Study of the Redox Potentials of Cobalt *Tetrakis*arylporphyrins and Their Use in Oxidation Reactions with Dioxygen

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy by

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To Andy and my Family

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CONTENTS

Chapter 2

Chapter Three

Chapter Four

Appendixes

Abstract

Study of the Redox Potentials of Cobalt *Tetrakis*arylporphyrins and Their Use in Oxidation Reactions with Dioxygen

The aim of the overall project was to develop a catalytic system using cobalt complexes of 5,10,15,20-*tetrakis*arylporphyrins and dioxygen. To develop such a system the research was divided into three parts.

In part one the synthesis of 5,10,15,20-*tetrakis*arylporphyrins was carried out. Some of the porphyrins synthesised were already described in the literature and some were new. Two methods of synthesis were used , the "one-pot" method and the "two-pot" method. Both methods were improved to maximise the yields and to facilitate the ease of isolation. The "one-pot" method was improved by using a statistical method, the Simplex, and the "two-pot" method by changing the reaction conditions in the second step. A combination of the two methods was also developed.

In part two the cobalt complexes of the porphyrins were made and their redox potentials measured using cyclic voltammetry. A correlation between substituents effect and the redox potential of the cobalt porphyrin complexes was investigated.

In part three an examination was made of the relationship between the redox potentials of the cobalt porphyrin complexes and their ability to act as oxidation catalysts in reactions with molecular oxygen. The capacity of cobalt porphyrin complexes to function as oxygen activators was therefore investigated. Three different dihydroquinones were chosen as oxidisable substrates. A thermochemical study of the reaction of the cobalt porphyrin complexes with dihydroquinones and dioxygen was done. Finally, a system was built and studied. Examination of the limitation of the system was done and attempts to overcome these were made.

Abbreviations

P - porphyrin ring

DMF - dimethyl formamide

L - ligand

NAD - nicotinamide adenine dinucleotide

Me - methyl group

rt - room temperature

Ac - acetate

Ph -phenyl group

LUMO - lowest unoccupied molecular orbital

HOMO - highest occupied molecular orbital

CV - cyclic voltammetry

DDQ - 2,6-dicyano-5,6-dichloro-1,4-benzoquinone

TCQ - 2,3,5,6-tetrachloro-1,4-benzoquinone

BQ - 1,4-benzoquinone

Q - quinone

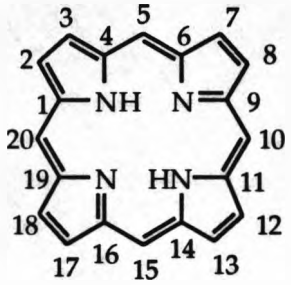
T - temperature

CA - carboxylic acid

NB - nitrobenzene

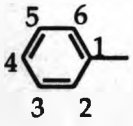
Nomenclature

In this thesis the nomenclature used for the porphyrin compounds was established by the Commission on the Nomenclature of Biological Chemistry in 1960. Accordingly in the basic porphyrin ring the carbon atoms are numbered from 1 to 20 as below:



Occasionally the pyrrolic positions 2, 3, 7, 8, 12, 13, 17 and 18 are called the β-positions and the positions 5, 10, 15, and 20 are called the *meso*-positions.

For the aryl groups in the 5,10,15,20-*tetrakis*arylporphyrins the numbering of the carbon atoms was done as in the example below. The carbon number 1 is directly bonded to the porphyrin ring:



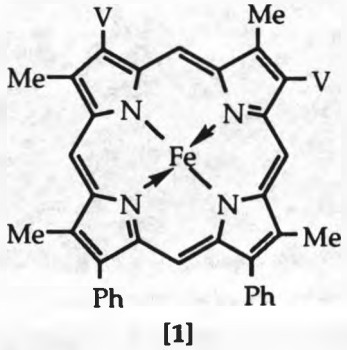
Chapter One

PORPHYRINS AND METALLOPORPHYRINS

1. PORPHYRINS AND METALLOPORPHYRINS

1.1. Historical Aspect

It could be said that the history of porphyrins goes back to the first reports about human illnesses involving porphyrins and their complexes. The investigation into these disorders was probably the driving force for the subsequent research into porphyrin structures.[1] In 1912, first proposals of the structure of hemin (the oxidised form of heme) and porphyrins as tetrapyrrolic conjugated ring systems were published.[1,2] In 1926, the synthesis of etioporphyrin I, II, III, was described. Later, in 1929, the "crowning achievement", the synthesis of the iron complex of protoporphyrin IX, [1], was reported, confirming an earlier formulation.[1,3,4] After these first events, new synthetic methods started to be the centre of interest and the general chemistry of porphyrins began to develop.

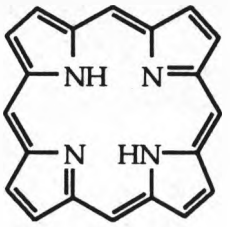


[1]

V-Vinyl
Me-Methyl
Ph-Phenyl

1.2. Structure and Properties

Porphyrins consist of four "pyrrole type" rings joined together by four methine bridges, and, for example, the structure **[2]** of porphin, the simplest member of this class of compound, is shown.[3,4]



[2]

These compounds of relatively large relative molecular mass have 22π electrons, although only 18 can be incorporated into any one delocalization pathway. They are aromatic and obey the Debuy Huckel (4n+2) rule. From X-ray investigations of porphyrins, it was shown from bond lengths that they have aromatic character, and also that the main ring system is planar (a basic requirement for aromaticity).[5,6] Measurements of their heats of combustion, and applications of nmr techniques provided further evidence for their aromatic character.[7,8,9,10]

The analysis of proton nmr spectra of porphyrin, reveals that the outer protons of the macrocycle ring appear at very low field (as with simple benzene compounds) the nitrogen protons appear at very high field, as would be expected from their position on the inside of the planar ring system. This double deshielding and shielding effect is caused by a strong induced circulation of the 18π electrons by the applied magnetic field that creates an induced magnetic field which is opposite to that applied in the centre of the ring but with the same direction at the outside. Figure 1 illustrates the effect for benzene.[11,12].

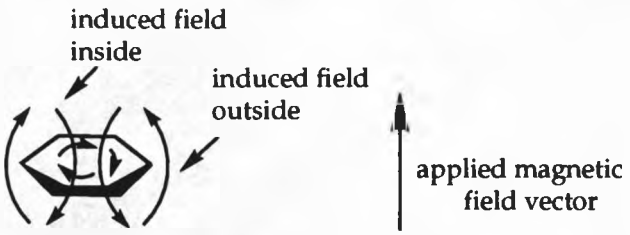


Figure 1. A magnetic field applied to benzene in solution induces an electronic ring current which creates torroidal induced magnetic field having direction vectors in one direction outside the ring and the opposite inside the ring

Another consequence of a porphyrin being highly conjugated is a decrease in the energy difference between the HOMO (highest occupied molecular orbital) and the LUMO (lowest unoccupied molecular orbital). This results in long wavelength electronic transitions in the visible region (420nm - 550nm) of the electromagnetic spectrum so that, as a consequence, porphyrins are coloured, usually red or reddish blue. One electronic absorption band ("Soret" band) at about 400nm, is very narrow and has a large extinction coefficient.[13,14] The band is characteristic of all tetrapyrrollic porphyrin systems which are fully conjugated. At longer wavelengths, the Soret is followed by other bands (the satellite or Q bands), which have smaller extinction coefficients. The position and intensity of the visible absorption bands vary with the nature of the side chains on the main porphyrin chromophoric system.[15,16]

The four centre imine-type nitrogen atoms, can undergo a series of acid-base equilibria as shown in Scheme 1, where P represents porphyrin:[17]

$$P^{2-} + H^+ \rightleftharpoons PH^-$$

$$PH^- + H^+ \rightleftharpoons PH_2$$

$$PH_2 + H^+ \rightleftharpoons PH_3^+$$

$$PH_3^+ + H^+ \rightleftharpoons PH_4^{2+}$$

Scheme 1.

PH_2 is only a weak acid and the porphyrin dianion P^{2-} and anion, PH^- are difficult to generate, needing the presence of a very strong base such as an alkoxide. For the protonated forms (PH_3^+, PH_4^{2+}), the relative instability of the mono-cation makes it difficult to observe. There is a greater barrier to the addition of the first proton to the free base than there is for the second proton.[18,19] However, with many porphyrins under special conditions the monocationated form is observable.[20] The free base and the dication are easily observed and are well characterised.

Porphyrins are good ligands for almost all the transition metals.[21] The visible absorption spectrum of a porphyrin changes in such a way when it is metallated as to give an easy way of identifying the metalloporphyrin. The changes are dependent on the type of metal, but all metalloporphyrins show a shift of the Soret band to shorter or longer wavelengths, and the collapse of the satellite (Q) bands into only one or two other bands.[22]

1.3. Catalysts: Functions and Objectives

The main part of the work developed in this research project involves the use of metalloporphyins as catalysts. Therefore to define what is a catalyst and how does it work is relevant.

In its simpler definition, a catalyst is a substance that increases the rate of a chemical reaction without itself being used up.

In biorganisms, there is an incredible number of chemical reactions, thermodynamically possible, but having very low rates in the absence of a catalyst. The very simple reaction of CO_2 with H_2O to give HCO_3^- and H^+ when catalysed by the enzyme, anhydrase, is 10^7 times faster than in its

absence, permitting the complete transfer of CO_2 from animal tissues to the blood stream and subsequently to the lungs for exhalation.[23]

To explain how a catalyst works, various theories have been developed but the most useful is the transition state theory.[24] In this, the processes by which the reagents collide are ignored and the only physical entities considered are the reagents in their ground state and the most unstable species on the reaction pathway, the transition state. The transition state is considered to occur at a peak along the reaction co-ordinate, figure 2.

Thermodynamics and kinetic analysis permit the calculation of the free energy between the transition state and the ground state, and the rate of formation of the latter.

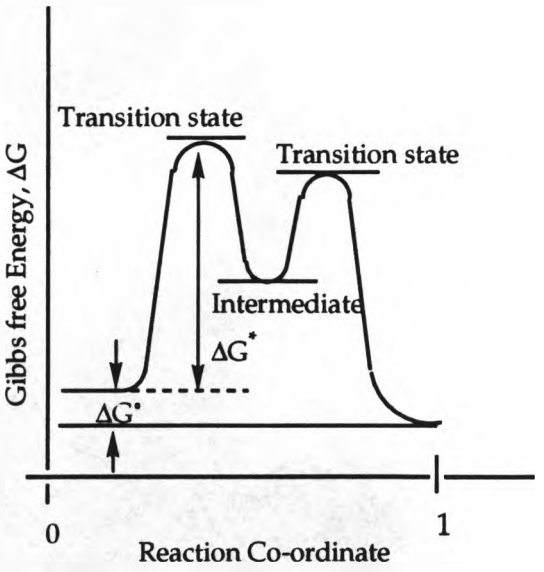


Figure 2. As a reaction proceeds from its start (0) to its finish (1), the total free energy (ΔG) in the system changes, reaching a maximum at a transition state. There may be regions of relative stability where intermediates in the reaction can, in theory, be isolated.

To understand catalysis we need to understand first why some reactions are so slow. A slow reaction has a high energy transition state, which means a very unfavourable transition state. As a reaction proceeds

from its start to its finish along the reaction co-ordinate, the overall free energy in the system changes; if the overall energy change in the reaction, ΔG°, is negative then energy is given out and vice versa. Between "0" and "1", the free energy of the system increases (ΔG^{*}) to a maximum where an unisolable structure called a transition state is formed. The energy change, ΔG°, determines whether or not a reaction can be expected to proceed spontaneously but the energy barrier, ΔG^{*}, determines how fast a reaction goes. A catalyst acts by reducing ΔG^{*} by providing an alternative mechanism for the reaction.

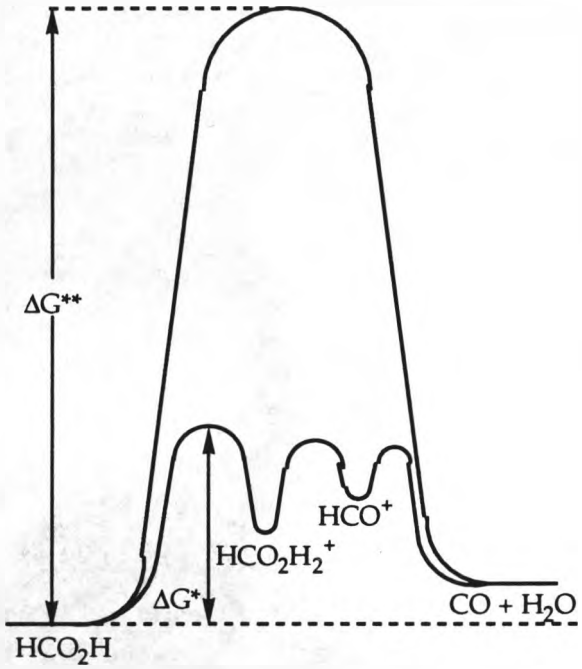


Figure 3. Decomposition of formic acid, HCO_2H, to give carbon monoxide and water. Without the use of a catalyst the free energy of the system is given by ΔG^{**}, which is lowered to ΔG^{*} when a catalyst is used.

