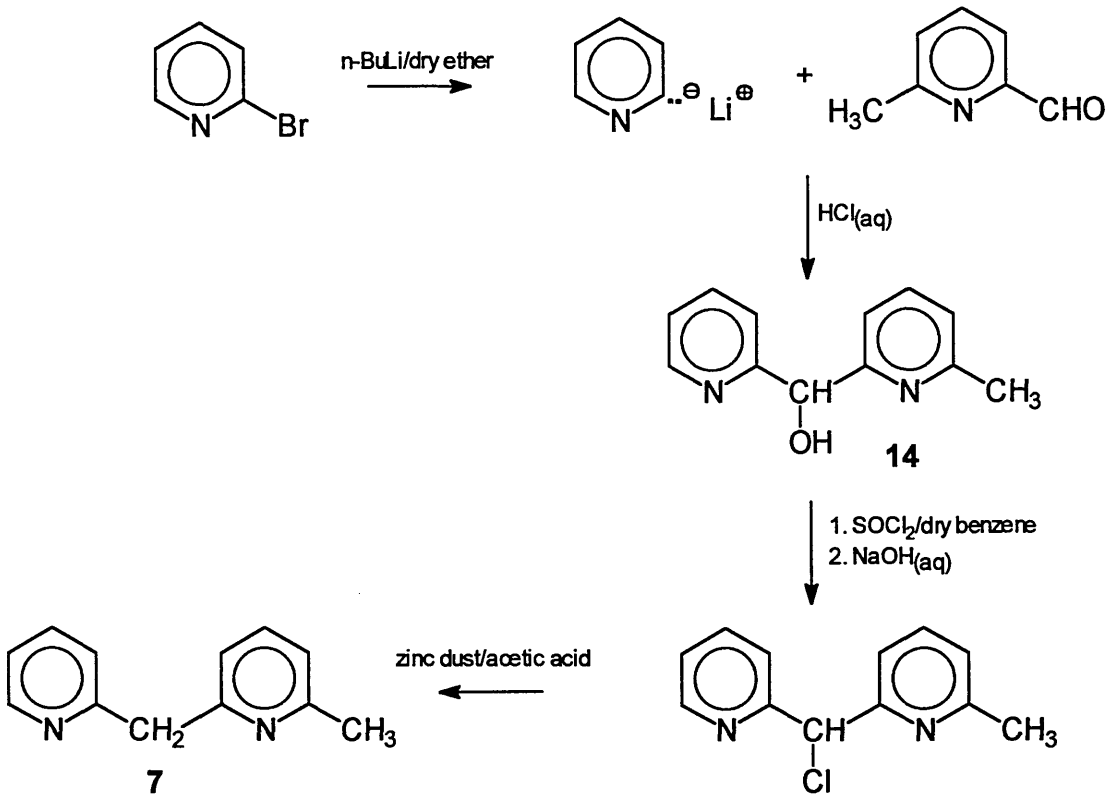
The difficulties encountered on trying to prepare the compound of interest **7** would seem to suggest that the cobaloxime complex falls apart quite easily under the conditions imposed during the photolysis reactions. The pyridine, which behaves as a ligand in the complex, is then free and is more effective at trapping the radicals formed. Attempts were therefore made to prepare the related alkylpyridylCo(dmgH)$_2$(H_2O) complex, where the pyridine basal ligand is replaced by a water molecule. However, these attempts have so far been unsuccessful.

As indicated earlier, the preparation of the 3-, and 4-pyridylmethylCo(dmgH)$_2$(pyridine) complexes was also attempted, but difficulties were encountered here due to the insolubility of the compounds formed. It was felt that that the problem with their synthesis was related to the nitrogen atom in the pyridine ring of the alkylpyridine substituent behaving as the pyridine ligand towards an adjacent complex, leading to the development of an insoluble polymeric structure. Due to these problems, a third approach was considered for the preparation of the pure isomeric dipyridylmethane structure, 2-methyl-6-(2-pyridylmethyl)pyridine **7**.

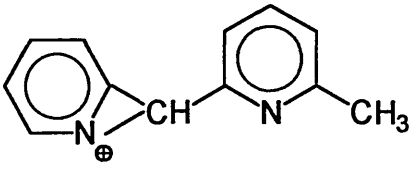
4.3.1.3. Method 3

In this approach the synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine **7** was attempted via a two step synthesis, which involved first preparing 2-pyridyl-6-(2-methylpyridyl)methanol **14**. This was done by treating 2-bromobenzene with n-butyllithium and the 2-pyridyl anion that resulted was formed via a metal-halogen exchange reaction. This was then allowed to react with 6-methyl-2-pyridinecarboxaldehyde to form the appropriate methanol structure **14**. The hydroxy group present in this compound was then reduced by first forming the chloro compound using thionyl chloride. This was then reduced to the hydrocarbon using zinc dust to form the desired compound 2-methyl-6-(2-pyridylmethyl)pyridine **7**, as illustrated in Scheme 8 below.

Scheme 8



This approach was successful in preparing the dipyridylmethane isomer, 2-methyl-6-(2-pyridylmethyl)pyridine and the isomer was purified so that full structural characterisation was possible. The structure was first confirmed by analysis using NMR with the protons in the CH_2 bridge being observed as a singlet at δ 4.30. MS analysis also confirmed the structure with a molecular ion being observed at *m/z* 184. A base peak was found at *m/z* 183 indicating the presence of the stable fragment ion shown below.

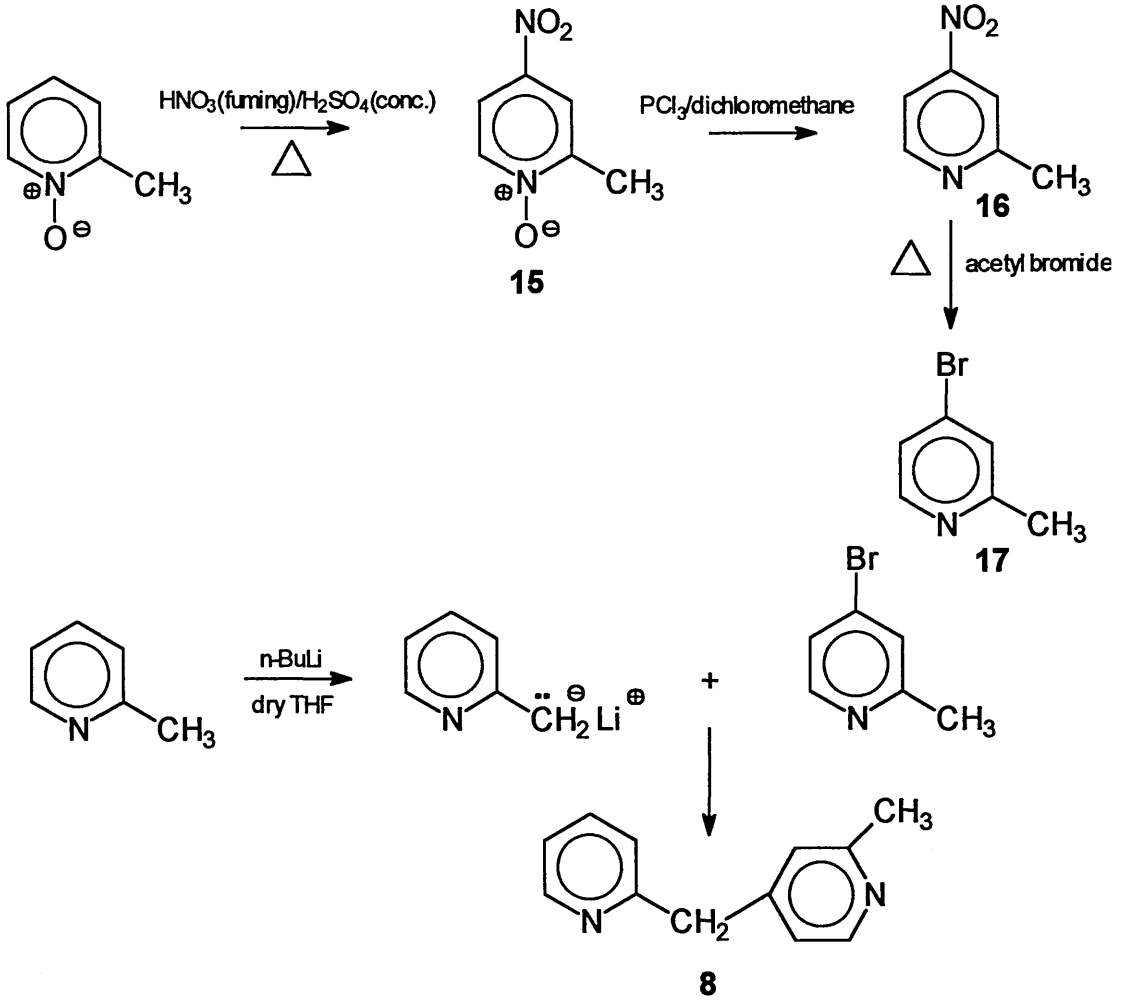


4.3.2. Preparation of 2-methyl-4-(2-pyridylmethyl)pyridine **8**

4.3.2.1. Method 1

This method involved a multistage reaction to first prepare 4-bromo-2-methylpyridine **17** by nitrating 2-methylpyridine-N-oxide and then reducing it to form 4-nitro-2-methylpyridine **16**. Acetyl bromide was then added to 4-nitro-2-methylpyridine and then, under the influence of heat, 4-bromo-2-methylpyridine **17** was formed. The next stage of the synthesis involved the reaction of 2-methylpyridine with n-butyllithium to form the related organolithium intermediate. This was then allowed to undergo a nucleophilic displacement reaction with 4-bromo-2-methylpyridine to form the desired structure, 2-methyl-4-(2-pyridylmethyl)pyridine **8**.

Scheme 9



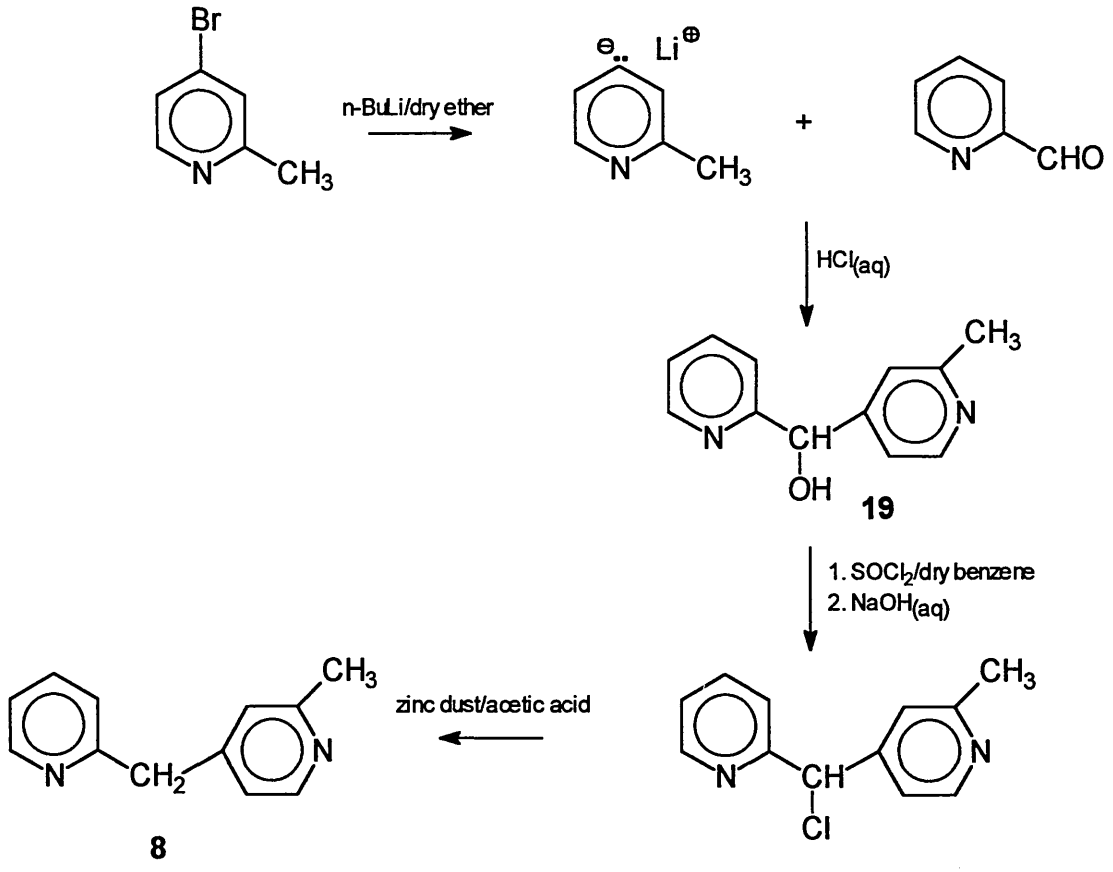
This method was as sucessful at preparing 2-methyl-4-(2-pyridylmethyl)pyridine **8** as it was for preparing the isomer 2-methyl-6-(2-pyridylmethyl)pyridine **7**. However, as in 4.3.1.1., attempts to purify this compound were unsuccessful due to the complexity of the mixture of products that resulted from the reaction. The data that was generated from the GC/MS analysis was used for identification purposes to compare with oxidation products that had been formed in the studies discussed in Chapters 2 and 3. However, a pure form of this compound was required so that structural characterisation could be carried out.

From the study discussed in 4.3.1., method 3 was found to be sucessful at preparing the dipyridylmethane isomer, 2-methyl-6-(2-pyridylmethyl)pyridine **7**. This approach was therefore used in an attempt to produce the isomer 2-methyl-4-(2-pyridylmethyl)pyridine **8**.

4.3.2.2. Method 2

4-Bromo-2-methylpyridine **17** was prepared by using the method outlined in 4.3.2.1. above. This was then allowed to react with n-butyllithium in a metal exchange reaction to generate the 4-pyridyl anion which was then added to pyridine-2-carboxaldehyde to form 2-pyridyl-4-(2-methylpyridyl)methanol **19**. The hydroxy group in this compound was then reduced to the hydrocarbon using thionyl chloride followed by zinc dust to form the desired compound, 2-methyl-4-(2-pyridylmethyl)pyridine **8**, as illustrated in Scheme 10 below.

Scheme 10



Problems were encountered on purifying the intermediate 2-pyridyl-4-(2-methylpyridyl)methanol **19** shown above. Although NMR analysis supported the formation of this compound, impurities still remained after purification using flash column chromatography. The next stage of the synthesis involving reduction of the hydroxy group using thionyl chloride and zinc was attempted but this stage was unsuccessful at producing the target compound. The lack of success was thought to be related to the impurities that were contained in the intermediate **19**.

4.4. Summary

The synthesis of the possible isomeric forms of the dipyridylethene **A** and dipyridylethane **B** structures was successful. The compounds that were prepared are well known and some of the isomers are available commercially. However, attempts at preparing possible isomeric dipyridylmethane **C** structures were less successful. Such compounds are not available commercially and little was found in the literature regarding their preparation. Thus, attempts to prepare some of the possible isomeric dipyridylmethane structures were carried out. The synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine **7** and 2-methyl-4-(2-pyridylmethyl)pyridine **8**, was achieved using the methods found in 4.3.1.1. and 4.3.2.1. respectively. However, these methods were unsuccessful at preparing pure forms of isomers **7** and **8**. Hence, other methods of preparing these compounds and purifying them were attempted and so far one method, shown in 4.3.1.3., has proved to be successful in the preparation and characterisation of 2-methyl-6-(2-pyridylmethyl)pyridine **7** in a pure state.