Alternatively, stabilisation of the transition state reduces its total energy, permitting the reaction to occur faster as in the example given for the decomposition of formic acid, (figure 3).[23] Formic acid decomposes very slowly at room temperature to produce water and carbon monoxide in a one step reaction. However if a strong acid is added, carbon monoxide

is produced rapidly. According to the literature, this catalysed reaction occurs in three steps. In a first step the protonation of formic acid occurs; this is the rate determining step. In the second step the protonated species decomposes to give water and HCO^+ which then liberates carbon monoxide by losing a proton, (figure 3).

A catalyst can act in different ways to lower the energy of the transition state. Some act without changing the mechanism of the reaction and by stabilizing an existing transition state, some involve provision of a different reaction pathway but, in all cases, a catalyst cannot make a thermodynamically impossible reaction occur; it can only make it proceed faster, with no change in the equilibrium constant related to ΔG°.[23,24]

Finally another definition to be introduced in this section is the turnover number of a catalyst. The turnover number refers to the number of cycles a catalyst is able to perform during a reaction before it becomes inactive.

1.4. Naturally Occurring Porphyrins

The importance of porphyrins in a variety of biological systems is probably due to the fact that their metal complexes are biologically accessible compounds whose functions can be varied by changing the metal, its oxidation state, or the nature of the organic substituents in the porphyrin structure. The versatility of these compounds is exhibited in their widespread occurrence in natural systems, such as blood and various enzymes.

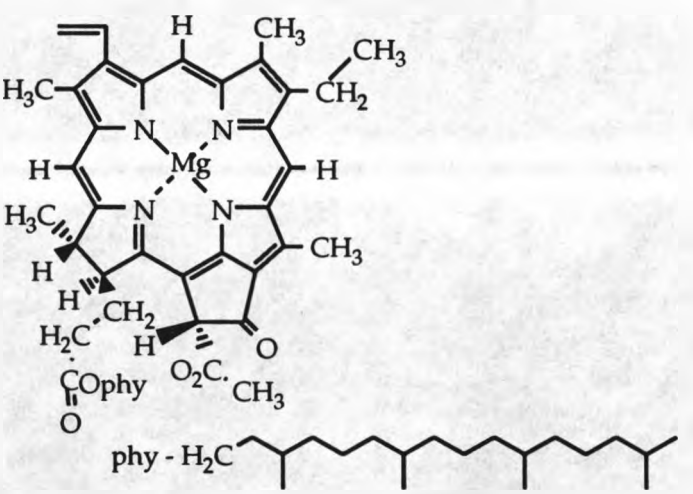
1.4.1. Porphyrins in plants

It is interesting to note that porphyrins play a central role in both animals and plants. At some point in the past, animal species developed the use of porphyrins but plants made use of modified porphyrins (chlorophyll). A few microorganisms also utilise porphyrins. From this viewpoint, all life on earth relies on the central role played by porphyrins. In the animal kingdom, porphyrins are used to transport oxygen from the atmosphere whilst, in the plant kingdom, chlorophyll with light energy is utilised to reduce carbon dioxide and generate oxygen.

1.4.1.1. Chlorophylls

Chlorophylls comprise the green colouring matter found in plants. They form a group of closely related pigments found in all organisms capable of photosynthesis.

The chlorophyll ring system is a metalloporphyrin of magnesium, in which a double bond in one of the pyrrole rings has been reduced to give a chlorin, **[3]**.

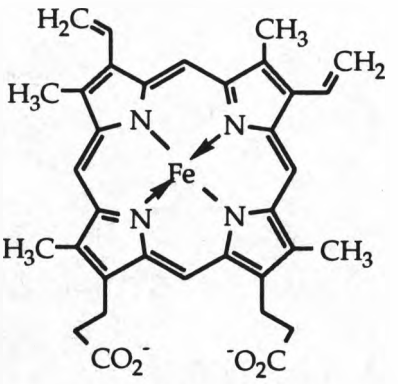


[3]

Studies on the structure of chlorophylls by spectroscopic techniques showed that there is chlorophyll aggregation *in vivo*, in which the carbonyl group of one molecule acts as a ligand to the magnesium atom of another molecule and so on, thereby building an oligomer. [25,26] Different chlorophylls perform slightly different functions *in vivo*. The large majority collect light energy (in the form of long wavelength electronic excitation) and transfer it to a few specialised chlorophyll molecules, where the conversion of light into chemical energy takes place.[25,26] The energy obtained goes on into the photosynthetic process, the first step being reduction by an electron. In nature, the number of different chlorophylls is not large, only about ten different ones having been isolated from the green parts of various plants.[27] In some organisms only one type chlorophyll can be detected whilst in others, a major chlorophyll is accompanied by other auxiliary green pigments.

1.4.1.2. Cytochromes

During photosynthesis, an electron transfer process is important as the process of electronic excitation by the incoming light. The electron "carriers" are various cytochromes of which the active centre is a heme group, such as the one shown for cytochrome C, **[4]**. This heme group is an iron porphyrin, that can be in either its +2 or +3 oxidation state.

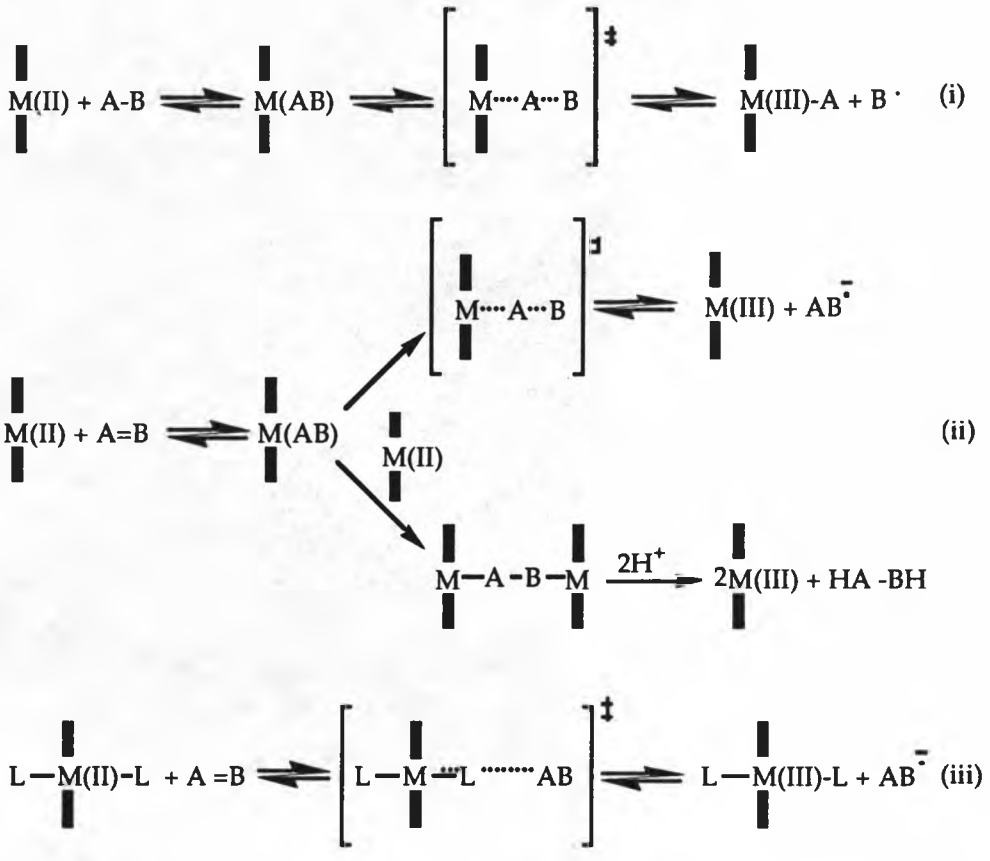


[4]

Cytochromes can act as redox intermediates in electron transfer processes. They are attached to a polypeptide chain which wraps itself around the porphyrin nucleus. A histidine and a methionine from the polypeptide chain provide a nitrogen and a sulphur atom respectively that are placed spacially in the fifth and sixth co-ordination sites of the central iron; the cytochrome reacts indirectly in the electron transfer mechanism.

There have been many studies attempting to explain how a cytochrome is oxidised or reduced in natural systems. Two general mechanisms for one electron oxidation or reduction have been proposed, viz., axial electron transfer and the peripheral electron transfer (Schemes 2 and 3).[28] In the axial electron transfer processes [equations (i) and (ii); Scheme 2] it is required that the oxidant or reductant become an axial ligand of the metal. In another process [equation (iii); Scheme 2], an appropriate orbital overlap is required between the axial ligand and the oxidant or the reductant.[28] In peripheral electron transfer processes, described by equation (i) and (ii) [Scheme 3], an electron is transfered through the porphyrin, rather than through the axial ligand as in equation (iii) [Scheme 2].[28] The peripheral process in equation (ii) [Scheme 3] is described in the literature as not likely to be reversible since a σ-bond is made or broken at position 5,10,15 or 20 of the porphyrin ring system.[28]

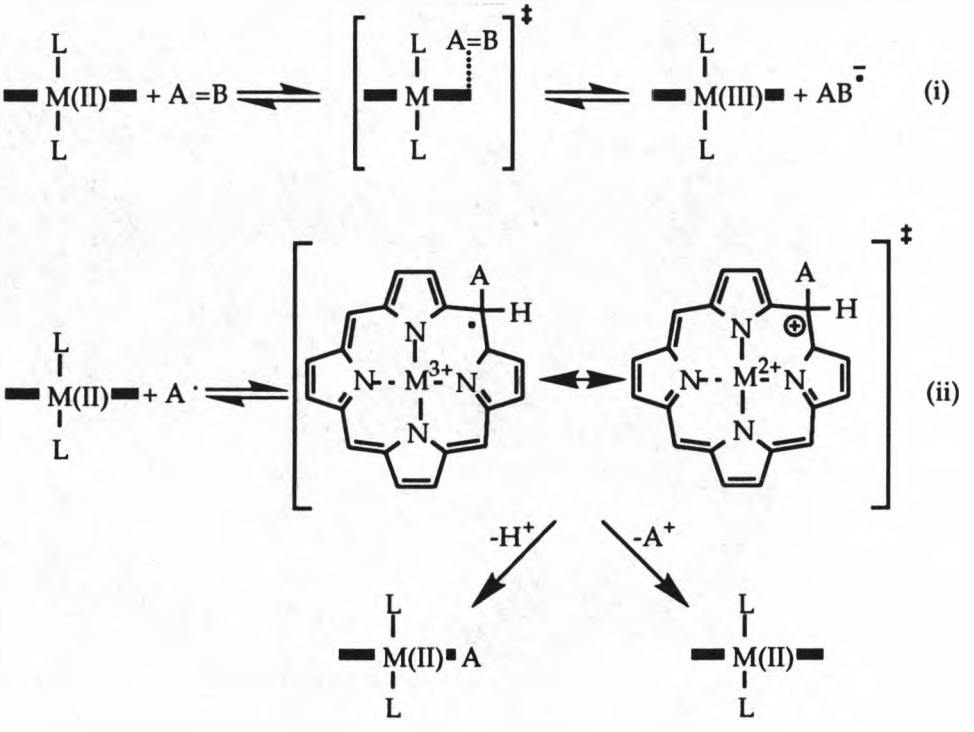
Both peripheral processes presented require that metal d-electrons are in conjugation with the porphyrin ring.



L - Ligand
AB - Organic or inorganic species being oxidised or reduced
[ ] - Indicates a transition state

M - Metalloporphyrins

Scheme 2.



L - Ligand
AB - Organic or inorganic species being oxidised or reduced
A· - Organic or inorganic radical
[ ] - Indicates a transition state
M
▌ - Metalloporphyrins

Scheme 3.

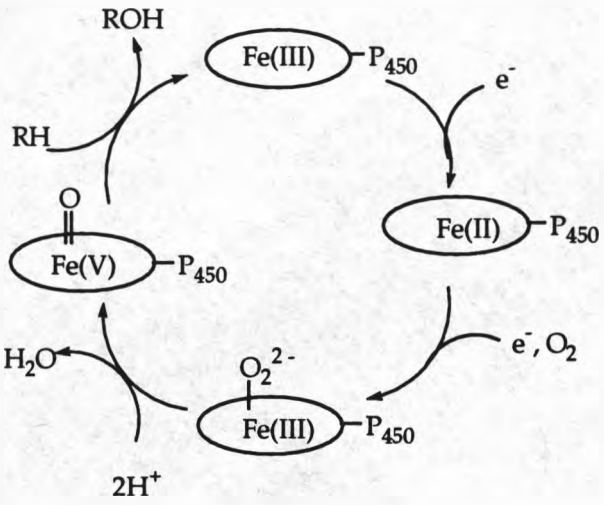
In particular for cytochrome C, it now seems agreed that, for peripheral mechanisms, the process proceds mainly along the lines discussed for equation (i) [Scheme 3]. However, all the results obtained during these investigations have some ambiguity surrounding them and, although that mechanism is the most widely accepted, the mechanism of equation (iii) [Scheme 2], in which electrons are transferred through the axial ligand, cannot be eliminated.[29,30] Clearly, where the axial positions are "protected" by an enveloping protein, this last process could not occur.

1.4.2. Porphyrins in animals

1.4.2.1. Cytochrome P450

Cytochrome P450 was discovered only in 1962, but this enzyme is widely distributed in the animal, plant, and microbial kingdoms. It participates as an oxygenase in various detoxification and biosynthetic pathways. Cytochrome P450 varies only slightly from species to species.[31] The active site of P450 contains an iron protoporphyrin IX **[1]**, held in a large hydrophobic depression in the tertiary structure of the apoprotein. The heme is bound by a combination of hydrophobic and coulombic attraction forces, and one or two co-ordinate covalent bonds from the protein to the central metal ion. The iron is always penta- or hexa-coordinated, four of the ligands being from the planar tetradentate porphyrin ring and the fifth being thought to be a thiolate anion contributed by a cysteine residue from the polypetide chain. The sixth coordination position of the iron is occupied by an exchangeable ligand. On reduction of the ferric metal to ferrous, this sixth position becomes the site of dioxygen binding.[31]

Cytochrome P450 uses molecular oxygen to oxidise substrates but introduces only one oxygen atom into them. The oxygen molecule is cleaved reductively and one of its oxygen atoms is reduced to water. The electrons for the reduction are provided through electron transfer from such a system as NADPH. Most P450 enzymes appear to follow the catalytic cycle of Scheme 4.[31,32,33]



Scheme 4.

The mechanism of oxygen activation and transfer by cytochrome P450 has been widely investigated. Although several aspects of the catalytic cycle for this enzyme are still controversial, the process outlined in Scheme 4 is consistent with existing data.[33,31]

The first step of the cycle is a reversible one eletron transfer from NADPH to Fe(III) of P450 to produce Fe(II). The second step is the binding and activation of dioxygen. Here, dioxygen binds to Fe(II) and one electron transfer to dioxygen takes place. This is followed by an electron transfer from NADPH to the ferric dioxygen complex to produce a ferric iron-coordinated peroxide complex, $[Fe(III)O_2^{2-}]P450$. The third step is the generation of an 'active oxygen' by heterolytic cleavage of the peroxide bond, involving protonation and extrusion of water such that the remaining oxygen atom contains the two oxidation equivalents previously associated with the peroxide. The new iron-coordinated atom has an unspecific local electron density, it has been writen as in Scheme 4 i.e., [Fe(V)=O] or as $[Fe(IV)\text{-}O^{-}]^{3+}$ or $[Fe(V)\text{-}O^{2-}]^{3+}$. The final step in the process lies in oxygenation of a subtrate by this active species to re-form a ferric complex and then to start another cycle.[31,34]

Another important feature of P450 enzymes is the protection that the aproprotein provides to the porphyrinic part. The apoprotein is folded around the central heme molecule, providing a hydrophobic medium and so alleviates the well-known problem of oxidation of ferrous to ferric iron that occurs readily in the presence of oxygen and water; the ferric state is useless for binding of oxygen. The protein serves also to protect the heme from easy approach by other molecules.[31,32]

1.4.2.2. Haemoglobin and myoglobin

The structures and reactions of haemoglobin and myoglobin have been described as, " An inspiration for research in co-ordination chemistry".[35] Haemoglobin transports oxygen in the blood from lungs to tissues and is responsible for its red colour. It is the major respiratory protein in the higher vertebrates. Haemoglobin has a quarternary structure that consists of four associated peptide chains, two α and two β. Each chain forms a tertiary structure, having a pocket in which a heme group is bound through van der Waals forces, hydrogen bonding, and co-ordinate bonding to an imidazole group of a histidine residue. The heme group is a planar four co-ordinate iron (II) protoporphyrin IX complex **[1]**, in which the nitrogen on the imidazole side-chain of histidine provides a fifth coodination donor group. The sixth co-ordination position is accessible to small neutral molecules such as oxygen and carbon monoxide.[36]

Myoglobin is a protein with only a single polypeptide chain and contains only one porphyrin group. Like haemoglobin, the peptide chain in myoglobin has a tertiary structure which includes a pocket containing a heme group and an iron complex of a protoporphyrin IX.[36] Myoglobin *stores* oxygen, rather than acting as an oxygen transport molecule and it

must be able to accept dioxygen from haemoglobin before releasing it to anoxic muscle tissues. Therefore, it must have a dioxygen affinity high enough to remove dioxygen from haemoglobin but low enough to allow its release to muscle tissues.[36]

It appears that, in both haemoglobin and myoglobin, a histidine is not absolutely essential for fixing the heme into the globin but it does have a fundamental effect on the binding of ligands. The pentacoordinated ferrous ion is displaced approximately 0.3-0.6Å out of the porphyrin plane towards the proximal imidazole side-chain of a histidine residue. In this configuration, the metal is somewhat protected from interaction with solvent. However, small molecules such us dioxygen can readily bind to the metal at its sixth co-ordination site.[36,35]

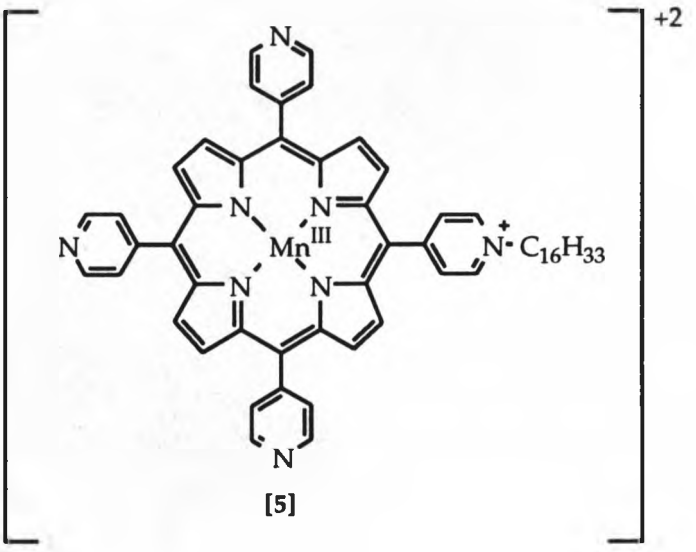
1.5. Synthetic Analogues of Porphyrins

Studies of the roles played by porphyrins in naturally occurring systems reveal how essential they are for life and how enormous is the potential for synthetic analogues. A few examples of their uses include: energy conversion; cancer therapy; Langmuir-Blodget film formation; modelling of enzymes. These topics are described below in slightly greater detail.

1.5.1. Energy conversion

Synthetic porphyrins are being studied as photochemical electron-transfer systems for conversion of solar energy into usable power.[37,38,39,40] Porphyrins are receiving attention as potential photosensitisers for photochemical electron transfer systems to effect solar energy

conversion.[37,38,39,40] For example water-soluble porphyrins can sensitise photocatalytic reduction of water or its oxidation, and are of potential use in photogalvanic cells.[38] Artificial photosynthetic systems have been developed with success for the generation of oxygen. In this type of "synthetic chloroplast", manganese (III) tetrapydridyl porphyrins were used, [5].[27]

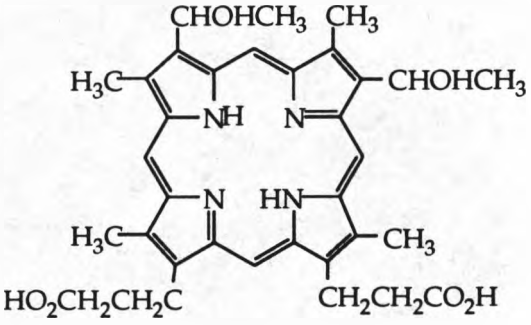


[5]

1.5.2. Photodynamic Cancer Therapy

Porphyrins are receiving attention in the field of photodynamic cancer therapy, where they act as photosensitisers for the conversion of triplet to singlet oxygen. For such therapy, a sensitiser should be red or near infrared light absorbing but preferably should not absorb elsewhere. The sensitiser should be selectively retained in a tumor relative to normal adjacent tissue.[41] The first generation of successful sensitizers are the porphyrins.[41] Basically, the porphyrins absorb the light and pass from the ground state to an excited, long lived triplet state where they can interact directly with molecular oxygen to produce the active oxygen singlet species which is able to destroy the cells close to its site of generation.[41,42,43,44,45]

Examples of such sensitisers now available are derivatives of haematoporphyrin [6] and aluminium complexes of phthalocyanine sulphonates [7].



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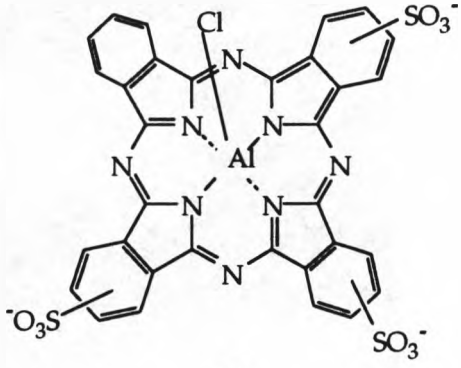


[7]

1.5.3 Langmuir-Blodgett Films

Langmuir-Blodgett films result from a deposition technique that can produce organic assemblies in which the (crystalline) structure and thickness may be controlled in a varied manner. In this technique, a floating monomolecular film is formed and is then transferred from the liquid-air interface onto a solid substrate.[46] By successive transfer, the film thickness can be built up in a moleculary ordered fashion. Once formed, the films can be used in such application as,

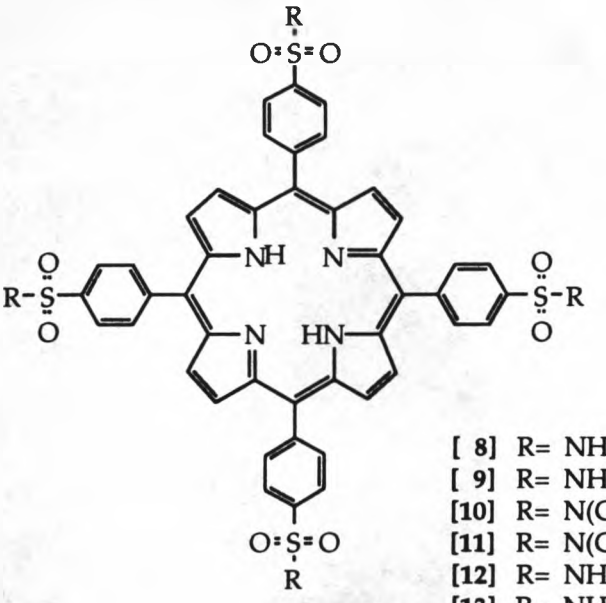
(i) microlithography for the production of integrated electronic circuits,

(ii) modification and enhancement of acoustic wave devices,

(iii) nonlinear optics in which the interaction of electromagnetic fields produce new waves with different phase, frequency or other propagation characteristics. One particular application is to form an electro-optic modulator for the telecommunications industry,

(iv) production of pyroelectric materials that could eventually be exploited in thermal imaging techniques.

Examples of film-forming porphyrins are provided by the sulphonamido porphyrins **[8 - 14]**.[47]



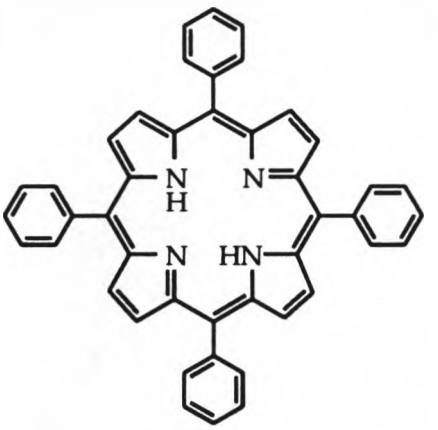
[8] R= NH_2
[9] R= $NHC(CH_2OH)_3$
[10] R= $N(CH_2COOH)_2$
[11] R= $N(CH(CH_3)_2)_2$
[12] R= NHC_4H_9
[13] R= NHC_8H_{17}
[14] R= $NHC_{12}H_{25}$

1.5.4. Enzyme Modelling

Research into modelling of enzyme actions using transition metals with various ligand is very diversified and it is arguably the most investigated potential of porphyrins. As a consequence, the amount of literature in this area is vast. Most studies on catalytic activity of biological models try to mimic the capacity for oxygen activation and oxygen transfer in enzymes.[36,48]

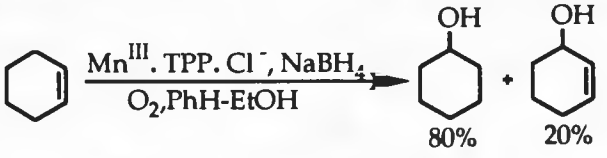
1.5.4.1. Modelling of enzymes using metalloporphyrins of iron and manganese

Iron and manganese are among the more widely used and investigated metals for enzymatic modelling because of their importance in natural systems. In this sort of research oxygen can be activated by the metalloporphyrins but, being a powerful oxidant, it usually induces initiation of free-radical autoxidation, leading to destruction of the activating porphyrins. Most research studies in this area have used other oxygen oxidation sources than molecular oxygen and these are discussed later.



[15]

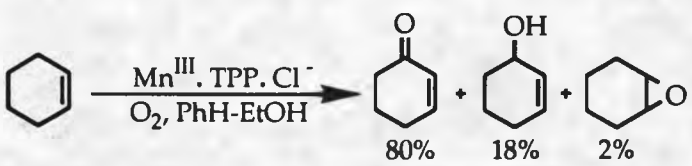
Much of the early research with model metalloporphyrins took advantage of the easy synthetic availability of the iron and manganese complexes of 5,10,15,20-*tetrakis*phenylporphyrin **[TPP; 15]** but there are a few examples in the literature of the use of iron and manganese metalloporphyrins with molecular oxygen. The systems that have been examined to attempt to mimic the reduction of oxygen by enzymes through use of a manganese(III) porphyrin in the presence of sodium borohydride, to oxidise alkenes as, for example, with cyclohexene.



Scheme 5.