4.5. Experimental

4.5.1. a) Synthesis of 2-pyridylmethyltriphenylphosphonium chloride **1a**

2-Picolyl chloride hydrochloride (0.0122 mol) was dissolved in a small amount of water (20 cm^3). An aqueous solution of sodium hydroxide (0.0122 mol, 5 cm^3) was then added to this and a fairly vigorous reaction was observed. After the reaction had appeared to reach completion, the aqueous mixture was extracted with diethyl ether (4 x 25 cm^3). The organic phases were combined and dried with magnesium sulphate and the excess organic solvent was removed under reduced pressure to leave approximately 10 cm^3 of a pale green ethereal solution. This solution now contained the free picolyl chloride and it was this that was used in the next stage of the synthesis which involved adding it to triphenylphosphine (0.0122 mol) dissolved in diethyl ether (10 cm^3). The mixture was then refluxed overnight to form a white precipitate which, on cooling, was filtered to give 1.2g of a white powder (27.8% crude yield).

^{1}H NMR ($CDCl_3$) - δ 5.7 (d, 2H), 7.0-8.2 (m, 19H). The doublet at δ 5.7 in ^{1}H NMR is characteristic of -CH_2 next to a phosphorus atom, as phosphorus (as ^{31}P, 100% abundance) has a nuclear spin quantum number of 1/2, like a proton ^{1}H.

4.5.1. b) Synthesis of *cis/trans* 1,2-bis-(2-pyridyl)ethene **1b**

Pyridine-2-carboxaldehyde (0.001 mol) was added to dry methanol (3 cm^3). Then, while stirring under a nitrogen atmosphere, sodium methoxide (0.001 mol, 5 cm^3) in methanol (2 cm^3) was added dropwise from a pressure equalising funnel. After allowing the reaction to proceed for approximately 30

minutes, the reaction mixture was extracted with diethyl ether (4 x 20 cm^3). The combined organic extracts were dried with magnesium sulphate and the excess solvent was removed under reduced presure to give 0.54g of a yellow oil which contained a crystalline solid. The solid was thought to be triphenylphosphine oxide which is an expected side product of the reaction. Analysis by thin layer chromatography (TLC) (9:1 dichloromethane:methanol) identified the presence of two spots which reacted quickly with potassium permanganate indicator. This is 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 as the compounds of interest were well known compounds and only retention time and mass spectral data were required for comparison with oxidation products observed. For this reason, the reaction products were analysed using GC/MS techniques.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), the products of this reaction were analysed using GC/MS techniques. Two major peaks were observed in the GC trace at retention time (t_R) 21.42 and 27.13 minutes, both exhibiting an apparent molecular ion at *m/z* 182 - Appendix 13.

4.5.2. Synthesis of *cis/trans* 1,2-bis-(3-pyridyl)ethene **2**

The method used was identical to that outlined in 4.5.1., only the 3-isomeric reagents were used where appropriate.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), two major peaks were observed in the GC trace at t_R 23.47 and 34.28 minutes, both exhibiting apparent molecular ions at *m/z* 182.

4.5.3. Synthesis of cis/trans 1,2-bis-(4-pyridyl)ethene **3**

The method used was identical to that outlined in 4.5.1., only the 4-isomeric reagents were used where appropriate.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), two major peaks were observed at t_R 21.44 and 29.06 minutes, both exhibiting apparent molecular ions at *m/z* 182.

4.5.4. Synthesis of 1,2-bis-(2-pyridyl)ethane **4**

A mixture of *cis/trans* 1,2-bis-(2-pyridyl)ethene (0.0024 mol) was dissolved in methanol (10 cm^3) and to this a small catalytic amount of platinum(IV) oxide was added. The reaction was stirred under a positive pressure of hydrogen and the reaction was monitored by thin layer chromatography (TLC - 9:1 dichloromethane:methanol). After several hours the spots of the *cis/trans* 1,2-

bis-(2-pyridyl)ethene **1** disappeared and a new spot developed which did not react with potssium permanganate indicator. This observation indicated the absence of any easily oxidisable groups in the product of the reaction, which is expected. On completion of the reaction, the catalyst was filtered and the excess methanol was removed under reduced pressure to give 0.40g (90.4% crude yield) of a yellow oil.

^{1}H NMR ($CDCl_3$) - δ 3.3 (s, 4H), 7.1-8.7 (m, 8H). The singlet observed at δ 3.3 is due to the protons in the -CH_2-CH_2- bridge between the two pyridine rings. All of these protons are equivalent and therefore a singlet is expected to represent the presence of this bridge.

No attempts were made to purify 1,2-bis-(2-pyridyl)ethane as only retention time and mass spectral data were required for comparison purposes. Therefore GC/MS analysis was carried out on the crude product.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), the product of this reaction was analysed using GC/MS techniques. A major peak was observed at a t_R 18.13 minutes and this compound exhibited an apparent molecular ion at *m/z* 184 - Appendix 4.

4.5.5. Synthesis of 1,2-bis-(3-pyridyl)ethane **5**

The method used here was identical to that outlined in 4.5.4., only the 3-iomeric reagents were used where appropriate.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), a major peak was observed at t_R 21.22 minutes and this compound exhibited n apparent molecular ion at *m/z* 184 - Appendix 3.

4.5.6. Synthesis of 1,2-bis-(4-pyridyl)ethane **6**

The method used here was identical to that outlined in 4.5.4., only the 4-isomeric reagents were used where appropriate.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), a major peak was observed at t_R 25.11 minutes and this compound exhibited an apparent molecular ion at *m/z* 184 - Appendix 8.

4.5.7. Synthesis of 2-Methyl-6-(2-pyridylmethyl)pyridine **7** - Method 1

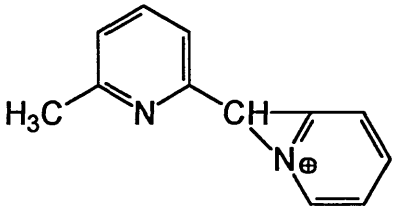
2,6-Lutidine (0.01 mol) was added to dry tetrahydrofuran (20 cm^3). The reaction vessel was purged with nitrogen and n-butyl lithium (0.01 mol) was added dropwise from a syringe after the reaction mixture had been cooled to -78°C using a dry ice/acetone bath. After complete addition of the n-butyl lithium, the reaction remained stirring at -78°C for approximately 15 minutes. 2-

Bromopyridine (0.01 mol) in dry tetrahydrofuran (10 cm^3) was then added dropwise from a pressure equalising funnel. The reaction mixture was returned to room temperature and the system was left stirring overnight.

Upon the workup of the reaction, an excess of water was added initially to remove any anhydrous lithium salts that may have been formed in the reaction. The aqueous solution that remained was then extracted with dichloromethane (6 x 25 cm^3). The extracts were combined and dried with magnesium sulphate and the excess solvent was removed under reduced pressure to give 2.35g of a brown liquid. Analysis by thin layer chromatography (50:50 dichloromethane:petroleum ether) indicated a complex mixture which contained unreacted starting materials. For this reason, attempts to identify the component of interest involved analysis of the product mixture using GC/MS techniques.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), a GC trace was obtained which contained a mixture of components. They included 2,6-lutidine and 2-bromopyridine at t_R 4.15 and 9.38 minutes, respectively. The component of interest, 2-methyl-6-(2-pyridylmethyl)pyridine was identified at t_R 18.37 minutes exhibiting an apparent molecular ion of 184 - Appendix 14. The base peak was observed at m/z 183 which may be due to the presence of the following fragment ion(2)



4.5.8. Synthesis of 2-pyridylmethylCo(dmgH)$_2$(pyridine) **9**[8]-[10]

Under a nitrogen atmosphere, dimethylglyoxime (0.02 mol), and cobalt(II) chloride hexahydrate were added to degassed methanol (40 cm^3) and stirred. Pyridine (0.011 mol) was then added to the flask via a syringe followed by a sodium hydroxide solution (0.04 mol, 5 cm^3 water). After the blue/black colour of the cobalt(I) species had developed, 2-chloromethylpyridine (from the related hydrochloride, 0.005 mol together with 2.5 cm^3 of 2M sodium hydroxide) in methanol (5 cm^3) was then injected into the reaction mixture and immediately the orange/brown colour of the cobalt(III) cobaloxime formed.

Upon workup, water (50 cm^3) was added to the mixture and an extraction was carried out using dichloromethane (3 x 100 cm^3). The extracts were combined and dried using magnesium sulphate. The excess dichloromethane was removed under reduced pressure to give 1.61g (35.0% crude yield) of a red solid. The solid smelt strongly of pyridine and therefore it was washed several times with petroleum ether (4 x 25 cm^3) to give 1.3g (28.3% crude yield) of a red/brown solid.

^{1}H NMR ($CDCl_3$) - δ 2.05 (s, 12H), 2.90 (s, 2H), 7.0-8.6 (m, 9H). The singlet at δ 2.05 indicates the presence of the methyl groups in the cobaloxime planar structure which are all equivalent and the singlet at δ 2.90 indicates the -CH_2 group linking the pyridine ring to the cobaloxime complex. The aromatic multiplets indicate the presence of heteroaromatic rings[9]. The NMR spectrum, however, also indicated the presence of impurities. Attempts were made to purify the complex using flash column chromatography (1 : 10 : 90, pyridine : methanol : dichloromethane) but this did not improve the purity of the complex as the NMR spectrum still exhibited extra peaks in the region of δ 2.5.

4.5.9. Synthesis of 2-Methyl-6-(2-pyridylmethyl)pyridine **7** - Method 2

The cobaloxime complex (0.00037 mol), 2-methylpyridylCo(dmgH)$_2$(pyridine), that had been prepared was added to ethanol (10 cm^3) together with 2-methylpyridine (0.00037 mol) and camphor sulphonic acid (0.00037 mol). Under a nitrogen atmosphere, the system was stirred and irradiated with a 500 watt light supply for 6 hours. After this time the mixture was allowed to cool and then analysed using GC/MS techniques.

GC/MS Analysis

Using instrument 2 and temperature programme 2 (Chapter 2, section 2.1.3.), the presence of a component exhibiting an apparent molecular ion at *m/z* 170 and a base peak at *m/z* 169 was observed, consistent with the formation of a single dipyridylmethane rather than the desired compound 2-methyl-6-(2-pyridylmethyl)pyridine **7** - Appendix 15.

4.5.10. Synthesis of 2-Methyl-6-(2-pyridylmethyl)pyridine **7** -Method 3

2-Bromopyridine (0.01 mol) was added to dry diethyl ether (10 cm^3) and the reaction vessel was purged with nitrogen. After reducing the temperature of the reaction mixture to -78°C using a dry ice/acetone bath, n-butyllithium (0.01 mol) was added dropwise via a syringe. On complete addition of the n-butyllitium, the reaction mixture was held at -78°C for approximately 15 minutes. 6-Methyl-2-pyridinecarboxaldehyde (0.01 mol) in diethyl ether (10 cm^3) was then added dropwise to the reaction from a pressure equalising dropping funnel. The reaction mixture was then allowed to return to room temperature and the system was left stirring overnight.

The workup of the reaction involved first adding dilute hydrochloric acid (~20 cm^3, 1 mol dm^{-3}) and a clear orange solution resulted. The mixture was then neutralised using sodium hydroxide (2 mol dm^{-3}) prior to extraction using dichloromethane (4 x 50 cm^3). The extracts were combined and dried using magnesium sulphate and the excess solvent was removed under reduced pressure to give 3.27g of a yellow oil. Analysis by TLC (9.5:0.5 dichloromethane:methanol) identified a complex mixture which contained a large spot which developed quickly using potassium permanganate as an indicator This spot was believed to be due to the formation of the intermediate 2-pyridyl-6-(2-methylpyridyl)methanol **14**. Purification using flash column chromatography and the solvent system used for TLC analysis produced 0.47g of a yellow oil (23.5% crude yield).

^{1}H NMR ($CDCl_3$) - δ 2.50 (s, 3H), 5.70 (s, 1H), 5.85 (s, 1H), 7.0-8.0 (m, 6H), 8.75 (d, 1H). The presence of the hydroxy (OH) group in **14** formed in the reaction was confirmed by the presence of the broad peak in the region of δ 5, which disappeared when the deuterated chloroform mixture was shaken with deuterated water. The doublet observed at δ 8.75 indicated the presence of an *ortho* hydrogen on the pyridine ring which is present in the structure of **14**. The NMR does support the formation of 2-pyridyl-6-(2-methylpyridyl)methanol **14** and therefore the hydroxy group was then reduced to form a $-CH_2$ bridge in a two step reaction to form 2-methyl-6-(2-pyridylmethyl)pyridine **15**[10].

2-Methyl-6-(2-pyridylhydroxymethyl)pyridine **14** (0.0037 mol) was added to benzene and, with stirring and ice cooling, thionyl chloride (0.004 mol) was added dropwise[11]. The reaction mixture was allowed to stir at room temperature for 1 hour. After this time, with ice cooling again, the system was made alkaline by the addition of sodium hydroxide (40% w/v aqueous solution) and two layers were formed. The layers were separated and the organic layer

was washed with cold water and dried using magnesium sulphate The excess solvent was removed under reduced pressure to give 0.47g of a red oil (58.3% crude yield). This was then dissolved in glacial acetic acid (5 cm^3) and to this stirred mixture, zinc dust (~1g) was added. The reaction was then heated overnight but not to reflux.

The workup involved allowing the reaction to cool and then adding it to water (20 cm^3). The mixture was then made alkaline using sodium hydroxide (2 mol dm^{-3}) prior to extraction with diethyl ether (4 x 25 cm^3). The extracts were combined and dried using magnesium sulphate and the excess solvent was removed under reduced pressure to give 0.27g (39.7% crude yield) of a yellow oil.

^{1}H NMR ($CDCl_3$) - δ 2.60 (s, 3H), 4.30 (s, 2H), 7.0-8.70 (m, 7H), 8.6 (d, 1H).

GC/MS Analysis

Instrument 1 and temperature programme 2 (Chapter 2, section 2.1.3.) identified the component of interest at t_R 15.57 minutes exhibiting an apparent molecular ion at *m/z* 184.

Accurate Mass Analysis

This analysis confirmed the mass and molecular formula of the compound formed in this reaction. The expected mass of this compound was calculated to be 184.10012 and the experimentally observed mass was found to be 184.10005.

4.5.11. Synthesis of 4-Nitro-2-methylpyrdine-N-oxide **15** [12]

To 2-Methylpyridine-N-oxide (0.05 mol) was added, with care, concentrated sulphuric acid (21.88 cm^3). Then, with ice cooling, fuming nitric acid (17.25 cm^3) was added dropwise to the mixture while maintaining the reaction temperature below 20°C. Upon complete addition, the mixture was heated to 100-105°C for 6 hours. After this time the reaction was allowed to cool to room temperature and was left stirring overnight.

The workup of the reaction involved adding the mixture to crushed ice. The system was then neutralised using sodium carbonate prior to extraction with dichloromethane (4 x 100 cm^3). The extracts were combined, washed with a saturated sodium chloride solution, and then dried using magnesium sulphate. The excess solvent was removed under reduced pressure to give 6.49g of a yellow powder (84.3% crude yield) which had a melting point at 148-151°C.

^{1}H NMR ($CDCl_3$) - δ 2.55 (s, 3H), 8.0 (m, 2H), 8.4 (d, 1H). The NMR spectrum compares with that found in the literature[12] thus supporting the identity of the product as the desired compound.

4.5.12. Synthesis of 4-Nitro-2-methylpyridine **16**[12]

4-Nitro-2-methylpyridine-N-oxide (0.041 mol) was dissolved in dichloromethane (80 cm^3). Phophorus trichloride (0.2 mol) dissolved in dichloromethane (80 cm^3) was added to this solution dropwise, under a nitrogen atmosphere, while the system was cooled in an ice bath. Upon complete addition of the phosphorus trichloride, the reaction mixture was allowed to stir at room temperature overnight.

The workup of the reaction involved pouring the mixture into crushed ice and then neutralising the system using aqueous ammonia prior to extraction with dichloromethane (4 x 100 cm^3). The extracts were combined and washed with a saturated sodium chloride solution and then dried using magnesium sulphate. The excess solvent was removed under reduced pressure to give 4.10g of a yellow solid (72.5% crude yield).