In the presence of a small amount of Mn(III)TPPCl and an excess of sodium borohydride, cyclohexene was treated with an excess of dioxygen. The reaction taking place (Scheme 5) occurs rapidly at room temperature without formation of products other than cyclohexanol and cyclohexenol in a 4;1 ratio. Further investigation concerning the origin of the cyclohexanol showed that, during reaction, the formation of cyclohexene epoxide occurs even in the presence of sodium borohydride but this is readily reduced exclusively to cyclohexanol . Cyclohexenone is formed also and is readily reduced to cyclohexenol and cyclohexanol but this route only accounts for 14% of the total of cyclohexanol, the remaining giving cyclohexenol.[49]

It was found that, in the absence of sodium borohydride, oxidation of cyclohexene occurred but there was a long induction period and oxidation could be quenched by addition of a radical inhibitor. This finding indicates clearly that, in the absence of sodium borohydride, reaction proceeds as a typical autoxidation, (Scheme 6).[49] The products of the autoxidation are cyclohexene epoxide, cyclohexenone and cyclohexenol.



Scheme 6.

Careful spectroscopic investigation indicated that at least two intermediates were involved in the reaction, viz., $TPPMn(IV)O_2^{2-}$ and $TPPMn(III)O_2^{-}$. Thus, the authors refer to the fact that the reducing reagent (sodium borohydride) and one of the intermediates seemed to be the active species in these reactions, which closely resembles the operative mechanism for oxidation by cytochrome P450, where the reducing reagent is NADPH.

Other substrates which have been investigated using the same catalytic system were olefins such as styrene, cyclooctene and (E)-1-phenyl-prop-1-ene.[163] With these alkenes only two types of product were obtained, namely ketones and their corresponding alcohols, the latter resulting from reduction of the first-formed ketones by excess of sodium borohydride.[50]

To overcome the problem that the system $NaBH_4/TPPMn(III)/O_2$ gives not only direct oxidation products but also those resulting from further reduction with sodium borohydride, a new system was developed with $TPPMn(III)/H_2$/colloidal Pt-O_2. It was reported that the need for an appropriate electron donor was essential to convert TPPMn(III) into TPPMn(II) which activates dioxygen to form a powerful oxidising species. It was found that colloidal platinum efficiently catalysed electron transfer from H_2 to TPPMn(III) to form TPPMn(II).[51] In an experiment with cyclohexene, the formation of cyclohexene oxide was detected as a major product. 3-Cyclohexenone and a very small amount of 3-cyclohexenol were also produced, but no detectable amount of cyclohexanol was formed. This system gave direct oxygenation products efficiently and in high yield, without serious perturbation from autoxidation or further reduction.[51] It was reported that studies to clarify the reductive oxygen activation mechanism were in progress.[51]

Iron and manganese complexes of 5,10,15,20-*tetrakis*phenylporphyrin have been studied for oxidation reactions in which iodosylbenzene was used as the oxygen donor without the need for a reductant. Iodosylbenzene is a an effective mono-oxygen souce for the P450 enzyme models in the absence of molecular oxygen and a reducing agent.[33,52,53] However, under the reaction conditions, TPPMn and TPPFe were either destroyed or inactivated through formation of a μ-oxo dimer (figure 4).

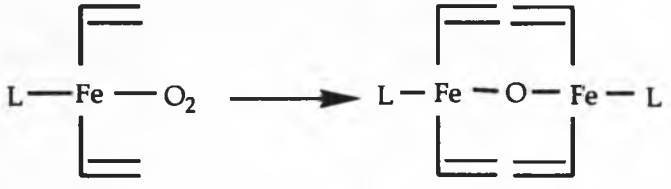
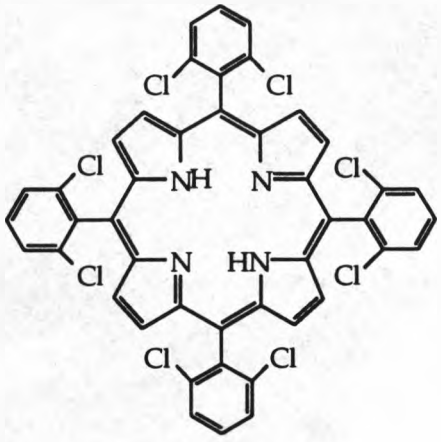


Figure 4. Reaction of TPP iron complex with molecular oxygen to form an inactive μ-oxo dimer.

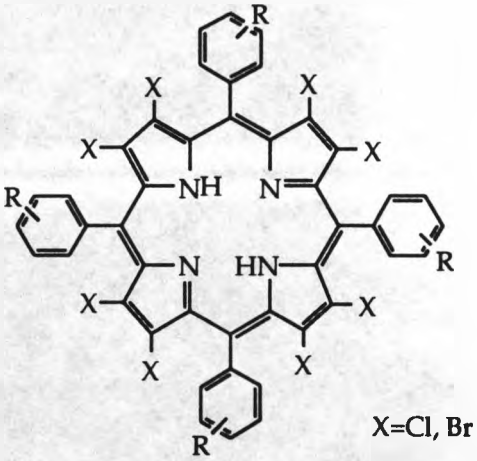
Increased interest in metalloporphyrin-catalysed reactions has promoted a search for more robust catalysts.

Tetraarylporphyrins bearing 2,6-substituents on the aryl rings, such as 2,6-dichlorophenylporphyrin **[TDCPP; 16]**, have proved to be much more resistant to autoxidation, probably due to the protection given to the 5,10,15,20-positions by the two large chlorine atoms preventing formation of the inert μ-oxo species or protecting the meso position from oxidative attack.



[16]

This catalyst has become widely used in oxidation experiments in which iodosylbenzene, iodosopentafluorobenzene, sodium hypochlorite, potassium monopersulphate, alkyl hydroperoxides and magnesium monoperoxyphthalate have been used as single oxygen donors.[54,55,56,57,58,59,60,61,62,63,64,65,66,67] It was found also that electronegative groups in the β-positions of the porphyrinic pyrrole rings increased the resistance of porphyrins to oxidative degradation [17].[61,60,65] With this in mind, attention then turned to methods for effecting, halogenation of porphyrins so as to perchlorinate, perbrominate or perfluorate the β-positions.[53,59,60,61,62,64,65]



X=Cl, Br

[17]

In some of the oxidation reactions using hydrogen peroxide and peroxycarboxylic acids as oxygen donors, it has been found that, when a ligand such as imidazole was present, the metalloporphyrins reacted much more efficiently. The ligand increased the rate of oxygen transfer from the donor to the catalyst and promoted the necessary heterolytic cleavage of the peroxy O-O bond, by utilizing higher oxidation states of the central metal.[54,60,65,67] The presence of other ligands, such as pyridine and substituted pyridines and substituted imidazoles, in reactions with other single oxygen donors was also investigated, the conclusion being that their presence had considerable influence on the rate of substrate oxidation.[68,69] Depending on electronic effects from the ring systems of the chosen ligands, the rates of the oxidation reactions could be varied, a result which is consistent with co-ordination of the extra ligand to the metal complex during reaction. Electron-donating groups on the ligand such as methyl, increase rates of oxidation whereas electron-withdrawing groups, such as cyano, decrease it. For instance, in the epoxidation of styrene, the time for formation of epoxide with 4-methylpyridine as extra ligand was 20 minutes as against 2 hours when using 4-cyanopyridine.[68] Later it was noticed that the manganese complex of 2,3,7,8,12,13,17,18-octachloro-5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, although a powerful catalyst for oxidation of alkenes, was inefficient in turnover number when used with equimolar amounts of an alkene substrate and hydrogen peroxide.[66] In spite of all the reported success for the use of β-halogenated complexes, a careful analysis was later published in which it was suggested that the extreme reaction conditions might have had a protective influence against the porphyrin oxidative degradation.[58] Thus, it appears that use of a large molar excess of substrate relative to oxidant served to protect the catalyst whereas, under more normal reaction conditions, the catalyst is not stable. The catalytic activity of manganese complexes of β-

perchlorinated 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin and manganese complexes of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin have been compared with the conclusion that the β-chlorine atoms do not give any inherent protection to the catalyst and that the catalytic efficiency of manganese 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin itself was consistently higher.[58] In other words, the highly chlorinated porphyrins were only useful under highly unusual reaction conditions.

1.5.4.2.Polymer-supported metalloporphyrin models of enzymes

Interest in heterogeneous catalysis and in immobilised enzyme models has led to the synthesis of another class of porphyrins, namely those connected in some way to polymers.[34,70,71,72,73,74] Polymer-supported porphyrins have been synthesised by using, (i) polymers containing N-donor ligands capable of binding to the metalloporphyrin in an axial position, (ii) covalent or electrostatic attachment of the polymer to the porphyrin ring, (iii) aromatic substituents introduced at bridging carbon position on the porphyrin ring and, (iv) inclusion complexes.

Polymer-supported metalloporphyrins are used in the same sort of oxidation reactions as the free metalloporphyrins analogues and the oxygen sources are again the same. In general, the site-isolated polymeric catalysts show greater activity than do free porphyrins. It is believed that this might be due to the prevention of deactivation or degradation occurring because of the polymer support. Recycling of the catalyst is easier because of the ease of separation of the catalyst from reaction products. Finally, selectivity increases due to the polymer support environment.[34,70,71,72]

1.5.4.3. Modelling of enzymes using porphyrin complexes of other metals than manganese or iron

In the literature, reports can be found for the use of metal complexes other than those of iron or manganese for investigation as models for enzymes. Some examples involve the use of aluminium, ruthenium, rhodium, molybdenum, niobium, tantalum, zinc, nickel, cobalt, etc.[75,76,77,78,79] Because of the interest of the present work in cobalt complexes, these are discussed separately in the next section.

1.6. Enzymatic Modelling Using Cobalt Complexes

Cobalt is a transition metal with normal valences of 2 or 3. The metal itself in its compact state is not attacked by oxygen or water at ordinary temperatures but, at elevated temperatures or in a finely divided form, it is oxidised by moist air.[80] Cobalt is silver-white when polished and, at room temperature, exists in a stable close-packed hexagonal lattice (α-cobalt).[80]

Cobalt salts exhibit remarkable colour phenomena in aqueous solution. It is thought that these colours are caused by either a change in hydration or solvation.[80] Or by the number of ligands surrounding the cobalt ion, where the color of the cobalt salts is determined solely by the degree of saturation of the residual valencies of the cobalt ion. "Saturated" compounds which have six groups around each cobalt(II) are pink or red whilst "unsaturated" compounds with only four groups are deep blue. To some extent, recent work tends to agree that the two different processes, change in hydration or solvation and change in the number of ligands, must be taking place to varying degrees.

The ready interchange between the +2 and +3 valence states is utilized for many purposes. Cobalt compounds are widely used in ceramics for several different purposes, such as glaze stain, where a very rich blue colour may be obtained by adding 5% of a cobalt salt to a glaze of high lead content or body stain, where the yellow colour given by iron to most clays used in pottery can be optically neutralised by addition of the complementary blue colour imparted by cobalt. For the artist's pigments, the phosphate, arsenate and aluminate are the most comonly used.[80]

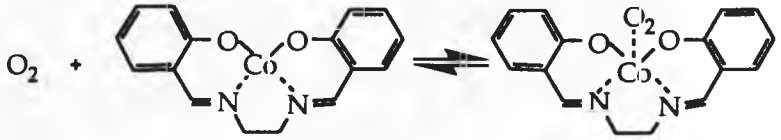
Cobalt is used in some glass manufacture, to impart colour. It has been found that some glasses which are pink at room temperature turn blue on heating, indicating that the average co-ordination sphere of cobalt decreases with increasing temperature. Occasionally cobalt is used for decolourising purposes in plate and window glasses, to neutralise the yellow tint of iron and selenium.

One of the first uses of cobalt compounds as catalysts lay in their excellent capacity for accelerating the drying of unsaturated oils in paints and varnishes through the action of oxygen. A number of cobalt salts, particularly organic compounds, is used for that purpose. One example is cobalt acetate which is used for drying linseed and soybean oil, a process of oxygenation and cross-linking of double bonds in components of the oils. The use of cobalt salts allows the use of some low priced semi-drying oils in place of faster reacting expensive ones. Any of the forms of cobalt(II) will "dry" these unsaturated oils.[80]

1.6.1. Cobalt carriers of dioxygen

In 1852 it was reported that aqueous ammoniacal solutions of cobalt(II) salts turned brown when exposed to air. These brown salts were called oxocobaltiates[48,81] and were characterised as containing the

diamagnetic cation, $[(H_3N)_5\text{-}Co(O_2)\text{-}Co(NH_3)_5]^{4+}$.[82] Although this was one of the first reports of a compound complexed with dioxygen, it was only in 1938 that synthetic, reversible cobalt-oxygen carriers were discovered.[83,84] The colour change seen on exposing N,N'-ethylene*bis*(salicylideneiminato)cobalt(II) (CoII[salen]; **[18]**) to air is due to reversible absorption of dioxygen to give structure **[19]**:



[18] **[19]**

Since the initial discovery of the absorption of dioxygen by (CoII[salen]; **[18]**), interest in Schiff's base cobalt complexes has continued. The main aims of the first investigations were to gain some understanding of the nature and properties of metabolic biological metal complexes which are so indispensable for oxidation and reduction, and to separate dioxygen from air.[85,84]

Extensive studies of the oxygen-carrier properties of cobalt(II) complexes with salen-type ligands have been reported.[84,85,86,87,88,89,90,91] It was found that application of these metal/ligand compounds as oxygen carriers was limited because their ability to complex with dioxygen deteriorated over a relatively short number of oxygenation/deoxygenation cycles, viz., they had poor turnover numbers. For example, CoII(salen) **[18]**, deteriorates to 70% of its original activity after only 300 cycles.[84] This deterioration has been attributed mainly to irreversible oxidation of parts of the organic ligand.[84,85,87] Neither the point of attack by the oxygen nor the products formed by it were indentified but the close proximity of the peroxide oxygen to the imine groups led to the supposition that initial attack might be at that double bond. Others believe that the deterioration

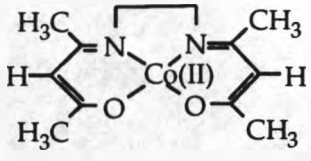
is due to irreversible oxidation of cobalt(II) to cobalt(III), caused by the solvent entering the co-ordination sphere of cobalt and increasing its oxidation potential.[84,85,87]

In parallel to these works, a dioxygen adduct of cobaltous *bis*(histidine) was reported.[92,93,94,95] This work demonstrated that reversible oxygenation of cobalt complexes was a general rather than an isolated phenomenon.[36] The behaviour of other substituted histidine compounds was studied and it was observed that whilst cobalt *bis*(histidine) does combine with dioxygen, it does not combine with carbon monoxide unlike haemoglobin and myoglobin.[93] The metal-to-dioxygen ratio in the cobalt *bis*(histidine)dioxygen complexes is 2:1, compared with only 1:1 in oxyhaemoglobin and oxymyoglobin complexes.[93] Later, in 1973, cobalt(II) complexes of histidine received more attention as oxygen carriers and new research was carried out with histidine, glycine and many other amino acids as ligands. It was found that, at the end of oxygen uptake, some of the carriers had decomposed to give cobalt(III) complexes. Another observation was that, for long reaction times with molecular oxygen, superoxide or peroxide, which was formed during reaction, attacks the histidine residue and leads to unidentifiable organic residues.[96]

In 1969, the mechanism by which dioxygen travels through the hydrophobic pocket of the protein to reach a co-ordination site on the iron atom in haemoglobin was published.[97] It seemed that it might be possible to simulate this hydrophobic environment of the protein through use of non-aqueous aprotic solvents.[97] This was found to be so and interest in Schiff base cobalt(II) complexes received a pronounced impetus from the work of two different groups[98,99,100] which reported that, under the appropriate conditions in non-aqueous solution, certain Schiff's base cobalt(II) complexes would bind reversibly one molecule of dioxygen per

two molecules of cobalt complex. It was found that this oxygen binding would only occur with a few solvents, such as dimethylformamide and dimethyl sulphoxide. Solvents such as toluene, chloroform or acetone would not allow oxygen adducts to form. The solvent was found to act as a ligand to the cobalt[98] and it appears that the role of the solvent ligand in binding *trans* to oxygen compensates for the charge transferred from the cobalt to dioxygen. Thus, the presence of a σ-donor was found to stabilise the metal-oxygen bond. To amplify this point, the addition of ligands such as acetate or thiocyanate to solutions of cobalt complexes in solvents such as toluene was examined and found to lead to formation of the oxygen adducts.[98] This same research group reported for the first time the formation of a 1:1 adduct of a cobalt Schiff base complex with dioxygen.[98] Solutions of N,N'-ethylenebis-(3-methoxysalicylideneiminato) cobalt(II) were found to bind reversibly to dioxygen in a 1:1 ratio.

In other research, it was shown that in the case of N,N'-ethylene*bis*(acetylacetoniminato)cobalt(II) (Co[acasen]; **[20]**), reversible formation of monomeric dioxygen adduct occurred at low temperatures in the presence of ligands such as substituted pyridines.

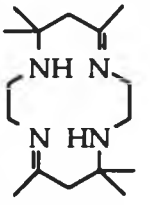


[20]

At a given pressure of dioxygen, the amount of oxygenated species formed increased with the base strength of the substituted pyridine. These substituted pyridine ligands were thought to stabilise the cobalt-oxygen bond by enabling octahedral co-ordination around the metal to be achieved.[100]

Three other groups of workers developed these studies further. The effect of equatorial and axial ligands on the formation and stability of dioxygen/cobalt complexes with ligands such as 1,4,8,11-tetraazacyclotetradecane **[21;** cyclam] and 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene **[22;** (Me_6(14)4,11-diene N_4)], was reported. It was found that binding of dioxygen is a function of axial and equatorial ligand composition. Change of the equatorial ligand can result in a dramatic change in oxygen affinity. For instance, substitution of cyclam **[21]** for Me_6(14)4,11-dieneN_4 **[22]** decreases oxygen affinity. The proferred explanation is that an increase in the oxidation state in the macrocyclic ligand decreases oxygen affinity by reducing the Co(II)/Co(III) oxidation potential.[101]

[21]



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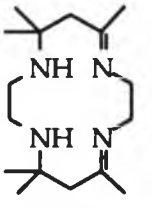
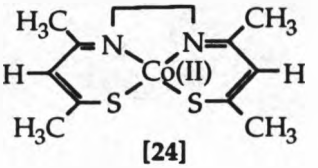


[23]

The synthesis and characterisation of cobalt(II) complexes with another macrocyclic Schiff's base ligand such as 5,7,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,14-diene (Me_6[14]4,14-dieneN$_4$) **[23]** was published.[102] It was observed that thermodynamic and steric requirements for co-ordination to cobalt(II) were fulfilled by a fifth ligand in one of the two available axial sites. The limited tendency to co-ordinate to a sixth ligand was due to electronic repulsion arising from the single unpaired electron in the dz^2 orbital of the cobalt(II) ion and to steric effects arising from axial methyl substituents on the carbons of the macrocyclic ligand.[102] The reversible binding of dioxygen by these compounds gave monomeric adducts.[102] It was proposed that there was a relationship

between the extent of electron transfer from cobalt(II) to oxygen and the redox properties of the complexes.[102]

Because of their great biological interest, studies have been reported on cobalt/oxygen (1:1) adducts with thioiminato cobalt(II) complexes, such as N,N'-ethylene*bis*(monothioacetylacetoneimine)cobalt(II) (Co[sacsacen]; **[24]**).



[24]

It was found that all of the complexes took up and released molecular oxygen reversibly in solutions containing small amounts of Lewis bases, such as pyridine, methylimidazole (MeIm) and dimethylformamide (DMF). Particularly with Co(sacsacen), the stability of the oxygen adduct was found to be a function of the solvent and the Lewis base present. The most stable of the systems studied was Co(sacsacenn)·MeIm·O2 in acetonitrile.[103] Generally, oxygen adducts with these cobalt/ligand complexes are less stable than their keto-iminato counterparts **[18, 20]**. It has been suggested that the reason is the poorer σ-donor ability of sulfur compared with a keto oxygen atom. In addition, it was proposed that the sulfur atom could drain electron density from the cobalt ion via π-back bonding interactions.[103] For these reasons, it was concluded that a π-donating para-substituted group in this type of ligand, should increase electron density in the chelate ring and reduce the π-back bonding between cobalt and sulfur, thereby increasing the electron density on the cobalt ion.[103] Although this was confirmed by the use of several different substituents in the para-positions, it was found also that when using the methoxy function (expected to be able to participate by resonance and

induction) stabilization of the oxygen adduct was not observed; no explanation was proffered.[103]

1.6.2. Cobalt porphyrin complexes as dioxygen carriers

About the time that the above cobalt ligands were being investigated as oxygen carriers, other research on cobalt(II) porphyrins was begun. The ability of such cobalt porphyrin complexes to bind reversibly to molecular oxygen was examined. The reactions investigated in the early research were not related to any catalytic capacity of these oxygen adducts but more to features of the systems themselves.

Attempts have been made to understand and correlate the factors involved in reactions leading to oxygen complexes such as those shown in equations (i) to (vi) of Scheme 7:

$$CoP + L \rightleftharpoons CoP \cdot L \qquad \text{"five-coordinate adduct"} \quad (i)$$

$$CoP \cdot L + L \rightleftharpoons CoP \cdot L_2 \qquad \text{"six-coordinate adduct"} \quad (ii)$$

$$CoP \cdot L + O_2 \rightleftharpoons CoP \cdot L : O_2 \qquad \text{"}O_2\text{ adduct"} \quad (iii)$$

$$CoP \cdot L_2 + O_2 \rightleftharpoons Co\,P \cdot L \cdot O_2 + L \qquad \text{"}O_2\text{ adduct"} \quad (iv)$$

$$CoP \cdot L + Co\,P \cdot L : O_2 \rightleftharpoons L \cdot CoP \cdot O_2 \cdot CoP \cdot L \qquad \text{"binuclear complex"} \quad (v)$$

$$CoP + O_2 \rightleftharpoons CoP \cdot O_2 \qquad \text{"ligand off"} \quad (vi)$$

P-Porphyrin ligand
L-Axial ligand (usually an amine)

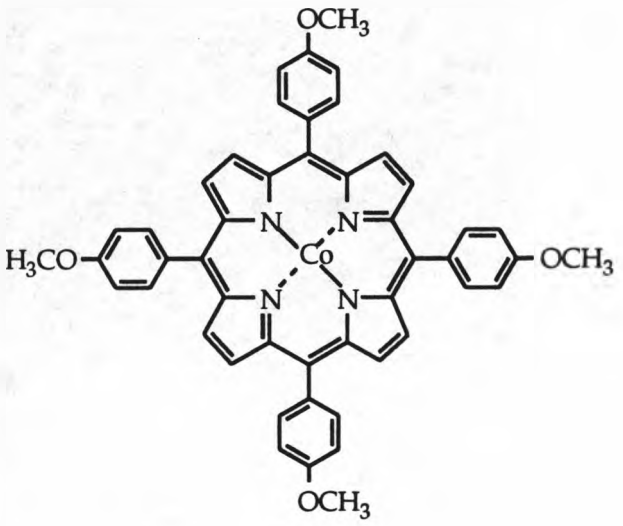
Scheme 7.

Equations (i) and (ii) [Scheme 7], show the formation of the five and six-coordinate cobalt complexes, where L is an axial ligand. Equations (iii) and (iv) [Scheme 7], describe the reactions of these complexes with dioxygen. In reaction (iii) of Scheme 7, the oxygen adduct is formed by reaction with a cobalt porphyin complex which already has an axial ligand. Most research groups agree that the presence of an axial ligand is essential to the formation of the oxygen adduct. In equation (iv) of Scheme 7, the formation of the oxygen adduct occurs with the replacement of one of two axial ligands. In equation (v) of Scheme 7, the formation of a binuclear complex from an oxygen adduct and a five coordinate cobalt complex is described. Finally, the reaction of a cobalt porphyrin complex with dioxygen without there being an axial ligand is the subject of study also, but most research groups do not consider this reaction as having significance. In the next section, the different studies and conclusions about the above reactions are presented. There are some disagreements on the interpretation of results and also some differences in detail but, overall, there is agreement on certain aspects.

1.6.3. Study of the reaction involved between cobalt porphyrin complexes and dioxygen

One section of research in this area was centred on the use of electron paramagnetic resonance spectroscopy (EPR) of cobalt complexes of 5,10,15,20-*tetrakis*arylporphyrins, in particular the cobalt(II) complex of 5,10,15,20-*tetrakis*(4-methoxyphenyl)porphyrin, **[25]**. Electron spin resonance is used for molecules containing unpaired electrons by observing the magnetic fields at which they come into resonance. Cobalt(II) has an electronic configuration with 7 electrons to distribute among its 5-d orbitals, d^7. As a consequence, cobalt(II) has an unpaired

electron in a d_z^2 orbital and was used in these studies.[104] The formation of a five-coordinate adduct, CoPL [reaction (i); Scheme 7], and of a six-coordinate adduct, CoL_2, [reaction (ii); Scheme 7], were investigated.