No analysis was carried out on the solid fomed in this reaction but it was assumed that the reaction had been successful and the solid formed was used in the next stage of the synthesis.

4.5.13. Synthesis of 4-Bromo-2-methylpyridine **17**[12]

Acetyl bromide (0.09 mol) was added, with care, to 4-nitro-2-methylpyridine (0.03 mol) and the mixture was stirred and refluxed overnight.

Upon workup, the mixture was first allowed to cool and was then added to crushed ice. The aqueous mixture was then neutralised using sodium carbonate prior to extraction with diethyl ether (4 x 50 cm^3). The combined extracts were washed with a solution of saturated sodium chloride and then dried using magnesium sulphate. The excess solvent was removed under reduced pressure to give 5.54 g of a pale yellow oil (108% crude yield). Analysis by TLC identified a mixture of components which contained a predominant amount of one product. This product was isolated using flash column chromatography and the solvent system used in the TLC analysis to give 3.83g of a yellow oil (74.3% yield).

^{1}H NMR ($CDCl_3$) - δ 2.5 (s, 3H), 7.4 (m, 2H), 8.3 (d, 1H). The data from this NMR compares with that obtained from the literature[12].

MS Analysis - The molecular envelope at *m/z* 171 was a 1:1 doublet at m/z 171 and 173 confirming the synthesis of a bromine containing compound.

4.5.14. Synthesis of 2-Methyl-4-(2-pyridylmethyl)pyridine **18** - Method 1

2-Methylpyridine (0.0052 mol) was added to dry tetrahydrofuran (20 cm^3) and stirred under a nitrogen atmosphere. The temperature of the reaction mixture was then lowered to -78°C using a dry ice/acetone bath and n-butyllithium (0.0052 mol) was injected into the reaction mixture. After 15 minutes, 4-bromo-2-methylpyridine in dry tetrahydrofuran (10 cm^3) was added dropwise from a pressure equalising funnel while the reaction was still cold. The reaction was then allowed to return to room temperature and it was left stirring overnight.

The workup involved adding an excess of water to solvate any anhydrous lithium salts that may have formed and the aqueous mixture was then extracted with dichloromethane (6 x 25 cm^3). The extracts were combined and dried using magnesium sulphate and the excess solvent was removed under reduced pressure to give 1.05g of an orange/brown oil. Analysis by TLC (50:50 dichloromethane:petroleum ether) identified a complex mixture which indicated the presence of starting materials. Therefore, attempts were made to identify the component of interest by using GC/MS techniques.

GC/MS Analysis

Using instrument 1 and temperature programme 1, a GC trace was obtained which contained a mixture of components. They included 2-methylpyridine and 4-bromo-2-methylpyridine at t_R 7.72 and 12.32 minutes, respectively. The component of interest, 2-methyl-4-(2-pyridylmethyl)pyridine was identified at t_R 29.46 minutes exhibiting an apparent molecular ion at m/z 184 - Appendix 16.

4.5.15. Synthesis of 2-Methyl-4-(2-pyridylmethyl)pyridine **18** - Method 2

4-Bromo-2-methylpyridine (0.0076 mol) was added to dry diethyl ether (10 cm^3) and stirred under a nitrogen atmosphere. The temperature of the reaction mixture was then lowered to -78°C using a dry ice/acetone bath and n-butyllithium (0.0076 mol) was injected into the reaction mixture. After 15 minutes, pyridine-2-carboxaldehyde (0.0076 mol) in dry diethyl ether (10 cm^3) was added dropwise from a pressure equalising funnel while the reaction was still cold. The reaction was then allowed to return to room temperature and it was left stirring overnight.

The workup involved first adding dilute hydrochloric acid (~20 cm^3, 1 mol dm^{-3}) and the mixture was then neutralised using sodium hydroxide (2 mol dm^{-3}) prior to extraction using dichlromethane (4 x 50 cm^3). The extracts were combined and dried using magnesium sulphate and the excess solvent was removed under reduced pressure to give 0.91g of a brown oil (59.9% crude yield). Analysis by TLC (9.5:0.5 dichloromethane:methanol) identified a complex mixture which contained a large spot which developed quickly using potassium permanganate as an indicator. Purification using flash column chromatography and the solvent system used for TLC analysis produced 0.25g of a brown oil (16.4% yield).

^{1}H NMR ($CDCl_3$) - δ 4.1 (s, 1H), 4.8 (s, 3H), 5.4 (s, 1H), 7-8.7 (m, 7H). The NMR spectrum contains the peaks of interest, in particular that for the OH group at δ 5.4. The presence of the OH group was confirmed by shaking the deuterated chloroform mixture with deuterated water and observing the disappearance of the peak at δ 5.4. However, the NMR identified the presence of impurities but the next stage of the synthesis was still attempted to reduce the hydroxy group to give the dipyridylmethane isomer **8**.

2-Methyl-4-(2-methylpyridyl)methanol **19** (0.001 mol) was added to benzene and, with stirring and ice cooling, thionyl chloride (0.004 mol) was added dropwise[11]. The reaction mixture was allowed to stir at room temperature for 1 hour. After this time, with ice cooling again, the system was made alkaline by the addition of sodium hydroxide (40% w/v aqueous solution) and two layers were formed. The layers were separated and the organic layer was washed with cold water and dried using magnesium sulphate The excess solvent was removed under reduced pressure to give 0.06g of a red oil (27.5% crude yield). This was then dissolved in glacial acetic acid (5 cm^3) and to this stirred mixture, zinc dust (~1g) was added. The reaction was then heated overnight but not to reflux.

The workup involved allowing the reaction to cool and then adding it to water (20 cm^3). The mixture was then made alkaline using sodium hydroxide (2 mol dm^{-3}) prior to extraction with diethyl ether (4 x 25 cm^3). The extracts were combined and dried using magnesium sulphate and the excess solvent was removed under reduced pressure to give 0.07g (38.0% crude yield) of a yellow oil.

GC/MS Analysis

Using instrument 1 and temperature programme 2, a GC trace was obtained which did not identify the presence of 2-methyl-4-(2-pyridylmethyl)pyridine.

4.6. References

1. a) Streitwieser A. & Heathcock C.H., Introduction to Organic Chemistry, Collier Macmillan Publishers, Third Edition, Chapter 11, pp 254 & Chapter 14, pp 39, b) Dictionary of OrganicCompounds - Cumulative Index Volumes 1-5, Chapman and Hall Publishers, Fifth Edition, pp298.
2. Osbourne A.G., Mass Spectral Studies of Biheteroaryls. Part 2. Diheteroarylalkanes, *Spectroscopy Letters*, 1985, **18**, 15-34.
3. Bhandal H., Patel V.F., Pattenden G. & Russell J.J., Cobalt Mediated Radical Reactions in Organic Synthesis. Oxidative Cyclisations of Aryl and Alkyl Halides leading to Functionalised Reduces Heterocycles and Butyrolactones, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2691-2701.
4. Brown T., Cooksey C.J., Crich D., Dronsfield A.T. & Ellis R., Generation and Trapping of Benzyl Radicals from Benzyl Iodides by Cobaloxime-Mediated Iodine Atom Abstractions, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2131-2136.
5. Brown T. & Cooksey C.J., Cobaloximes, Education in Chemistry, May 1987, 77-80.
6. Branchaud B.P., Meier M.S. & Malekzadeh M.N., New Synthetic Methods via Free Radicals. Free-Radical Generation via Photolytic Homolysis of Alkyl-Cobaloxime C-Co Bonds. Efficient Radical Trapping with useful Functional Groups, *J. Org. Chem.*, 1987, **52**, 212-217.
7. Branchaud B.P. & Choi Y.L., Cobaloxime-Mediated Radical Alkyl-Heteroaromatic Substitution, *J. Org. Chem.*, 1988, **53**, 4638-4641.
8. Brown T., personal communication.
9. Ashcroft M.R., Atkins M.P., Golding B.T., Johnson M.D. & Sellars P.J., Synthetic Methods for Alkyl(pyridine)cobaloximes: 3,3,3-Triphenylpropyl- and Methylbut-3-enyl-(pyridine)cobaloxime, *J. Chem. Research (S)*, 1982, 216-217.

10. Gupa B.D. & Roy S., NMR Spectra of Cobaloximes: Unexpected Equivalence of Methyl Groups, *Tetrahedron Letters*, 1985, **26**, 3609-3612.

11. Leonard N.J. & Ryder B.L., The Stereoisomers of *vic*-Dialkylpiperidines. The 2-*n*-Butyl-3-Methylpiperidines, *J. Org. Chem.*, 1953, **18**, 598.

12. Ashimori A., Uno T., Uchida T., Ohtaki Y., Fukaya C., Watanabe M & Yokoyama K., Novel 1,2-dihydropyridine Calcium Antagonists. I. Synthesis and Hypotensive Activity of 4-(Substituted Pyridyl)-1,4-dihydropyrdine Derivatives, *Chem. Pharm. Bull.*, 1990, **38**, 2446-2458.

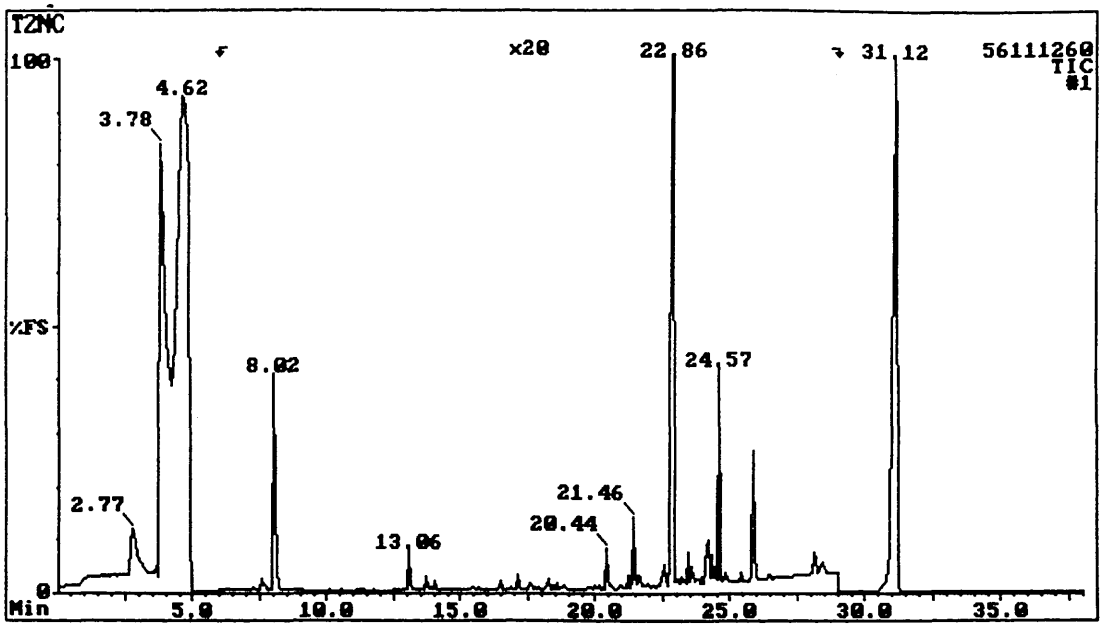
Appendix

1. Gas chromatogram of the uncatalysed autoclave oxidation of 2-methylpyridine
2. Mass spectra of 2-hydroxy-6-methylpyridine formed in the uncatalysed autoclave oxidation of 2-methylpyridine and of the standard material, 2-hydroxy-6-methylpyridine
3. Mass spectra of 4-methyl-2-(4-pyridylmethyl)pyridine formed in the uncatalysed autoclave oxidation of 4-methylpyridine and of the standard material, 1,2-bis-(4-pyridyl)ethane
4. Mass spectra of 2-methyl-6-(2-pyridylmethyl)pyridine and 1,2-bis-(2-pyridyl)ethane formed in the iron(III)/hydrogen peroxide catalysed autoclave oxidation of 2-methylpyridine and of the standard material 1,2-bis-(2-pyridyl)ethane
5. Mass spectra of 2,2'dimethyl-4,4'-bipyridine and 2,2'-dimethyl-6,6'-bipyridine formed in the iron(III)/hydrogen peroxide catalysed autoclave oxidation of 2-methylpyridine and of the standard material, 4,4'-dimethyl-2,2'-bipyridine
6. Mass spectrum of 4-hydroxy-2-methylpyridine formed in the iron(III)/hydrogen peroxide catalysed autoclave oxidation of 2-methylpyridine
7. Mass spectra of 2,2'-bipyridine formed in the copper(II)/hydrogen peroxide catalysed autoclave oxidation of 2-methylpyridine and a mass spectra of the standard material, 2,2'-bipyridine
8. Mass spectra of 5-methyl-2-(3-pyridylmethyl)pyridine formed in the copper(II)/hydrogen peroxide catalysed autoclave oxidation of 3-methylpyridine and of the standard material, 1,2-bis-(3-pyridyl)ethane
9. Mass spectra of 5-methyl-2-(2-pyridyl)pyridine, 2-(3-pyridylmethyl)pyridine, and 4-(3-pyridylmethyl)pyridine formed in the copper(II)/hydrogen peroxide catalysed autoclave oxidation of 3-methylpyridine

10. Mass spectra of 1,2-bis-(4-pyridyl)ethane formed in the copper(II)/hydrogen peroxide catalysed autoclave oxidation of 4-methylpyridine
11. Chromatogram of the Fenton-catalysed oxidation of 2-methylpyridine spiked with pyridine-2-carboxylic acid
12. Mass spectra of 3-hydroxymethylpyridine and 2-hydroxy-5-methylpyridine formed in the Fenton-catalysed oxidation of 3-methylpyridine and of the standard material, 2-hydroxymethylpyridine
13. Mass spectra of *cis/trans* 1,2-bis-(2-pyridyl)ethene
14. Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine (Method 1) and a mass spectrum of this component
15. Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine (Method 2) and a mass spectrum of the component exhibiting an apparent molecular ion at *m/z* 170
16. Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-4-(2-pyridylmethyl)pyridine (Method 2) and a mass spectrum of this component.

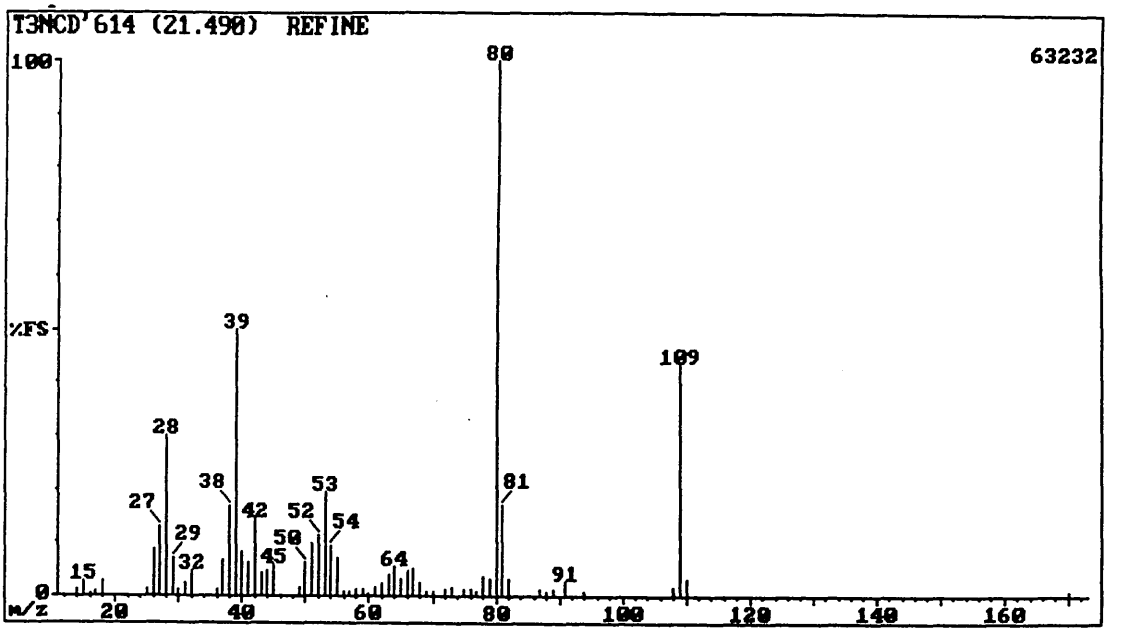
Appendix 1

Gas chromatogram of the uncatalysed autoclave oxidation of 2-methylpyridine

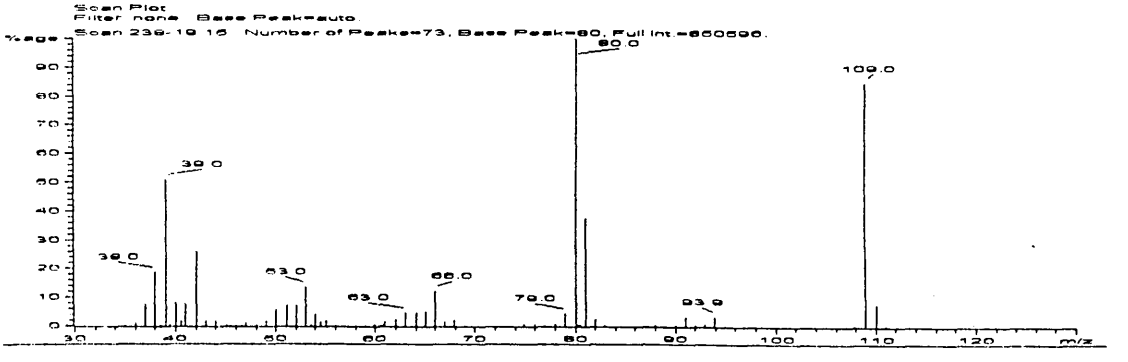


Appendix 2

Mass spectrum of 2-hydroxy-6-methylpyridine formed in the uncatalysed autoclave oxidation of 2-methylpyridine

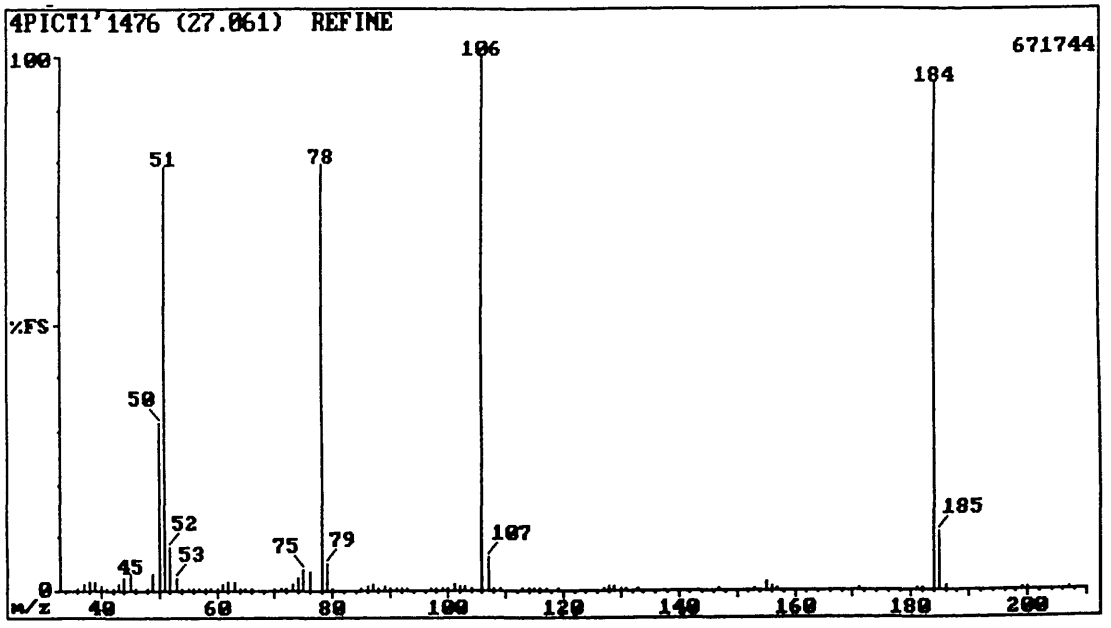


Mass spectrum of the standard material 2-hydroxy-6-methylpyridine

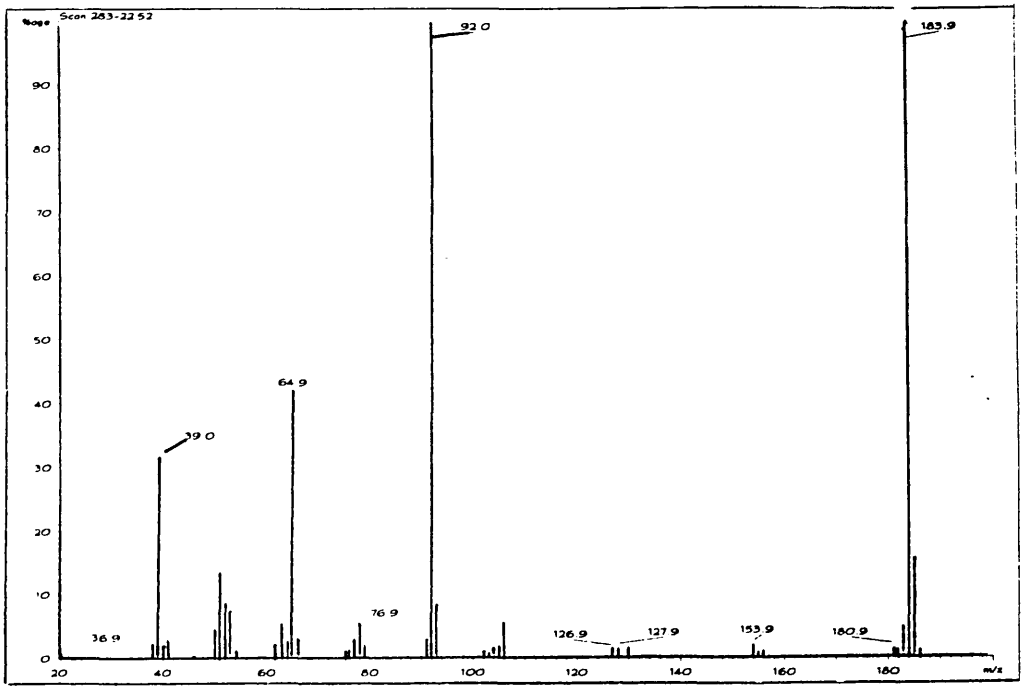


Appendix 3

Mass spectrum of 4-methyl-2-(4-pyridylmethyl)pyridine formed in the uncatalysed autoclave oxidation of 4-methylpyridine



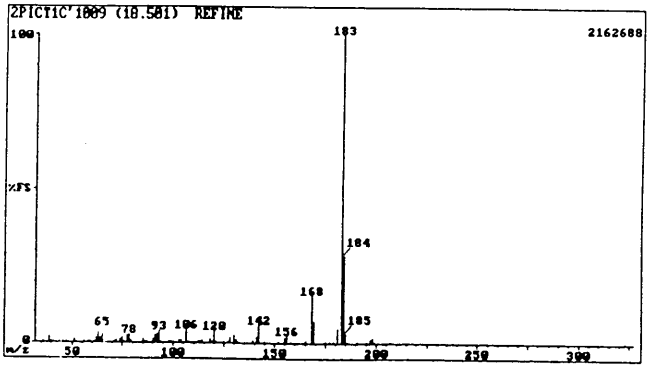
Mass spectrum of the standard material 1,2-bis-(4-pyridyl)ethane



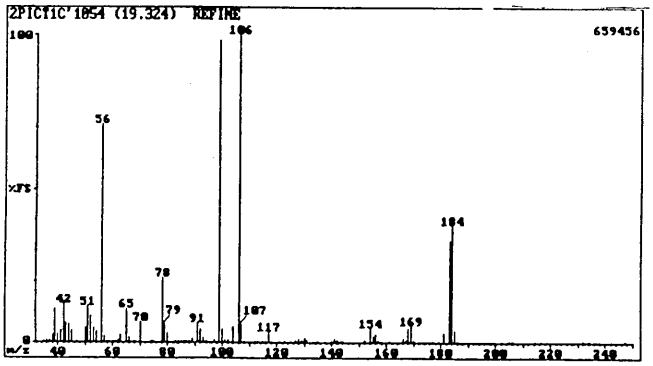
Appendix 4

Mass spectra of 2-methyl-6-(2-pyridylmethyl)pyridine (i) and 1,2-bis-(2-pyridyl)ethane (ii) formed in the iron(III)/hydrogen peroxide-catalysed autoclave oxidation of 2-methylpyridine

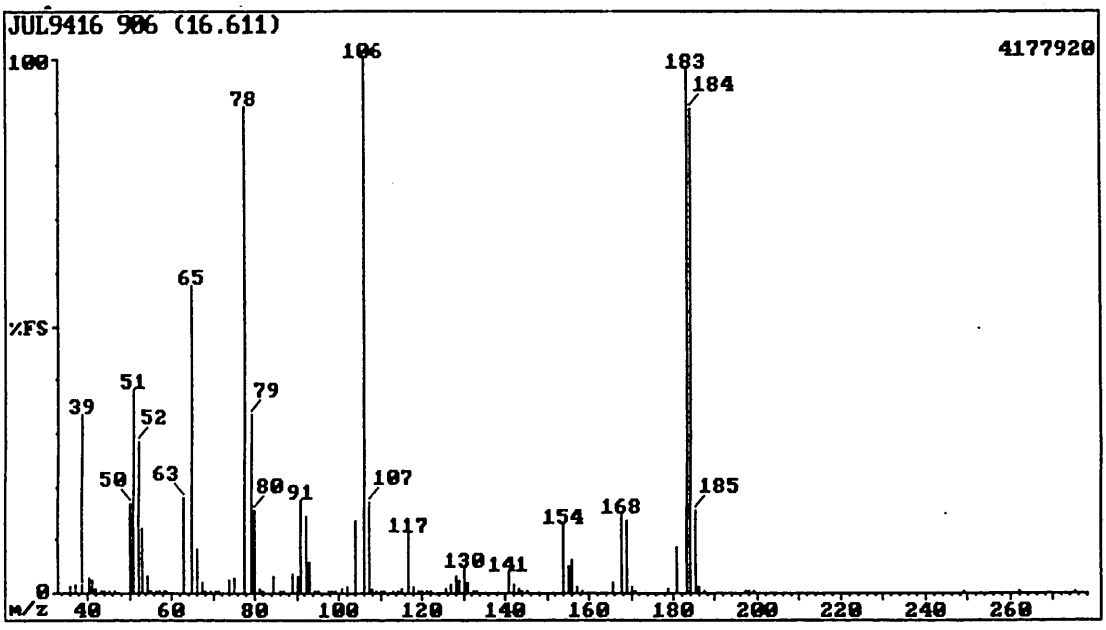
(i)



(ii)



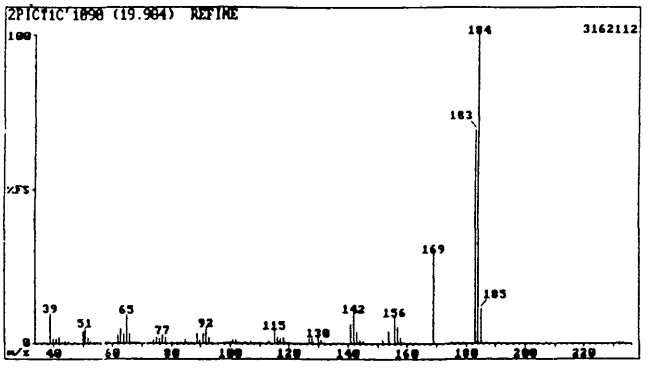
Mass spectra of the standard material 1,2-bis-(2-pyridyl)ethane



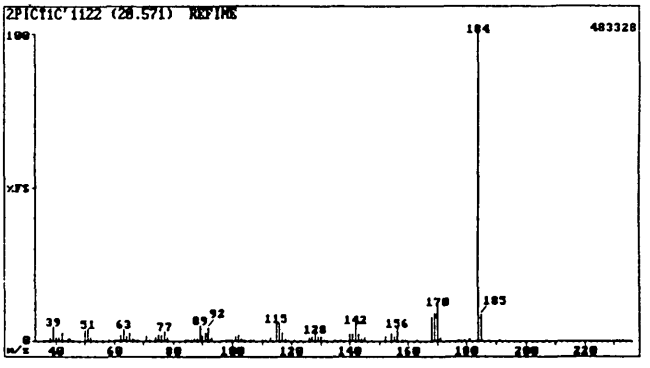
Appendix 5

Mass spectra of 2,2'-dimethyl-4,4'-bipyridine (i) and 2,2'-dimethyl-6,6'-bipyridine (ii) formed in the iron(III)-catalysed autoclave oxidation of 2-methylpyridine

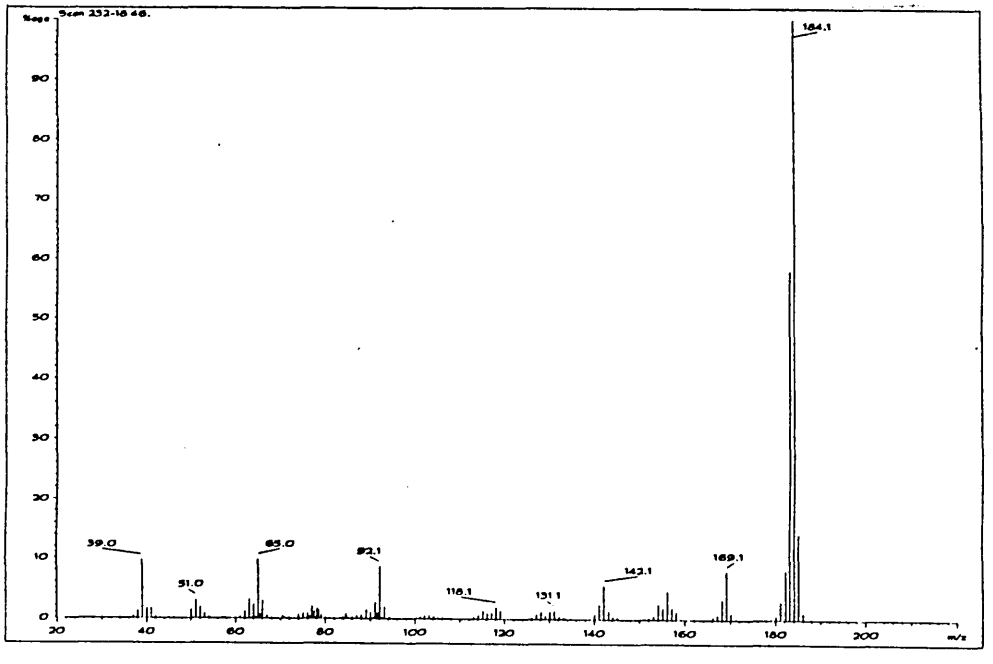
(i)



(ii)