[25]

No correlation was found between EPR parameters and the basicity of any axial ligands required for formation of a five-coordinate complex but there was a correlation between basicity and formation of a 2:1 adduct ($CoP{\cdot}L_2$) as shown in reaction (ii) of Scheme 7. However, some ligands such as N-methylimidazole, which are more basic than some substituted pyridines and therefore are better σ-donors, do not form 2:1 complexes, probably because of their poorer π-accepting capacity compared with pyridines. It was concluded that other factors in addition to ligand basicity were important in influencing complex formation. There appears to be a sensitive balance between the σ-donating and π-accepting ability of the ligand and the formation of a 2:1 adduct.[104]

Reaction (iii) of Scheme 7, in which the reaction of a five-coordinate cobalt complex with dioxygen takes place to produce the oxygen adduct $CoP{\cdot}L{\cdot}O_2$, was also studied by EPR spectroscopy. It was found that the ease of formation of an oxygen adduct is a function of ligand basicity and that it

is difficult to remove all of the dioxygen from adducts when more strongly binding axial ligands are used. The difficulty in removing oxygen was thought to be caused by formation of a strong bond between cobalt and oxygen driven by a basic axial ligand facilitating electron transfer from cobalt to oxygen.[104]

Studies into the formation of $CoP{\cdot}L{\cdot}O_2$ in reaction (iii) and (iv) of Scheme 7 showed the new complex to be $Co(III)O_2^{\cdot-}$ in which oxygen exists formally as a superoxide ion.[105] It has been suggested by others[106,107] that an electron is transferred from the d_z^2 orbital of the cobalt to a $2p\pi^*$ (antibonding) orbital of the oxygen molecule in which the degeneracy of the two $2p\pi^*$ orbitals had been split by bond formation with cobalt. When studying the Gibbs free energy (ΔG) and enthalpy (ΔH) for formation of $PCo{\cdot}L{\cdot}O_2$ in reaction (iii) of Scheme 7, in the presence of different ligands, no correlation was found between these thermodynamic parameters and the pK_a values for the ligands. This led to the deduction that the σ-donor strength of a ligand does not appear to be important in determining the stability of the $Co\text{-}O_2$ bond. However, it was found that aromatic amines such as pyridines and imidazoles provided a slight stabilization of the Co-O bond. Thus it was considered that π back-bonding from cobalt to the ligand might be important in strengthening the $Co\text{-}O_2$ bond. The π back-bonding should decrease electron density on the cobalt(III) product and this would strengthen its bonding to the electron rich O_2^- product species. An interestingly similar magnitude for ΔH for reaction (i) and (iii) of Scheme 7 (formation of $Co{\cdot}P{\cdot}L$ and $CoP{\cdot}L{\cdot}O_2^-$ respectively) was observed. A considerably more negative heat of formation of the $Co\text{-}O_2$ bond had been expected because there is an electron transfer from cobalt(II) to dioxygen upon bond formation that does not occur on formation of the five-coordinate complex, in which the electron is clearly localized on cobalt(II). In spite of this, it was reported that these two reactions differ in

one important respect, namely that the addition of a ligand to the four-coordinate cobalt(II) porphyrin complex acts to activate the cobalt(II) for reactions with dioxygen but addition of a sixth ligand was found to be very unfavourable.[105]

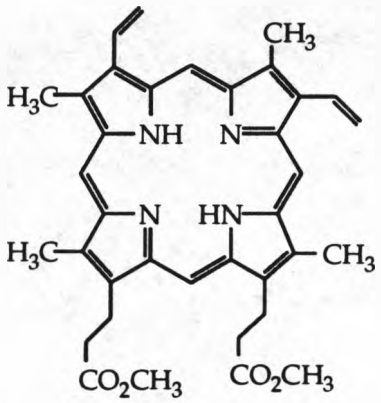
Reaction of cobalt(II) porphyrins with oxygen where cobalt(II) is four co-ordinated and where no axial ligand is present ("ligand off") were also considered [reaction (vi); Scheme 7]. The stabilities of a $CoP{\cdot}O_2$ adduct in a "ligand off " or "ligand on" context were compared and it was found that the "ligand off" adduct is at least 100 times less stable than the "ligand on" adduct.[105] ^{1}H-Nmr techniques have been used to confirm some of these conclusions.[108]

An investigation into steric and electronic effects in cobalt(II) porphyrins was carried out later with *para*-substituted 5,10,15,20-*tetrakis*aryl porphyrins of cobalt(II).[109,110] It appears that the cobalt atom is more sensitive to electronic effects within the porphyrin ring than it is to the basicity of the axial ligand. This was explained in terms of the π back-bonding tendencies of cobalt and the fact that the porphyrins are good π-acceptors.[109,110]

Redox reactions of these particular *para*-substituted cobalt porphyrins were investigated in several different solvents. In strongly co-ordinating solvents, oxidation of cobalt(II) to cobalt(III) was observed to occur more readily. A regular relationship between the half-wave potential for oxidation of cobalt(II) to cobalt(III) and the co-ordinating ability of aprotic solvents was observed.[109] The results were in agreement with others already published.[111,112] There seems to be a direct correlation between the redox potentials of cobalt chelates and their ability to behave as oxygen carriers.[111,112] Oxygen uptake correlates linearly with the half-wave potential and the correlation holds in spite of changes to the

framework and the π delocalization properties of the tetradentate porphyrin ligand.[111,112]

The same reactions presented on Scheme 7 have been examined using other techniques.[113,114,115,116] Measurements have been carried out using visible spectroscopic techniques on the cobalt complex of protoporphyrin IX dimethyl ester **[26]**.



[26]

According to these results the presence of an axial ligand is a necessary requirement for oxygen binding to any cobalt(II) porphyrin system. There is also a need for a sufficient electron-rich metal atom that can bind molecular oxygen reversibly, in agreement with other investigations in which it was established that, as the electron density on the metal atom increases, the strength of the M-O_2 bond increases.[100,117] In these studies, it was found that, in the presence of an axial ligand, the visible spectra under aerobic conditions differ from the spectra obtained under anaerobic conditions because of the formation of the oxygen adduct (figure 5).[114]

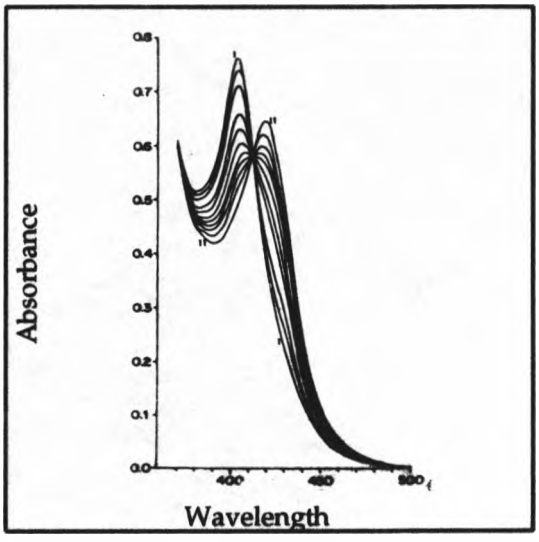


Figure 5. Changes in the absorption spectrum at the Soret band wavelength region during reaction of a cobalt(II) porphyrin complex with dioxygen. The Soret band at 404nm, due to unreacted cobalt(II) porphyrin complex decreases as a new band at 428nm due to the oxygen complex increases.[115]

As well as changes at the Soret wavelength, another alteration occurs to the Q band at around 555nm on formation of an L•PCo(III)•O_2 adduct, the band being split into two. Formation of the complex, CoP•L, in the absence of air resulted in a decrease in the intensity of the Soret band and was accompanied by a small blue shift of the Q bands. With the formation of the complex, CoP•L_2, a new Soret band appears in the region of 420nm (figure 6).

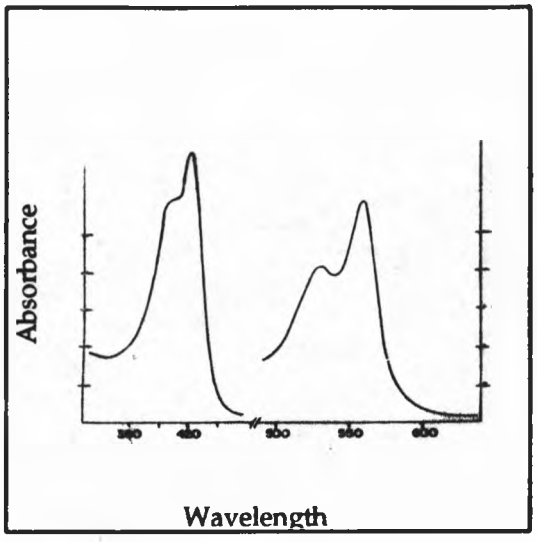


Figure 6. Visible spectrum of CoP run in piperidine at room temperature. The use of a high concentration of piperidine was needed in order to form a six-coordinated complex. Raising the temperature resulted in a decrease of the intensity of the band due to the six-coordinate complex. In the Soret region at around 400nm, a new band appeared at around 420nm due to the formation of a six-coordinate complex.[115]

Considering all the available data, it is found that the equilibrium constant (K) for reaction (iii) [Scheme 7; formation of a Co(III)P•L•O_2^- adduct with ligands such as dimethylformamide (DMF), imidazole and methylimidazole] was much greater than might have been expected on the grounds of their basicities. This finding was explained in terms of the π-donor properties of the ligands. The formation of a bond between dioxygen and various metal complexes was considered to be due to σ-donation from an sp^2 lone-pair on oxygen into the d_z^2 orbital on cobalt, accompanied by synergistic π back-bonding from filled cobalt d_{xy} or d_{yz} orbitals into empty π* (antibonding) orbitals on oxygen. Since ligands coordinate *trans* to the oxygen they compete for π-electron density on the cobalt; the binding of O_2 to CoP•L should be sensitive to the π–donating or accepting ability of an axial ligand (L). A good π-acceptor ligand should decrease the π-electron density on the metal, resulting in a weaker Co-O_2

bond and a greater electron density on the metal will make the same bond stronger.[115]

In analysing these data, use was made of a method referred to as the Hill equation.[118] This equation is an adaptation of the Benesi/Hildebrand analysis used for calculating thermodynamic parameters from spectroscopic observables.[119] Apparently, this has been considered by others as not to be a good procedure because the method suffers from many pitfalls.[119] Using a different approach,[120,121,122] an analysis was made of all the data obtained by uv/visible and EPR spectroscopic techniques. From this analysis it was concluded that earlier results were not reliable.[119] However, in a riposte, re-analysis of all data proved that the published work was reliable.[116]

More recently, analysis of reaction (iii) [Scheme 7; formation of $CoP{\bullet}L{\bullet}O_2$] in terms of σ-and π-bond effects was carried out, having in mind the previously reported data.[36] The commonly accepted order of energies of the d-orbitals for a planar low-spin cobalt(II) complex, such as one with a porphyrin, is shown in figure 7.[108,111] When the cobalt complex binds to dioxygen, the order of energies for the d-orbitals suffers the change shown in figure 8. As can be seen, formation of the cobalt dioxygen adduct involves the metal d_z^2 orbital and the dioxygen π^* antibonding orbital. Occupation of the antibonding $2\pi^*$ molecular orbital is generally unfavourable.

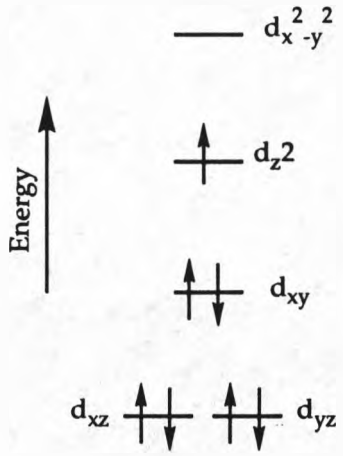


Figure 7. Assumed order of d-orbital energies for planar low spin cobalt(II) complexes.[59]

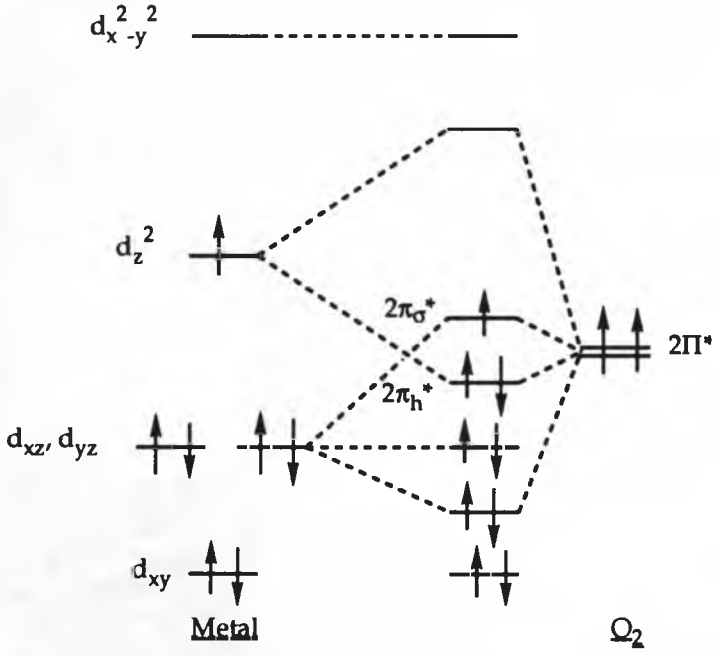


Figure 8. Qualitative molecular orbital diagram for formation of Co(III). O_2 complexes by overlap of d-orbitals on the metal with p orbitals on O_2.[30]

The Sigma effect

As the ability of a ligand to donate electron density (ligand donor strength) to the metal centre increases, the d_z^2 orbital energy increases. This interaction facilitates transfer of an electron from a predominantly

metal-based molecular orbital to a molecular orbital with substantial dioxygen character. This increase in electron density on the dioxygen ligand with concomitantly more cobalt(III) character would be expected to lead to greater stability of the dioxygen complex.

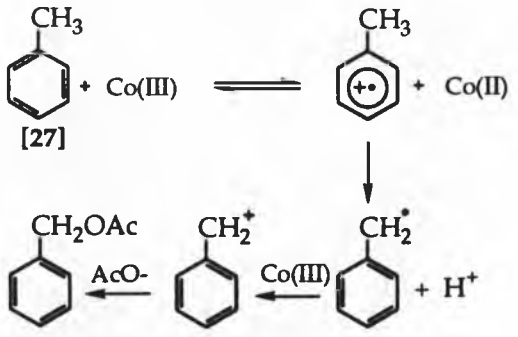
The Pi effect

When ligands are capable of π-bonding, two cases must be considered for π-donors and π-acceptors. The presence of a π-donor ligand would introduce orbitals of appropriate symmetry to interact with the doubly-degenerate d_{xz}, d_{yz} orbitals. Thus π back-bonding between cobalt and dioxygen would be enhanced by donated electron density into the $2\pi^*\sigma$ molecular orbital. This is an antibonding orbital and localisation of the electron density should destabilize a dioxygen complex. A π-acceptor ligand withdraws electron density from the $2\pi^*\sigma$ antibonding molecular orbital, thereby stabilising the complex.[36]

1.6.4. *Chemical reactions in which cobalt has been used as a catalyst*

Due to the main concerns of the present research the reactions where cobalt porphyrin complexes and dioxygen are used will be mainly referred. In these reactions, the complexes are those of 5,10,15,20-*tetrakis*aryl porphyrins which are convenient for catalytic research, due to their ease of synthesis and relative stability.