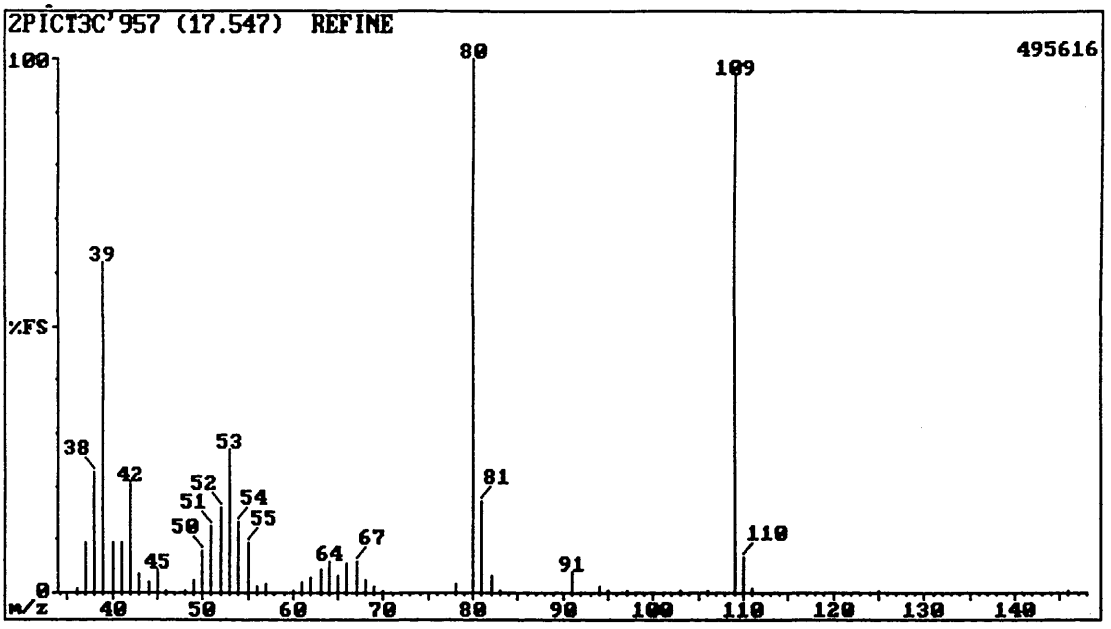


Mass spectra of the standard material 4,4'-dimethyl-2,2'-bipyridine



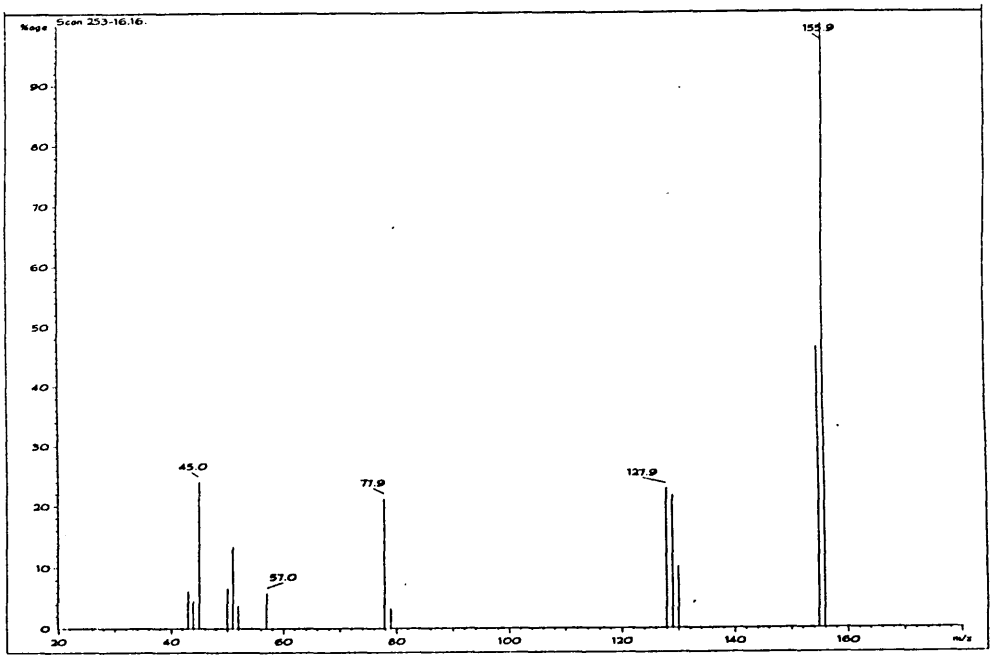
Appendix 6

Mass spectrum of 4-hydroxy-2-methylpyridine formed in the iron(III)/hydrogen peroxide catalysed autoclave oxidation of 2-methylpyridine

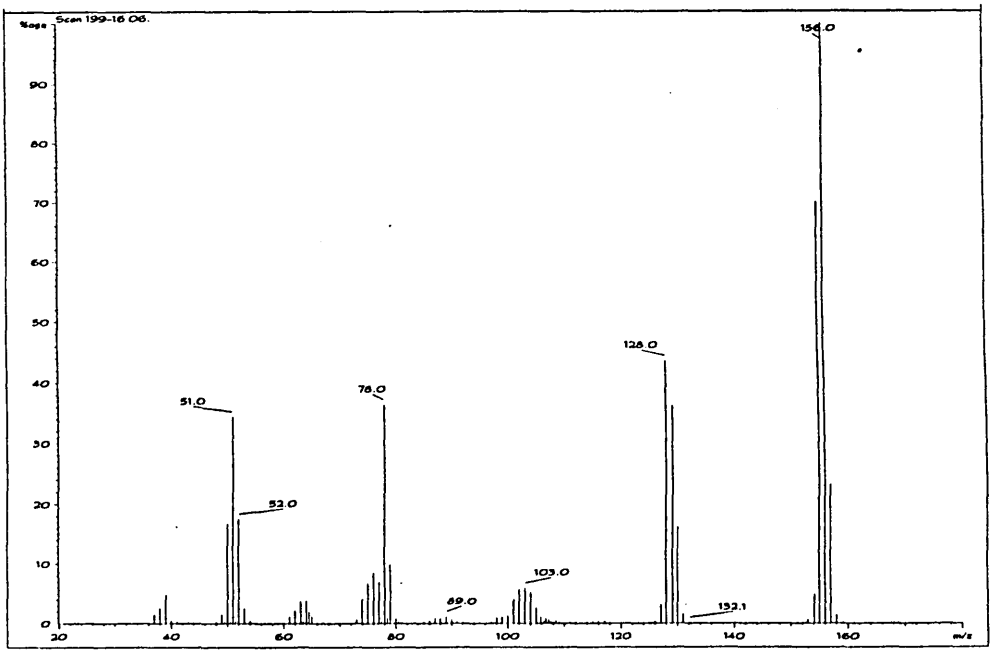


Appendix 7

Mass spectrum of 2,2'-bipyridine formed in the copper(II)/hydrogen peroxide-catalysed autoclave oxidation of 2-methylpyridine

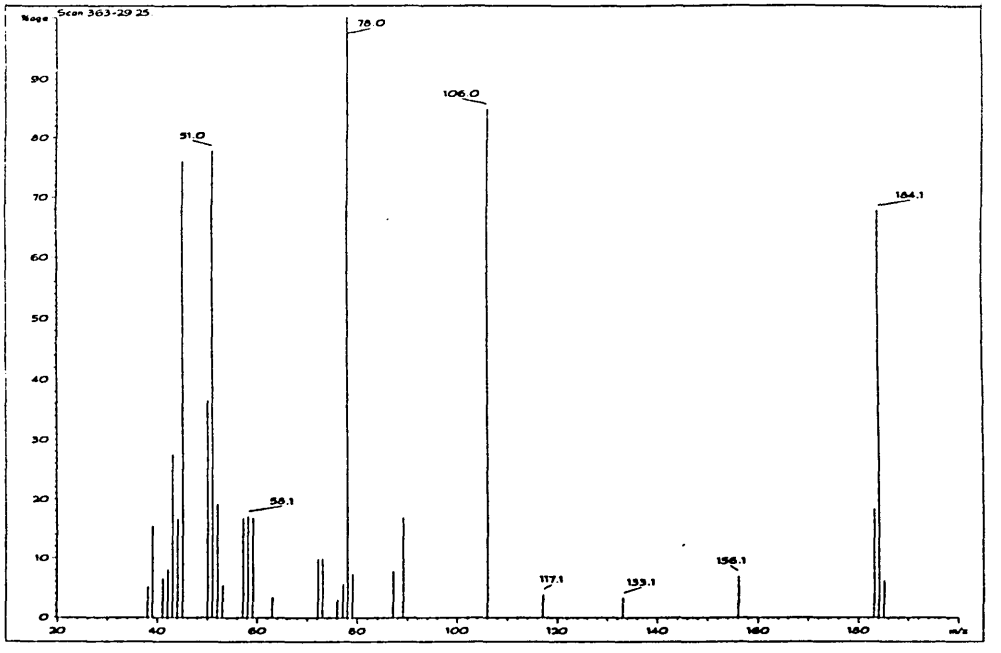


Mass spectrum of the standard material 2,2'-bipyridine

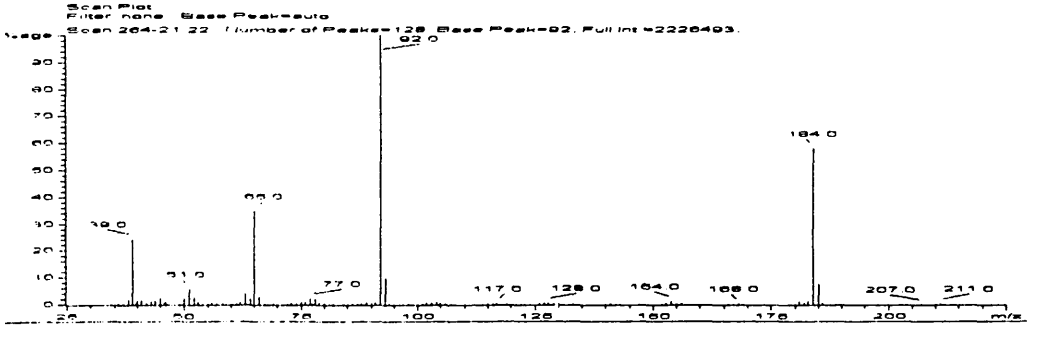


Appendix 8

Mass spectrum of 5-methyl-2-(3-pyridylmethyl)pyridine formed in the copper(II)/hydrogen peroxide-catalysed autoclave oxidation of 3-methylpyridine



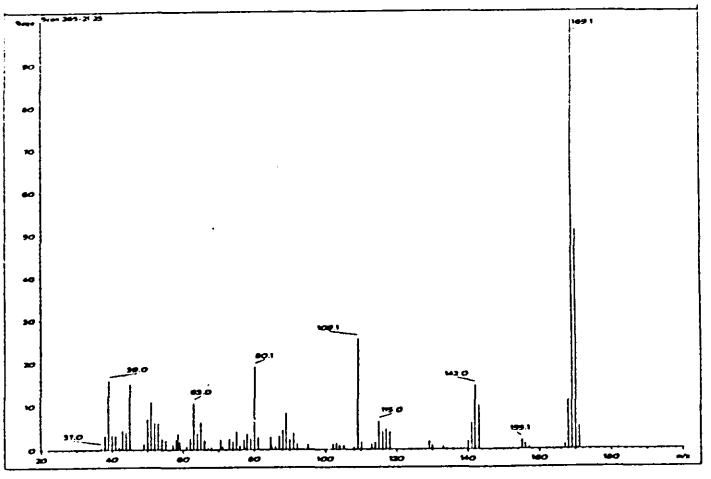
Mass spectrum of the standard material 1,2-bis-(3-pyridyl)ethane



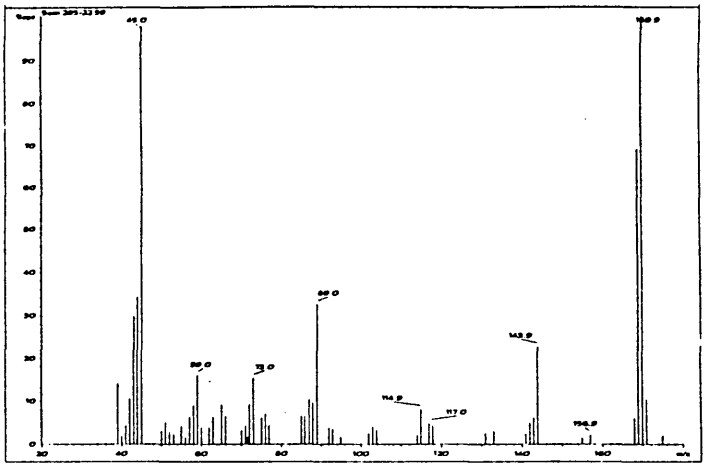
Appendix 9

Mass spectrum of2-(3-pyridylmethyl)pyrdine (i), 5-methyl-2-(2-pyridyl)pyridine (ii), and 4-(3-pyridylmethyl)pyridine (iii) formed in the copper(II)/hydrogen peroxide-catalysed autoclave oxidation of 3-methylpyridine

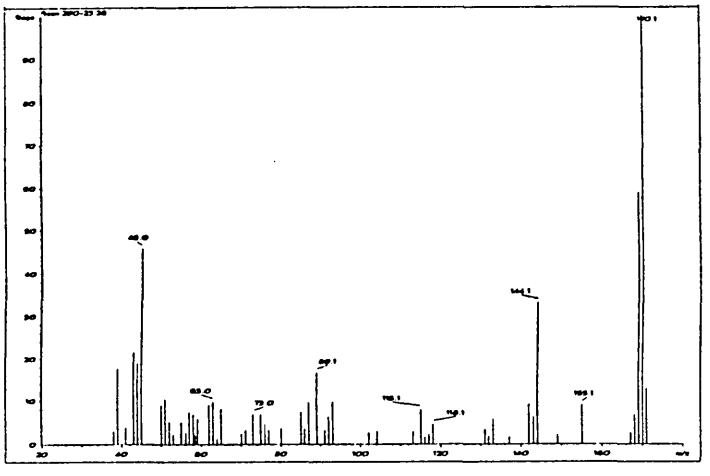
(i)



(ii)

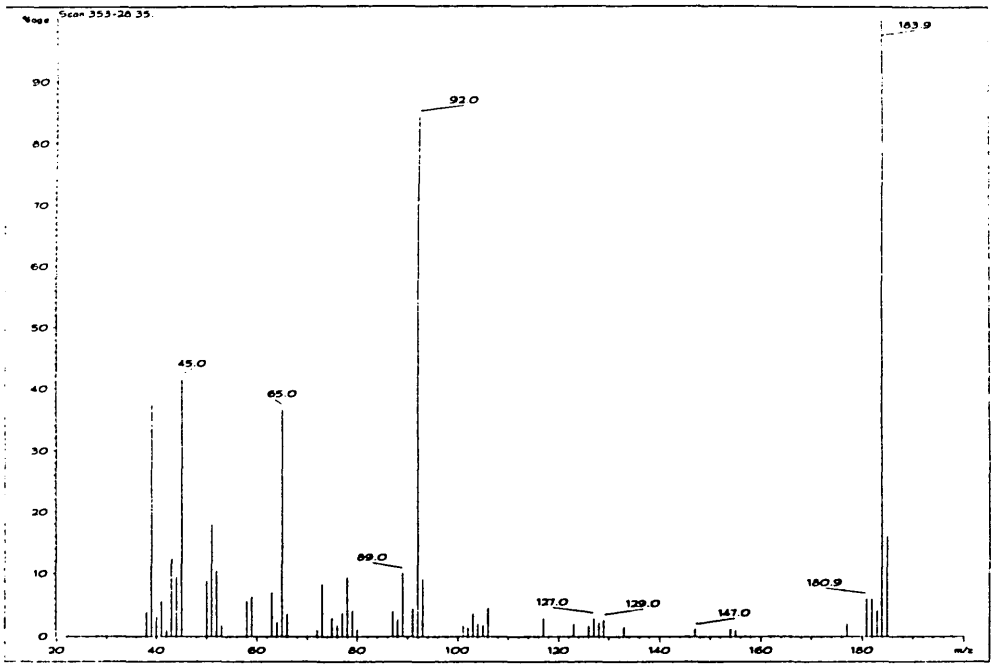


(iii)



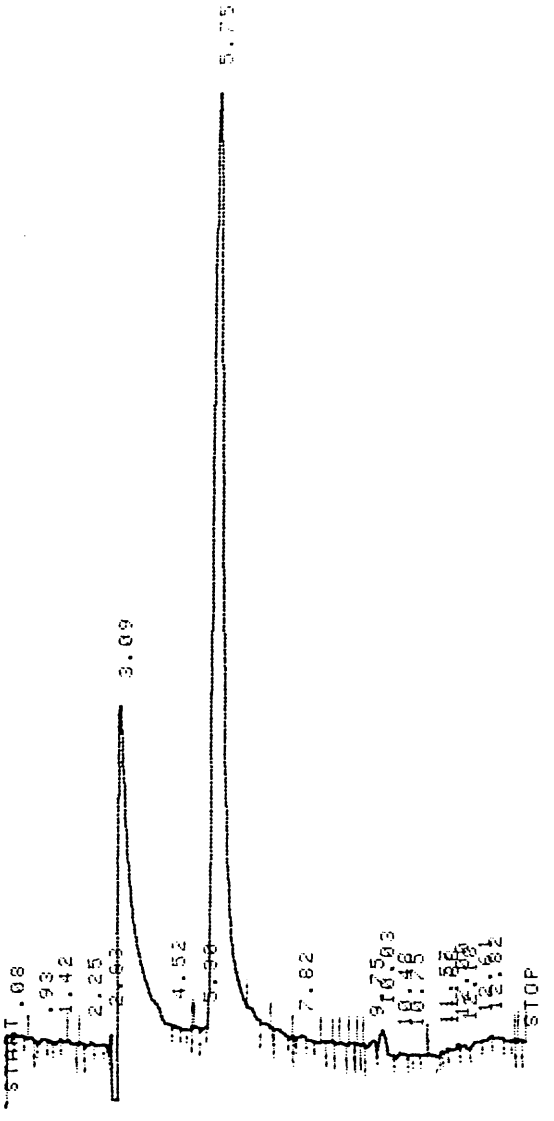
Appendix 10

Mass spectrum of 1,2-bis-(4-pyridyl)ethane formed in the copper(II)/hydrogen peroxide-catalysed autoclave oxidation of 4-methylpyridine



Appendix 11

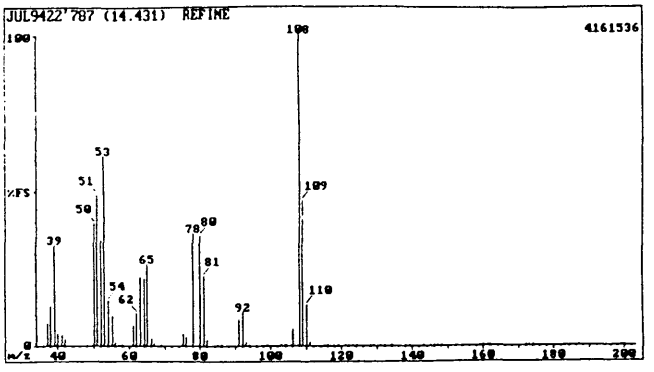
Chromatogram of the Fenton-catalysed oxidation of 2-methylpyridine



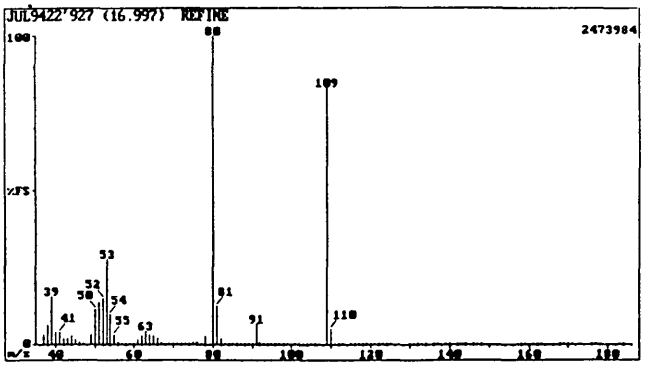
Appendix 12

Mass spectra of 3-hydroxymethylpyridine (i) and 2-hydroxy-5-methylpyridine (ii) formed in the Fenton-catalysed oxidation of 3-methylpyridine

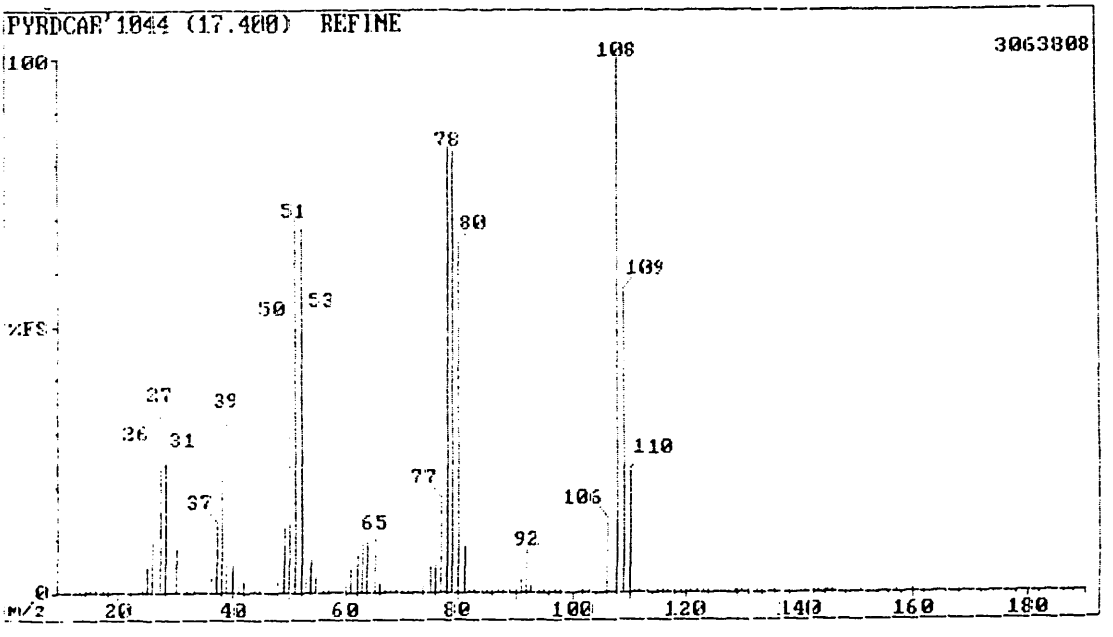
(i)



(ii)

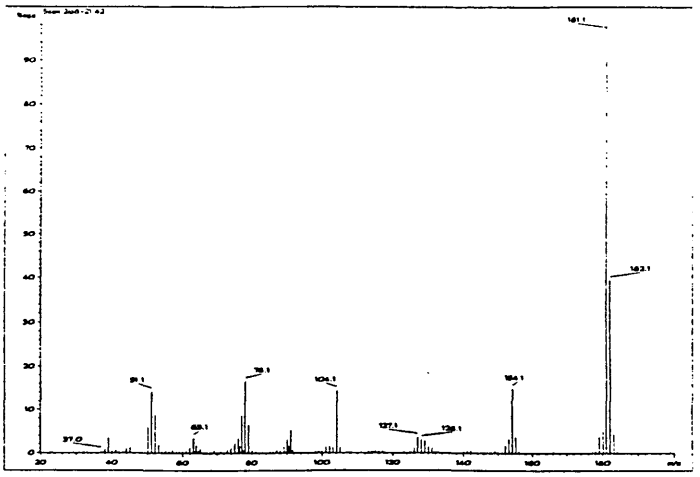


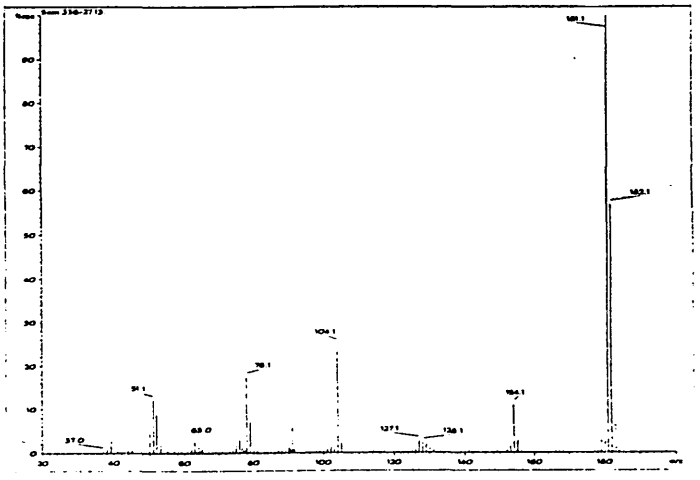
Mass spectrum of the standard material 2-hydroxymethylpyridine



Appendix 13

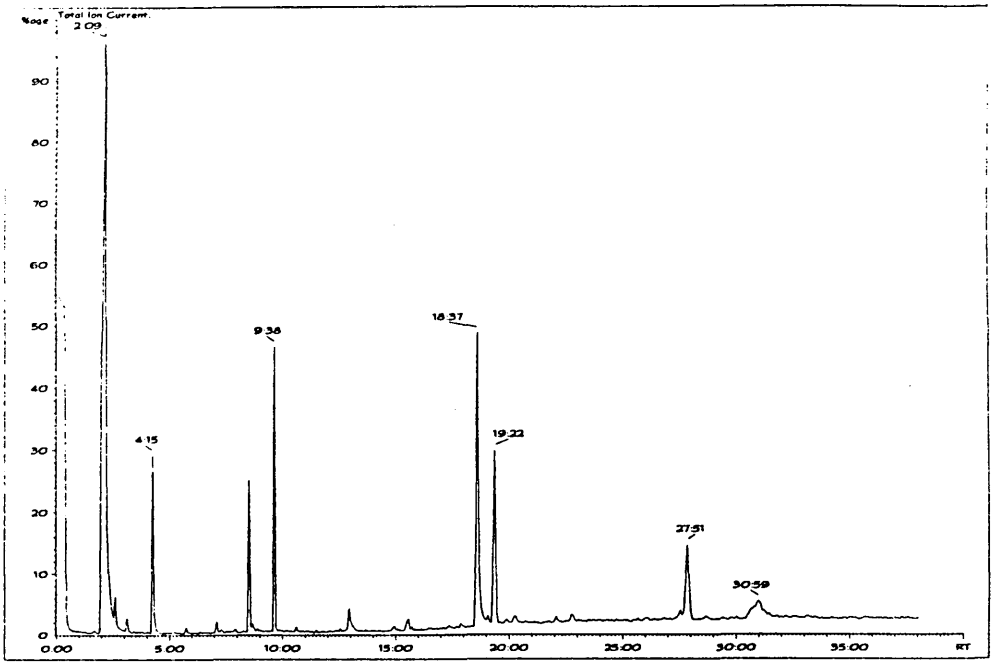
Mass spectra of cis/trans 1,2-bis-(2-pyridyl)ethane



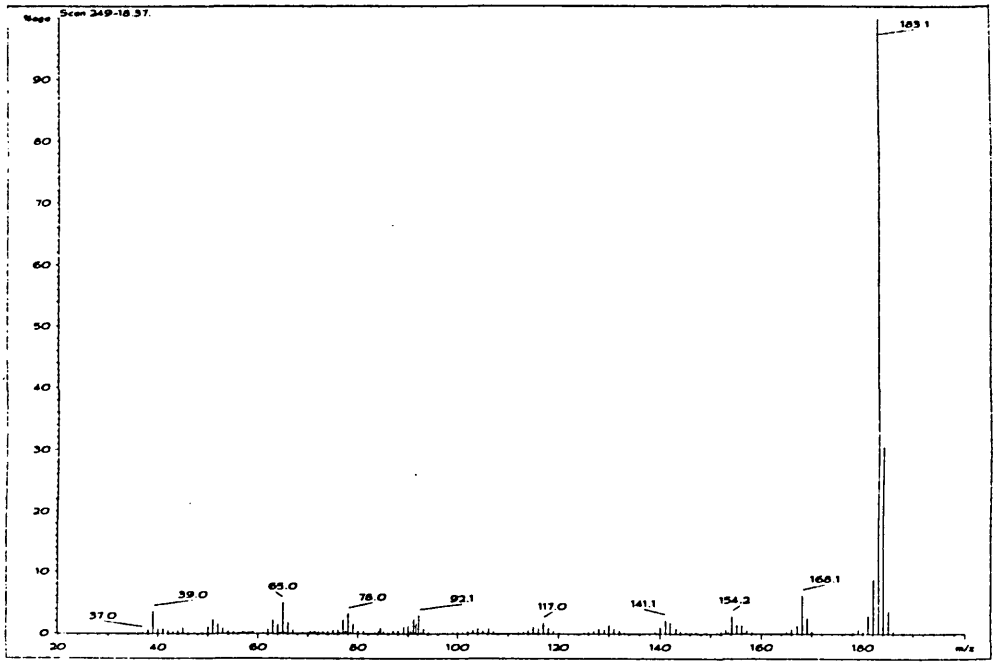


Appendix 14

Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine - Method 1

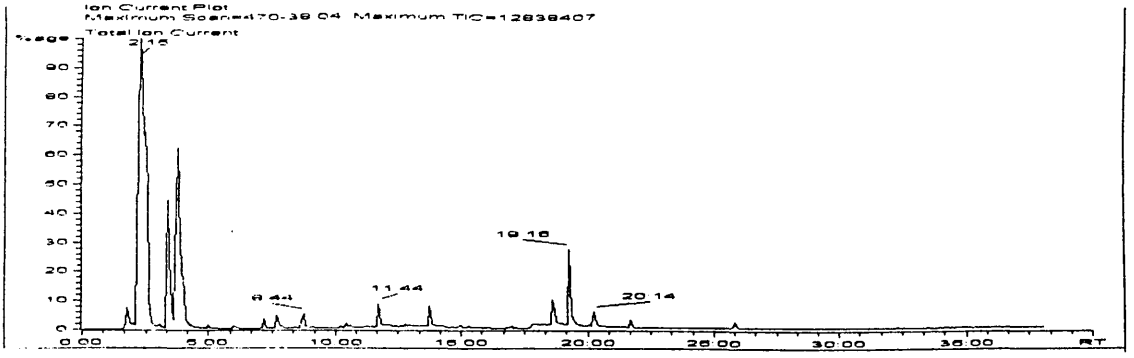


Mass spectrum of 2-methyl-6-(2-pyridylmethyl)pyridine at retention time 18.37 minutes

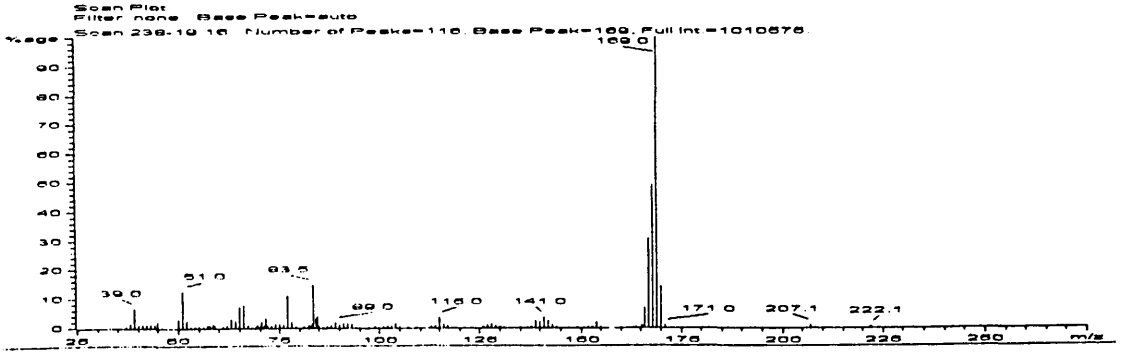


Appendix 15

Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-6-(2-pyridylmethyl)pyridine - Method 2