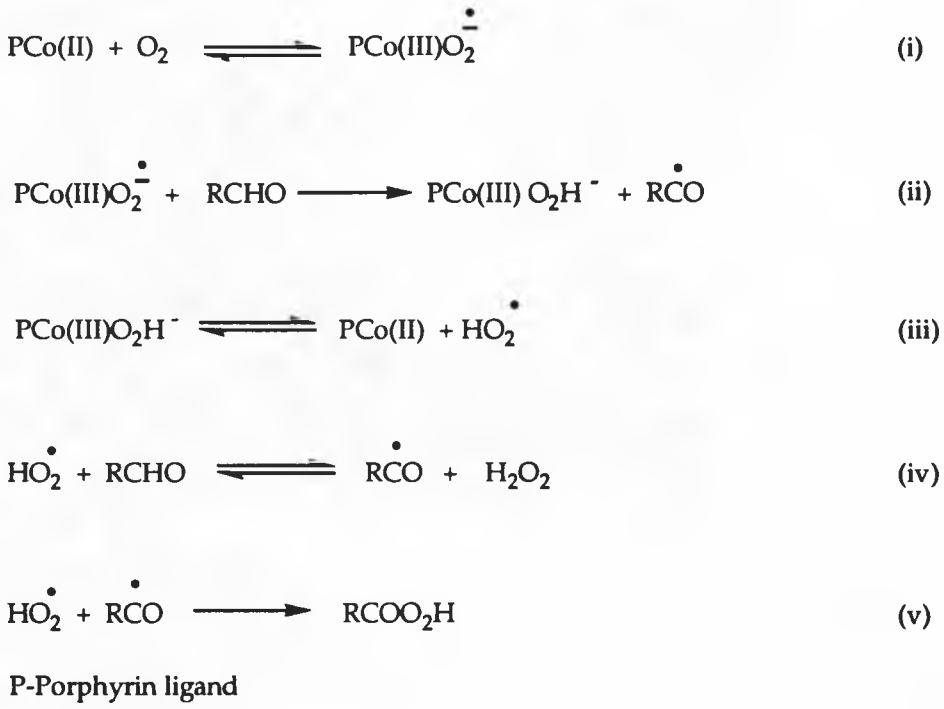
Investigation of cobalt as a catalyst does not only explore its capacity to react with dioxygen. Early reactions using cobalt as a catalyst for oxidation made use of its properties of being both an electron donor and an acceptor, as shown in the examples of Scheme 8, in which cobalt is used to catalyse the oxidation of toluene **[27]**.[123,124]



Scheme 8.

The above mechanism involves the reversible interaction of cobalt(III) with the aromatic ring leading to a radical-cation. The radical-cation in a subsequent step loses an α-proton to give a benzyl radical which is rapidly oxidised by cobalt(III) to the corresponding benzyl acetate.[123] It was recognised that the catalytic oxidation proceeded only when cobaltic ions were present and that no oxidation would take place if cobalt was present in the form of cobalt(II).[123] The fact that cobaltic ions were responsible for oxidation suggested that the catalytic oxidation proceeded predominantly *via* an electron transfer-process.[123] In fact if using substituted toluenes in this reaction high selectivity towards the catalytic oxidation was observed, which could also be explained by admitting a reaction step involving electron transfer from the substituted toluenes to the cobaltic ion.[123]

Auto-oxidation of acetaldehyde to give peracetic acid is not observed in the absence of a catalyst, but, in the presence of a catalyst such as a cobalt porphyrin complex, it immediately takes place.[125] Auto-oxidation of acetaldehyde using cobalt porphyrin catalyst starts with activation of oxygen to form the superoxide ion [reaction (i); Scheme 9]. The activated dioxygen is able to abstract a hydrogen atom from the aldehyde [reaction (ii); Scheme 9],[125,126] and the catalyst is recovered by formation of a hydroperoxy radical [reaction (iii); Scheme 9].



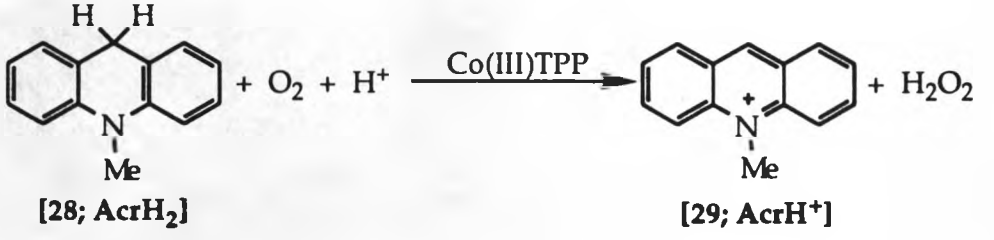
Scheme 9.

The hydroperoxy radical has been reported to react with other free radicals to became an inert compound such as peroxyacetic acid [reaction (v); Scheme 9]. No hydrogen peroxide could be detected by titration, but it was thought that this possibility should be considered [reaction (iv); Scheme 9].[125] In this last work, it was found that, for the different cobalt porphyrin complexes investigated, the order of their reactivities did not correspond to that of their redox potentials. It was shown that the effect of the substituents cannot be explained only from the viewpoint of the electron-donating or attracting properties of the substituents. The presence of additives, such as pyridine, DMF and water, was found to increase the catalytic activity of the cobalt porphyrin complexes in the order: pyridine> DMF> water. This order was explained firstly in terms of decreasing coordination to the metal, resulting in activation of the oxygen towards the metal and secondly in terms of the donating power of the different additives.[126] However, depending on the amounts used, it was found that

the presence of such additives can suppress oxygen binding because of the degree of competitive co-ordination that increases with increasing pK_a of the additives.[126]

Auto-oxidation of hydrocarbons like cumene, furan and cyclooctene by a cobalt porphyrin complex and oxygen occurs in a similar way to the oxidation of aldehydes. However, for some of the cyclic olefinic hydrocarbons an electrophilic addition of molecular oxygen to the double bond activated by the cobalt porphyrin had to be considered, together with hydrogen abstraction. It was concluded that 73% of the auto-oxidation reaction was *via* addition to double bonds and this was explained in terms of the strength of a C-H bond that is high enough to stop an activated oxygen molecule from abstracting a hydrogen atom, balanced by the ease of addition to a double bond. To verify this type of mechanism, a correlation was sought and found between the vibration frequency of the carbon double bond ($\upsilon_{C=C}$) of the different cycloolefins and the rate constants of initiation reactions.[127]

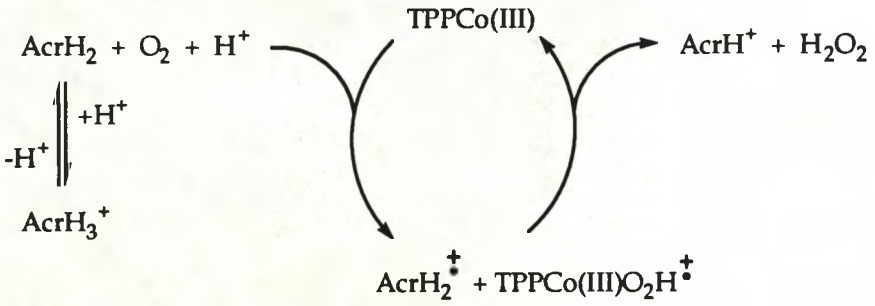
NADH plays a vital role as an electron source for the four-electron reduction of dioxygen in the respiratory chain. However, this efficiency is difficult to mimic by most models.[128] A two-electron and four-electron reduction of dioxygen was done by a model system for NADH-dependent oxygenases. These made use of an NADH model compound, 10-methylacridan **[28]**, in the presence of perchloric acid with metalloporphyrins of cobalt as catalyst (Scheme 10).[128]



[28; $AcrH_2$] **[29; $AcrH^+$]**

Scheme 10.

The proposed mechanism involves electron transfer from $AcrH_2$ to Co(III)TPP, catalysed by the presence of dioxygen and $HClO_4$, to form the complex $Co(III)TPP{\cdot}O_2H^{+\cdot}$ (Scheme 11). This step is followed by hydrogen transfer from $AcrH_2^{+\cdot}$ to $Co(III)TPP{\cdot}O2H^{+\cdot}$ to yield $AcrH^+$ and H_2O_2, followed by regeneration of Co(III)TPP. $AcrH_2$ is protonated by $HClO_4$ as shown in Scheme 11 but this new species ($AcrH_3^+$) is inactive as a reductant.[128]

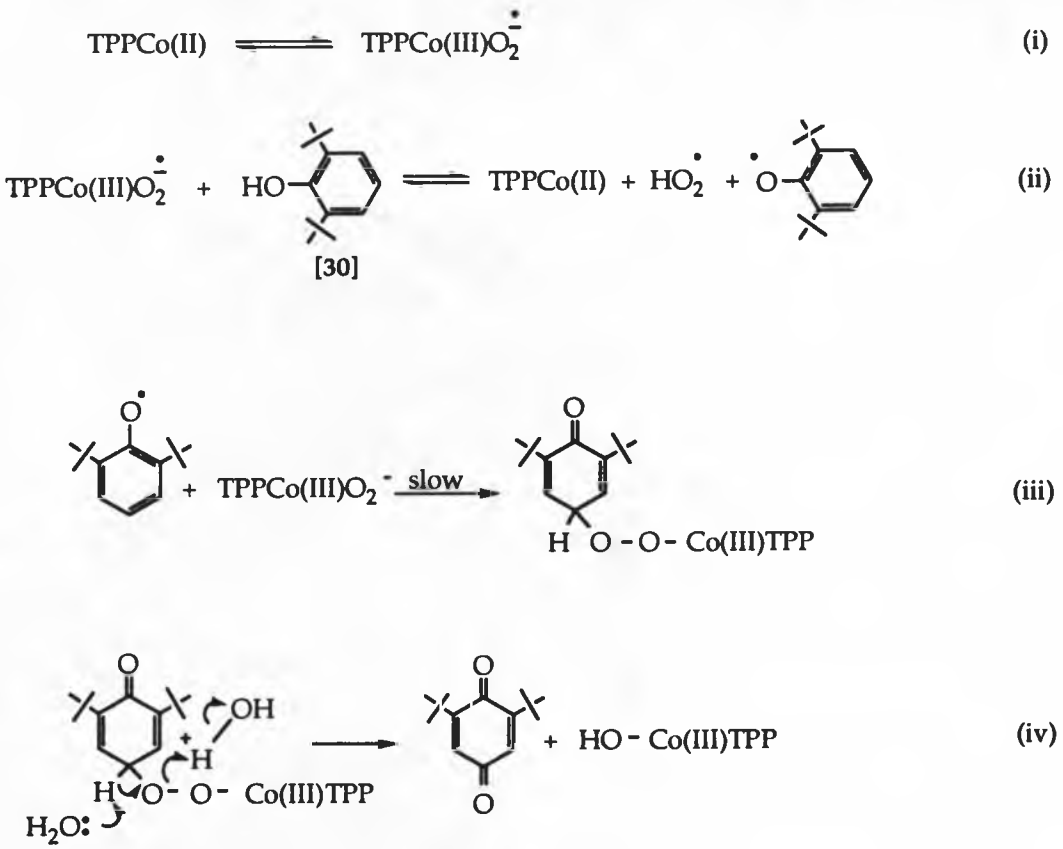


Scheme 11.

Combining the system shown in Scheme 11 (where a two electron transfer process occurs) with iodide anion which is readily oxidized to iodine, a four-electron reduction of dioxygen to water could be performed.[128] In fact, in the presence of Co(III)TPP and $HClO_4$, the four-electron reduction of dioxygen by iodide occurs efficiently.[128] On the other hand, iodide (I_2) readily oxidises $AcrH_2$ to yield $AcrH^+$ and iodine. Therefore, by combining both systems it was possible to carry out a four-electron reduction of dioxygen to water.[128] Studies of the mechanism of this last system were reported to be under way.[128]

Oxidation of phenols such as 2,6-di-*tert*-butylphenol **[30]** to yield quinones can be catalysed by cobalt porphyrins, the mechanism proposed being shown in Scheme 12.[129] Here, Co(II)TPP takes up an oxygen molecule to form a dioxygen intermediate which abstracts the hydrogen atom of the OH group of the phenol [reactions (i) and (ii); Scheme 12]. The

phenoxide radical initiates the reactions. The coordination of dioxygen to Co(II)TPP enhances the activity of the oxygen so that it reacts with phenoxide [reaction (iii); Scheme 12] and this complex finally reacts with water to give the quinone [reaction (iv); Scheme 12]. The new species that are formed, TPPCo(III)OH, are able to react with the OH group of phenol to produce a phenoxide radical and to regenerate TPPCo(II). It was found that, at high temperatures, coupling of two phenoxide radicals was favoured [reaction (vi); Scheme 12], because of the decrease in the solubility of oxygen which meant less dioxygen complex formation.