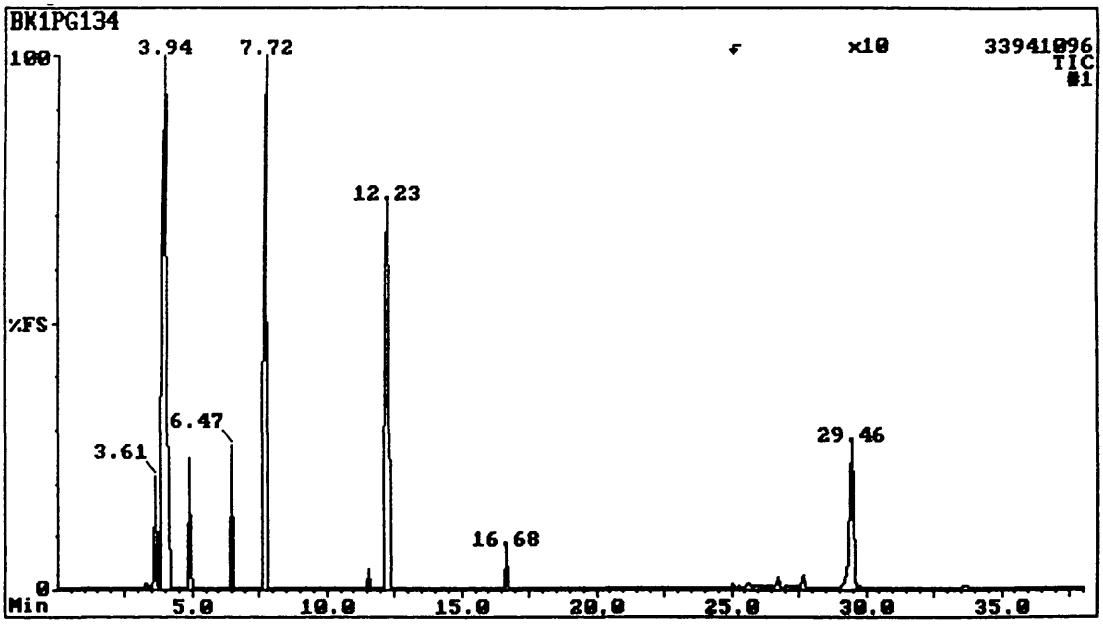


Mass spectrum of the component exhibiting an apparent molecular ion at *m/z* 170 at retention time 19.16 minutes

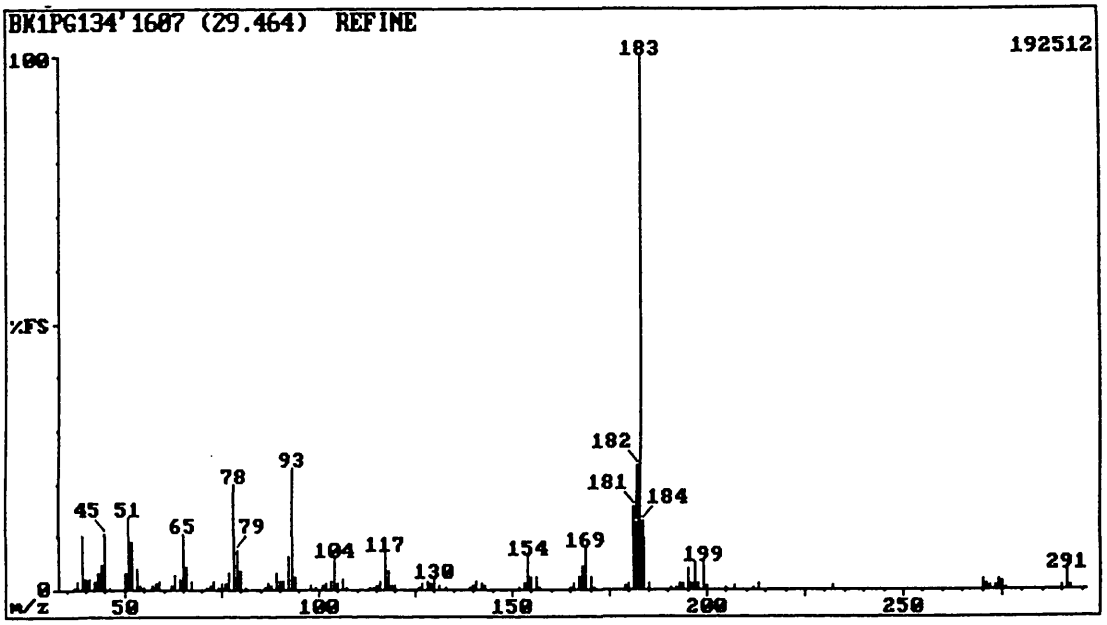


Appendix 16

Gas chromatogram of the reaction mixture formed in the synthesis of 2-methyl-4-(2-pyridylmethyl)pyridine - Method 1



Mass spectrum of 2-methyl-4-(2-pyridylmethyl)pyridine at retention time 29.46 minutes



Programme of Related Studies

Poster Presentations:

1. Research and Development Topics in Analytical Chemistry - Royal Society of Chemistry

   University of Bradford - July 1993

   University of Hertfordshire - July 1994

   University of Hull - July 1995

2. American Society of Mass Spectrometry

   Atlanta - May 1995

Oral Presentations:

1. Research Seminar

   Sheffield Hallam University - June 1994

2. Predoctoral Chemistry Symposium - Autumn Meeting

   University of Glasgow - September 1994

Meetings Attended:

1. Radicals in Organic Chemistry (Lecture Course)

   University of Sheffield - Autumn Term 1992 - Spring Term 1993

2. Annual Meeting on Stereochemistry

   University of Sheffield - December 1992, 1993

3. Oxidation in Organic Chemistry

   SCI - February 1993

4. Research Seminars

   Sheffield Hallam University - October 1992 - October 1995

Acknowledgements

I would like to thank Prof David Allen whose constant advice, encouragement and humour have made the completion of this Thesis possible. Thanks also go to Dr Malcolm Clench for his help throughout the project, all the technical staff at Sheffield Hallam University, in particular Joan Hague who constantly provided me with working instrumentation, and Leigh Environmental for their financial support.

My gratitude also goes out to my Mum and Dad who have supported me, both with words of encouragement and financially, throughout my education and I would not have made it this far without them. Finally, thanks go to Andrew who has been there for me for the past three years, through thick and thin, and who has helped to make it all lots of fun!

Published Paper

Allen D.W., Clench M.R. & Morris J., Investigation of the Products of Oxidation of Methylpyridines Under Aqueous Conditions by Gas Chromatography-Mass Spectrometry, *Analyst*, 1994, **119**, 903-907.

Investigation of the Products of Oxidation of Methylpyridines Under Aqueous Conditions by Gas Chromatography–Mass Spectrometry

David W. Allen, Malcolm R. Clench* and Jacqueline Morris

Division of Chemistry, School of Science, Sheffield Hallam University, Pond Street, Sheffield, UK S1 1WB

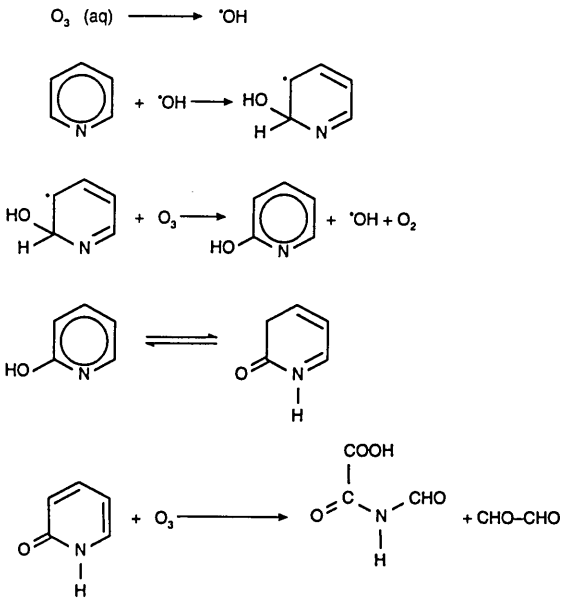
Wet air oxidation is a waste treatment process known to break down organic compounds at elevated temperatures and pressures under aqueous conditions. We have investigated, by gas chromatography–mass spectrometry, the products arising from the wet air oxidation of 2-, 3- and 4-methylpyridines carried out in a laboratory autoclave. The results indicate that radical chemistry is responsible for the products. The oxidation of each of the methylpyridines by use of Fenton's reagent was also studied, because this is known to generate hydroxyl radicals. Similarities were observed between products generated by Fenton-catalysed oxidations carried out in the laboratory and the uncatalysed autoclave reactions. Further experiments, where Fenton's reagent was incorporated in the laboratory autoclave reactions, were carried out. An improved level of decomposition of the methylpyridines was achieved by the incorporation of a hydroxyl radical-producing catalyst.

Keywords: Wet-air oxidation; methylpyridines; Fenton oxidation; gas chromatography mass spectrometry

Introduction

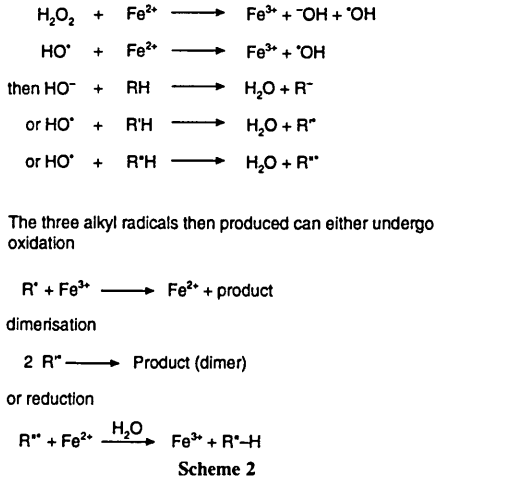
A potential route for the disposal of hazardous waste streams is *via* complete oxidation to simple products such as carbon dioxide and water.[1] Various commercial systems are available for this purpose,[2] which involve heating the waste stream to a high temperature (175–345 °C) while air is passed through the system under high pressure (20–200 atm) (1 atm = 101.325 kPa). However, it has been observed[3] that incomplete oxidation often occurs. This yields an effluent containing a mixture of products from the stepwise oxidation of organic compounds contained in the original waste stream.

We have become interested in examining the products formed from oxidation of specific compound classes under conditions that simulate commercial waste-treatment systems. Here, we report the results of the analysis of products arising from the oxidation of picolines (methylpyridines) in a laboratory autoclave and the effects of catalysis of such systems by use of Fenton's reagent.[4] Andreozzi *et al.*[5] have examined the ozonation of pyridine in aqueous solution and have proposed a mechanism for this process involving hydroxyl radicals, as shown in Scheme 1. Various studies have suggested that hydroxyl radicals play an important part in both wet air oxidation and ozonation reactions.[6] Chowdbury and Ross[7] have examined the use of catalysts in wet air oxidation; however, in that work the oxidation of specific compound classes was not studied. Rather, a general trend was noted that catalysis increases the extent of oxidation at low temperatures and pressures, with copper(II) ion in the presence of hydrogen peroxide being particularly effective.



Scheme 1

Fenton's reagent is a mixture of acidified aqueous hydrogen peroxide and a ferrous salt.[8] It is well known as an effective oxidant for a range of organic substances. It has been proposed that the actual oxidant in Fenton chemistry is also the hydroxyl radical.[4] Oxidation in Fenton chemistry is thought to follow the pathway shown in Scheme 2. In the



Scheme 2

* To whom correspondence should be addressed.

presence of an organic substrate, Fenton's reagent can also give rise to radicals other than hydroxyl (*i.e.*, RO· and HOO·) and these could contribute to the over-all oxidation process. In the presence of metal ions, metal–oxygen complexes (*e.g.*, FeO^{2+}) could also be involved.

Hence, it was felt that an investigation of the products of these reactions might suggest suitable catalysts for use in commercial waste-treatment plants for the destruction of waste streams containing aromatic nitrogen-containing compounds. These compounds are, for example, found in effluents from coal gasification and oil shale processing.[9] The method chosen for the analysis of the resulting products of oxidation was gas chromatography–mass spectrometry (GC–MS), as it was expected that complex mixtures would be produced.

Experimental

Experiments at Ambient Temperatures and Pressures

Uncatalysed reactions

2-, 3- or 4-Picoline (0.01 mol in 25 cm^3 of 1 mol dm^{-3} H_2SO_4) was added to H_2SO_4 (25 cm^3, 1 mol dm^{-3}) followed by dropwise addition of hydrogen peroxide (30% m/v, 0.1 mol). The system was stirred overnight under nitrogen.

Fenton chemistry

2-, 3- or 4-picoline (0.01 mol in 25 cm^3 of 1 mol dm^{-3} H_2SO_4) was added to a solution of H_2SO_4 (1 mol dm^{-3}, 25 cm^3) containing iron(II) sulfate (0.01 mol) followed by dropwise addition of hydrogen peroxide (30% m/v, 0.1 mol). The system was stirred overnight under nitrogen.

Autoclave Reactions

Uncatalysed reactions

An aqueous solution of the appropriate picoline (5% m/v, 1 dm^3) was heated to 250 °C during approximately 1 h under air pressure (250 atm). The autoclave was maintained under these conditions for 2.5 h.

Fenton chemistry

Iron(II) sulfate (0.003 mol) was added to the appropriate aqueous picoline solution (5% m/v, 1 dm^3). This was heated to 250 °C during approximately 1 h under air pressure (250 atm). The autoclave was maintained under these conditions for 2.5 h with addition of three aliquots of hydrogen peroxide (30% m/v), 30 cm^3 after 15 min, 30 cm^3 after 45 min and 35 cm^3 after 75 min.

Product Isolation

An aliquot (5 cm^3) of each sample was extracted, after adjusting the pH to approximately 7 by addition of NaOH (2 mol dm^{-3}), with diethyl ether (4 × 10 cm^3). After drying (over $MgSO_4$), the extract was then evaporated to approximately 2 cm^3 under reduced pressure. The ether-insoluble products remaining in the aqueous phase were then isolated by removing the excess of water on a rotary evaporator. The residue was then dissolved in methanol.

GC–MS

Both ethereal and methanolic extracts were analysed by GC–MS. The instrument used was a VG (Manchester, UK) Trio 1 quadrupole MS system fitted with a Hewlett-Packard (Avondale, PA, USA) 5890 gas chromatograph. The instrument was operated under the following conditions:

Column	50 m × 0.32 mm i.d. Supelcowax
Carrier gas	Helium
Temperature programme	40–250 °C at 10 °C min^{-1}
Injection volume	1 mm^3 splitless
Ion source	Electron impact (70 eV)
Source current	150 μA
Source temp.	200 °C
Scan rate	1 s $scan^{-1}$
Scan range	20–300 daltons

Results and Discussion

As anticipated, at ambient temperatures and pressures in the laboratory, no oxidation products were observed in the absence of the iron(II) catalyst. Table 1 shows the percentage of unoxidized picoline remaining after each of the catalysed experiments and the uncatalysed autoclave experiments. This is an indication of the degree of oxidation taking place. As can be clearly seen, the presence of the catalyst leads to a marked increase in the amount of oxidation taking place over that of uncatalysed reactions. The apparent reduction in percentage of the starting material oxidized in the catalysed autoclave reactions over that of the ambient catalysed experiments is in fact a function of the lower molar amounts of catalyst used in these experiments.

Representative data are shown as follows. Fig. 1 depicts the total ion current chromatogram (TIC) obtained from the

Table 1 Extent of oxidation of methylpyridines

Methylpyridine	Conditions	Catalysed/ uncatalysed	Starting material oxidized (mol %)
2-Methylpyridine	Autoclave	Uncatalysed	71.4
	Autoclave	Catalysed	61.1
	Ambient	Catalysed	97.5
3-Methylpyridine	Autoclave	Uncatalysed	2.7
	Autoclave	Catalysed	75.7
	Ambient	Catalysed	96.8
4-Methylpyridine	Autoclave	Uncatalysed	87.8
	Autoclave	Catalysed	98.8
	Ambient	Catalysed	98.1

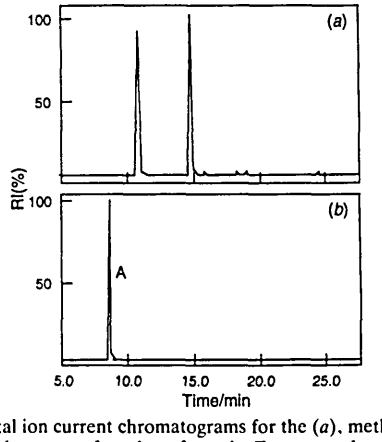


Fig. 1 Total ion current chromatograms for the (*a*), methanolic and (*b*), ethereal extracts of products from the Fenton catalysed oxidation of 2-picoline under ambient conditions. A, 2-picoline

ethereal extraction of the Fenton-catalysed laboratory oxidation of 2-picoline; Fig. 2 the TIC from the corresponding uncatalysed autoclave sample; and Fig. 3 the TIC from the catalysed autoclave sample. These reaction mixtures model potential aqueous waste streams after treatment of the initial waste *via* an oxidation process. As can be seen in Figs. 1–3, a mixture of products was observed in each instance.

Table 2(*a*–*c*) summarizes the products identified in the uncatalysed autoclave reaction mixtures from oxidation of 2-, 3- and 4-picoline, respectively. For 2-picoline, products have been identified as saturated and unsaturated dimers derived from the starting material, on the basis of their retention times, mass spectra and, as indicated in the table, by appropriate comparison of these with data for authentic samples. Representative mass spectra are shown in Fig. 4 [the mass spectrum of Component 2 (t_R = 13.7 min)], in Fig. 5 [the mass spectrum of Component 3 (t_R = 22.2 min)] and in Fig. 6 [the mass spectrum of Component 4 (t_R = 22.8 min)]. In Fig. 5 the intense $(M-H)^+$ ion at *m/z* 181 and fragmentation to yield *m/z* 104 is similar to that of an authentic sample of (*E*)-1,2-bis-(2-pyridyl)ethene (Fig. 7). The formation of dimers is indicative of the radical chemistry proposed previously as the mechanism of oxidation of such aromatic systems.[10] Also observed were simple oxidation products, *e.g.*, the aldehyde 2-(2-pyridyl)ethanal [Component 2 (t_R = 13.7 min] and the corresponding alcohol 2-(2-pyridylethanol) [Component 4 (t_R = 22.8 min].

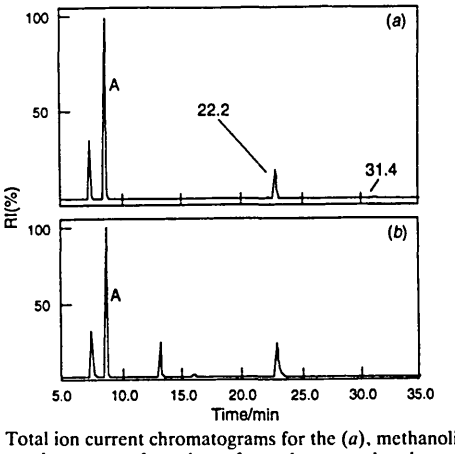


Fig. 2 Total ion current chromatograms for the (*a*), methanolic and (*b*), ethereal extracts of products from the uncatalysed autoclave oxidation of 2-picoline. A, 2-picoline ×29

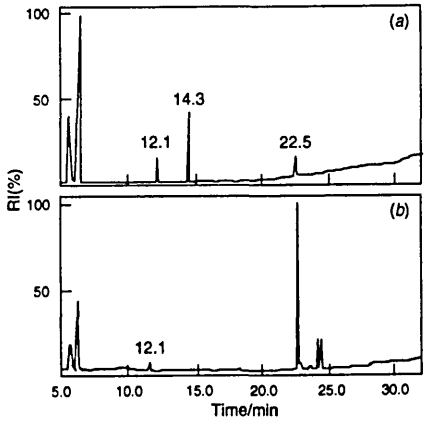


Fig. 3 Total ion current chromatograms for the (*a*), methanolic and (*b*), ethereal extracts of products from the Fenton catalysed autoclave oxidation of 2-picoline

Table 2 Principal products arising from the uncatalysed autoclave oxidation of alkylpyridines

Component	t_R/min	RMM*	Proposed structure
(*a*) *2-Methylpyridine*—			
1	7.5	79	Pyridine
2	13.7	121	2-(2-Pyridyl)ethanal
3	22.2	182	(*E*)-1,2-Bis-(2-pyridyl)ethene
4	22.8	123	2-(2-Pyridyl)ethanol
5	31.4	184	2- or 4-(2-Pyridylmethyl)-6-methylpyridine or 1,2-bis-(2-pyridyl)ethane
(*b*) *3-Methylpyridine*—			
1	10.6	123	A hydroxylated pyridine-3-carboxaldehyde or pyridine-3-carboxaldehyde *N*-oxide
2	14.8	107	3-Pyridylmethanal
3	15.1	137	Unknown
(*c*) *4-Methylpyridine*—			
1	10.8	60	Acetic acid
2	15.8	121	2-(4-Pyridyl)ethanol
3	26.2	123	2-(4-Pyridyl)ethanol
4	27.0	184	1,2-Bis-(4-pyridyl)ethane or 2- or 4-(4-Pyridylmethyl)-4-methylpyridine

* RMM = relative molecular mass.

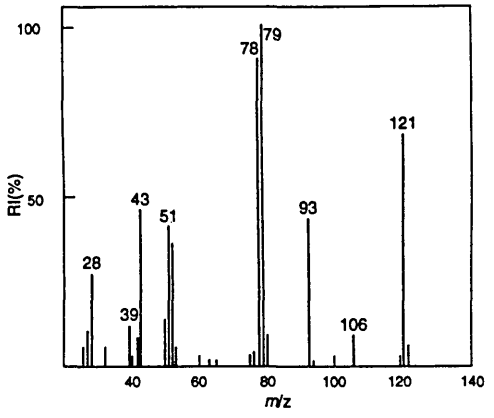


Fig. 4 Mass spectrum of component 2 (**Fig. 2**) t_R = 13.7 min, identified as 2-(2-pyridyl)ethanal

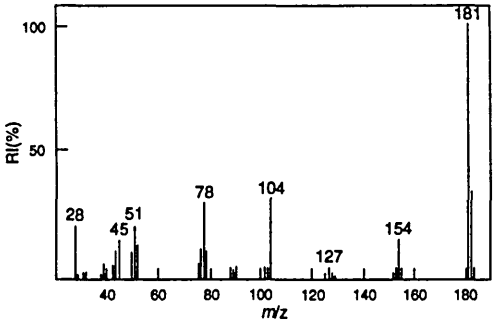


Fig. 5 Mass spectrum of component 3 (**Fig. 2**) t_R = 22.2 min, identified as an unsaturated dimer of 2-picoline

In the example of 3-picoline [Table 2(*b*)], dimeric structures were not observed, the main products being simple oxidation products, with some evidence of hydroxyl attachment to the aromatic ring. For 4-picoline [Table 2(*c*)] the formation of dimeric structures was again a dominant feature, and formation of acetic acid provided evidence of oxidative ring cleavage.

Table 3(*a–c*) summarizes the products detected from the Fenton-catalysed oxidation of the picolines carried out under ambient temperature and pressure. The presence of Fenton's reagent, as expected, promoted oxidation even under ambient conditions.[8] From 2-picoline [Table 3(*a*)] the major products formed were acetic acid and acetamide, together with trace amounts of many other as yet unidentified components. In the example of 3-picoline [Table 3(*b*)] a complex series of oxidation products was observed, including simple oxidation products, dimers and oxidative ring-cleavage products. For 4-picoline [Table 3(*c*)] the principal products observed were the unsaturated dimer, (*E*)-1,2-bis-(4-pyridyl)ethene [Component 5 (t_R = 23.6 min)], 4-pyridylmethanol, formamide, acetamide and acetic acid.

Table 4(*a–c*) summarizes the results from the Fenton-catalysed autoclave oxidation of the picolines. In each instance the oxidation proceeded further than the above uncatalysed conditions, as shown by the presence of acetic acid in all of the reaction mixtures and by the reduced amount of the starting material remaining (Table 1).

The results from the incorporation of Fenton's reagent into these experiments to oxidize picolines support proposals that free-radical chemistry is involved in the industrial wet air-oxidation waste-treatment processes. A comparison of products from the uncatalysed autoclave systems with the ambient Fenton-catalysed systems shows similar products being formed in both systems. In particular, the formation of saturated dimers is most readily accounted for by invoking free-radical chemistry. Incorporation of Fenton's reagent into the autoclave experiments does appear to promote oxidative ring-cleavage reactions over the uncatalysed systems. The mechanism for this is as yet unknown although it could be inferred from the results of these analyses that it is likely to be closely related to that proposed by Andreozzi *et al.*[5] The key step, as described by Andreozzi *et al.* in the ring cleavage of pyridines, is the formation of a hydroxypyridine with its corresponding non-aromatic tautomer. This occurs *via* attack on the aromatic ring by a hydroxyl radical generated in aqueous ozonation experiments. A similar mechanism has been proposed for wet air oxidation of polycyclic aromatic hydrocarbons.[3] The use of Fenton's reagent, which is known to generate hydroxyl radicals, would be expected to promote this initial ring attack stage of the cleavage process in our

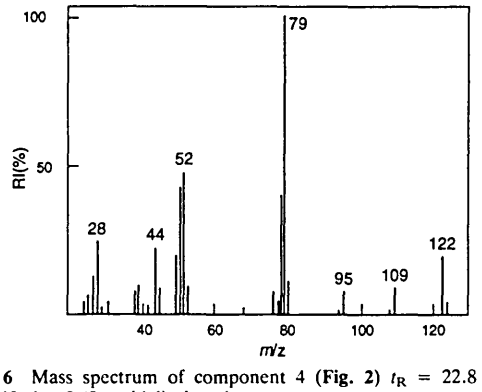


Fig. 6 Mass spectrum of component 4 (**Fig. 2**) t_R = 22.8 min, identified as 2-(2-pyridyl)ethanol

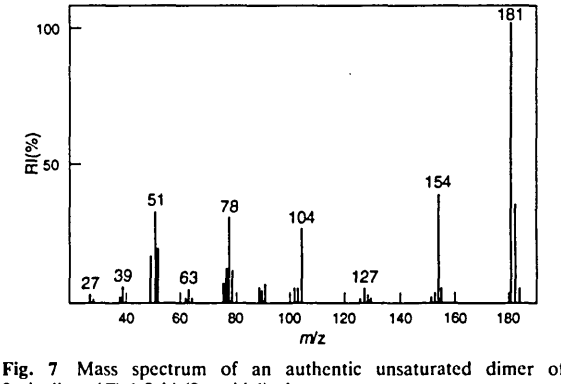


Fig. 7 Mass spectrum of an authentic unsaturated dimer of 2-picoline,-(*E*)-1,2-*bis*(2-pyridyl)ethene

Table 3 Principal products arising from the oxidation of alkylpyridines using Fenton's reagent under ambient temperatures and pressures

Component	t_R/min	RMM*	Proposed structure
(*a*) *2-Methylpyridine*—			
1	11.41	60	Acetic acid
2	15.48	59	Acetamide
(*b*) *3-Methylpyridine*—			
1	14.8	107	3-Pyridylmethanal
2	15.4	59	Acetamide
3	23.4	109	3-Methylpyridine *N*-oxide
4	23.5	182	(*E*)- or (*Z*)-1,2-Bis-(3-pyridyl) ethene
5	27.5	184	1,2-Bis-(3-pyridyl)ethane or 2- or 4- or 6-(3-Pyridylmethyl) 3-methylpyridine
6	27.9	184	As Component 5
7	32.0	198	(*E*)- or (*Z*)-1-(3-pyridyl)-2-(3-pyridyl *N*-oxide)ethene or a hydroxylated 1,2-bis-(3-pyridyl)ethene
(*c*) *4-Methylpyridine*—			
1	11.3	60	Acetic acid
2	15.4	59	Acetamide
3	15.7	45	Formamide
4	16.7	109	4-Pyridylmethanol
5	23.6	182	(*E*)-1,2-Bis-(4-pyridyl)ethene

* RMM = relative molecular mass.

Table 4 Principal products arising from the autoclave oxidation of alkylpyridines using Fenton's reagent

Component	t_R/min	RMM*	Proposed structure
(*a*) *2-Methylpyridine*—			
1	4.73	79	Pyridine
2	12.12	121	2-(2-Pyridyl)ethanal
3	14.33	59	Acetamide
4	22.54	123	2-(2-Pyridyl)ethanol
(*b*) *3-Methylpyridine*—			
1	10.7	60	Acetic acid
2	14.8	107	3-Pyridylmethanal
3	20.4	109	A hydroxylated 3-methylpyridine
4	22.6	109	As Component 3
5	23.2	109	3-Methylpyridine *N*-oxide
6	23.6	170	2-Pyridyl-(3-pyridyl)methane
(*c*) *4-Methylpyridine*—			
1	10.9	60	Acetic acid
2	14.0	107	4-Pyridylmethanal

* RMM = relative molecular mass.

experiments. Pyridines are known to behave as radical-trapping systems, leading to the formation of 2- and 4-substituted pyridines.[11] Identification of acetamide and acetic acid in our reaction products is clearly evidence of an oxidative ring-cleavage process.

Conclusions

GC–MS has been used to identify products arising from the oxidation of picolines under a variety of conditions. Evidence for the involvement of hydroxyl radicals in the oxidation process has been adduced. Fenton's reagent, a known source of hydroxyl radicals, has been shown to promote ring-cleavage processes in pyridine chemistry. The object of this work was to establish a system for the complete destructive oxidation of picolines. Towards this aim, radical-promoting catalysts seem worthy of further investigation.

We are grateful to Leigh Environmental Ltd., 1 Station Road, Four Ashes, Wolverhampton, UK WV10 7DQ, for their financial support for this work.

References

1 Pruden, B. B., and Le, H., *Can. J. Chem. Eng.*, 1976, **54**, 319.
2 Jackman, A. P., and Powell, R. L., *Hazardous Waste Treatment Technologies*, Noyes Publications, New Jersey, USA, 1991, pp. 90–134.
3 Larson, R. A., Ju, H., Soneyink, V. L., Recktenwalt, M. A., and Dowd, P. A., *Water Res.*, 1988, **22**, 337.
4 Walling, C., *Acc. Chem. Res.*, 1975, **8**, 125.
5 Andreozzi, R., Insola, A., Caprio, V., and D'Amore, M. G., *Water Res.*, 1991, **25**, 655.
6 Balloid, C. R., Faith, B. M., and Masi, O., *Environ. Prog.*, 1982, **1**, 217 and references cited therein.
7 Chowdbury, A. K., and Ross, L. W., *AIChE Symp. Ser.*, 1975, **7**, 46.
8 Ito, S., Mitarai, A., Hikino, K., Hirama, M., and Sasaki, K., *J. Org. Chem.*, 1992, **57**, 6937.
9 Pelizzari, E. D., Castillo, N. P., Willis, S., Smith, D., and Bursey, J. T., in *Measurement of Organic Pollutants in Water and Wastewater*, ASTM STP 686, ed. Van Hall, C. E., American Society for Testing and Materials, Philadelphia, 1979, pp. 256–274.
10 McKechnie, M., Nonhebel, D. C., and Scullion, I., *J. Chem. Res. (Synop.)*, 1993, 286.
11 Barton, D. H. R., and Doller, D., *Acc. Chem. Res.*, 1992, **25**, 502.

Paper 3/05289C
Received September 3, 1993
Accepted February 8, 1994