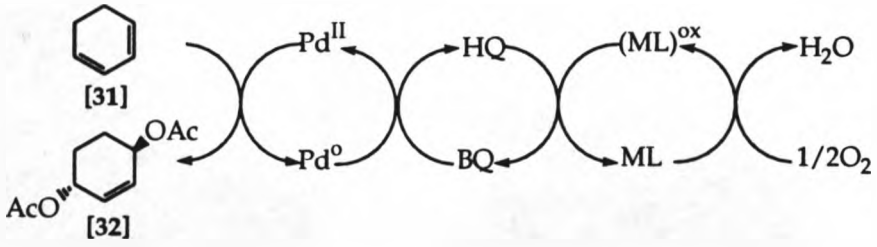


Scheme 12

In the above reaction, comparison of the cobalt complex of 5,10,15,20-*tetrakis*phenylporphyrin with similar complexes of other metals showed that the cobalt complex was more selective and more active in its catalytic action.[129] Comparison of the rate of the oxidation reaction (Scheme 12) in three different solvents (DMF, toluene, and toluene/pyridine) proved that the reactions carried out in DMF and toluene/pyridine were much faster than the ones carried out in toluene

alone. This observation was explained in terms of the formation of a CoTPP·DMF or CoTPP·pyridine complex that facilitated electron transfer in the coordinated oxygen. However, the reactions in DMF were still faster[129] than the ones in toluene/pyridine and this was explained in terms of a strong stabilizing effect of DMF on cobalt/dioxygen complexes. The effects of solvents and axial ligands were considered without reaching any definite conclusions and leaving this matter open to further reseach.[129]

Some other very interesting systems in which cobalt porphyrins are being used, are those involving multistep electron transfer, such as the one illustrated in Scheme 13 for the oxidation of 1,3-cyclohexadiene **[31]** to 1,4-diacetoxy-2-cyclohexene **[32]**.[130,131,132] This triple catalytic cycle proved to be efficient, particularly the electron transfer step from hydroquinone to the oxygen complexes [$(ML)_{ox}$], as well as the oxygen uptake by the cobalt porphyrin.[130,131,132]

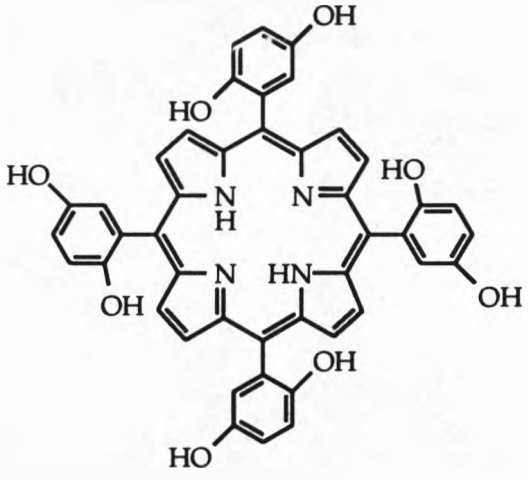


ML- Metal-containing porphyrin
HQ- Hydroquinone
BQ- Benzoquinone

Scheme 13.

In this triple catalytic system, selective interactions between each consecutive catalyst are involved and the reoxidation of hydroquinones (HQ) to benzoquinones (BQ) is a crucial step. This reoxidation takes place by reaction with a cobalt(III) complex that is produced by reaction of a cobalt(II) complex with dioxygen (Scheme 13). The benzoquinone can react with palladium(0) so as to be reduced back to the hydroquinone. The palladium(II) is an active catalyst for the 1,4-diacetoxylation of 1,3-dienes,

and, in the process, the palladium(II) is oxidised again back to palladium(0) (Scheme 13). In these systems the use of a porphyrin containing a hydroquinone substituent, such as the one shown in structure **[33]**, accelerated the electron transfer process, possibly due to *intra*molecular electron transfer from a hydroquinone unit to the oxidised cobalt atom *via* the π-electron system of the porphyrin.[131]



[33]

The overall aim of the project is to develop a catalytic system using cobalt complexes of different 5,10,15,20-*tetrakis*arylporphyrins and dioxygen. This will require improvements in syntheses and isolation of such porphyrins. The redox potentials of the cobalt complexes of these 5,10,15,20-*tetrakis*arylporphyrins will be measured in order to find a correlation between their structure and the redox potential and to get insight into the ability of the cobalt porphyrin to act as a catalyst for the oxidation of dihydroquinones to quinones with dioxygen. The ultimate aim will then be to incorporate this process as part of a catalytic cycle for the oxidation of methyl arenes to aldehydes with dioxygen since quinones are known to bring about this oxidation.

Chapter Two

Synthesis of 5,10,15,20-*tetrakisa*rylporphyrins

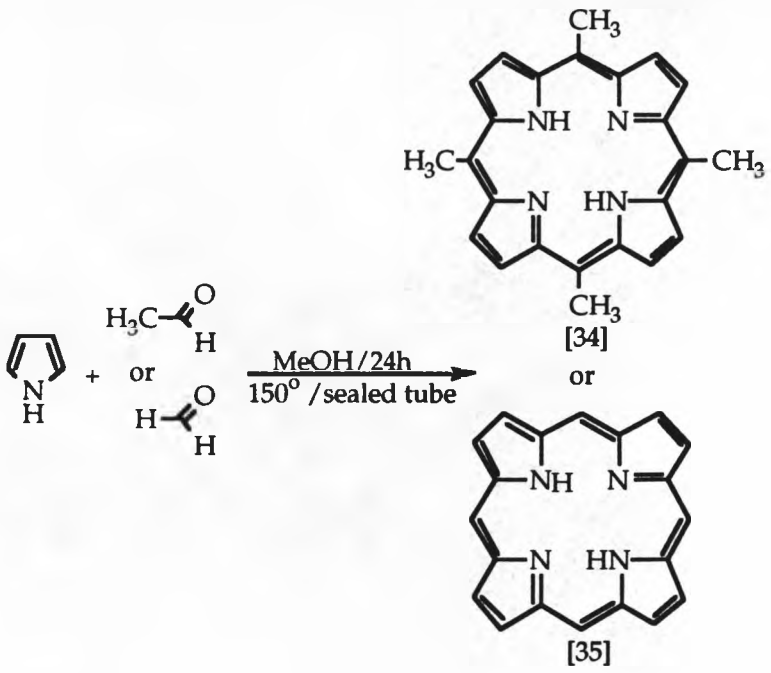
2. SYNTHESIS OF 5,10,15,20-*TETRAKIS*ARYLPORPHYRINS

2.1. First Methods of Synthesis: Historical Aspect

One important target for an organic chemist is to improve the synthesis of any compounds he works with. In the field of porphyrin chemistry there has been quite a remarkable evolution of the synthetic process over the years.

In 1935, *tetrakis*-alkylporphyrins were synthesised for the first time.[133] The formation of 5,10,15,20-*tetrakis*-methylporphyrin **[34]** and porphin **[2]** was observed after dissolving pyrrole in, respectively, a solution of gaseous acetaldehyde or formaldehyde in methanol and then heating the mixture in a sealed tube at 140-150°C for twentyfour hours. Yields were very low and, under such conditions, only a very limited number of such porphyrin structures could be synthesised (Scheme 14).[133,134,135,136]

An application of these reactions between pyrrole and aldehydes was later reported, in 1941, by the same research group, whereby pyrrole and benzaldehyde were condensed in pyridine solution, in a sealed tube at 170°C for fortyeight hours. However, the severe conditions still existed and only a limited number of porphyrins could be synthesised.[133,134,135,136]

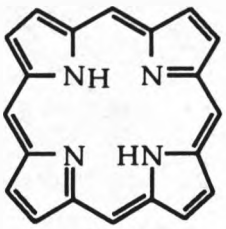


Scheme 14.

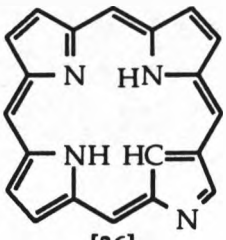
2.2. Detection of the Formation of Other Compounds During Porphyrin Synthesis

2.2.1. The Carboporphines

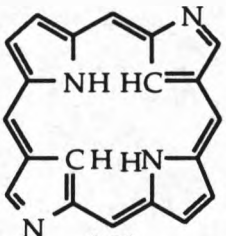
At around the same time as the work described in section 2.1, other research groups noticed the formation of isomers of porphyrins.[137,138,139] These isomers could be separated chromatographically[137] and some of the more probable structures proposed for these compounds are shown **[35 - 41]**.



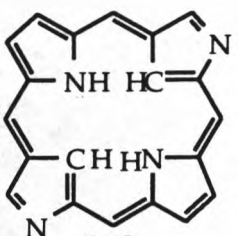
[35]



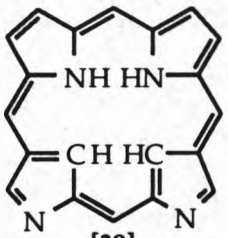
[36]



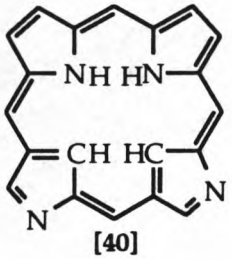
[37]



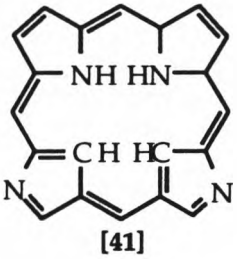
[38]



[39]



[40]

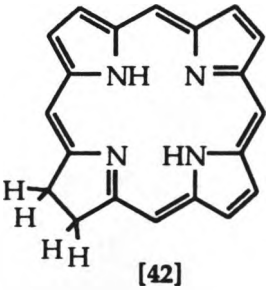


[41]

Since the α-carbon (or position 2) in the pyrrole ring has more nucleophilic character than the β-carbon, the α are more reactive towards electrophilic attack than are the β-positions. Because of this effect, the porphyrin with structure **[35]**, where only the α-positions of pyrrole have reacted, was assumed to be the main product, in agreement with the reactivity of pyrrole.[137] The probability that two β-carbons could suffer electrophilic attack to give porphyrins **[37- 41]** was expected to be much smaller than where only one has reacted, as illustrated by structure **[36]**. This prediction conforms with the low yields obtained for compounds identified as having structures **[37 - 41]**.[137] On further analysis of the compounds obtained during these syntheses, at least two substances appeared to be formed and were thought to have structures **[35- 36]**.

2.2.2. The Chlorins

Following the work discussed above, a report was published, in which two main products were described as being formed in sufficiently large amounts as to permit direct analysis.[138] The copper salts of both these major products were compared by uv/visible absorption spectroscopy and found to be different. One product was a porphyrin. Reduction of the zinc salt of the porphyrin compound with sodium converted it into the other and uv/visible absorption spectra of both compounds before and after hydrogenation showed that one of the two components was again partially converted into the other. These results were interpreted in terms of the reduced porphyrin derivative being the chlorin **[42]** and thus was proposed as a major product of the reaction between pyrrole and an aldehyde.

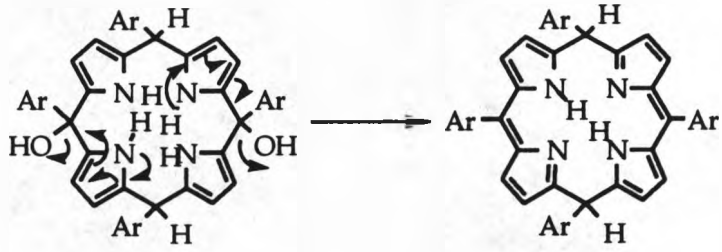


[42]

The chlorin structure was found to consist of a porphyrinic system in which the β-positions of one of the pyrrole rings had been reduced **[42]**.[138] Later work followed in which the chlorin system was synthesised as a model for chlorophyll, a naturally occuring chlorin.[139]

Attempts have been made to explain the formation of chlorins during synthesis of porphyrins from pyrroles and aldehydes.[140,141,142] The formation of chlorin is proposed as being due to initial formation of a macrocycle having structure **[43]** which can lose two water molecules to

give the dihydroporphyrin **[44]**; this last compound either undergoes dehydrogenation to give porphyrin or rearranges to chlorin.[140]

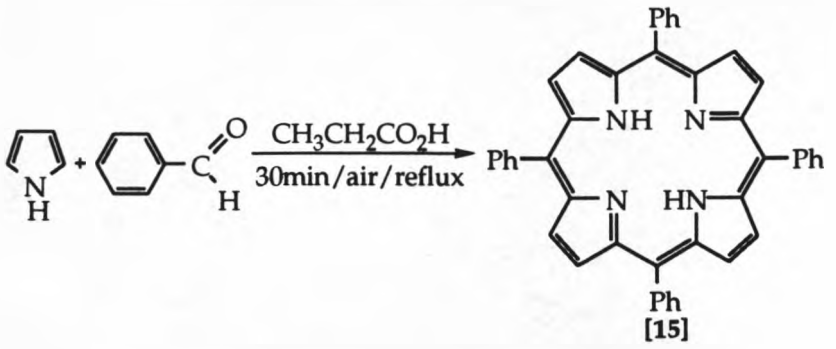


[43] **[44]**

It has been proposed also that chlorin formation might occur through further reduction of porphyrin.[141] In this case the formation of species **[43]** is not considered.[141]

2.3. Evolution of Methods for Porphyrin Synthesis: Historical

The next improvement in "one-pot" porphyrin synthesis came when benzaldehyde and pyrrole were allowed to react for 30 minutes in propionic acid in the presence of air. The yield of 5,10,15,20-*tetrakis*-phenylporphyrin **[15]**, was greatly improved from the earlier trace quantities to about 20% and, importantly, the technique could be applied to a larger range of aldehydes (Scheme 15).[143]



Scheme 15.

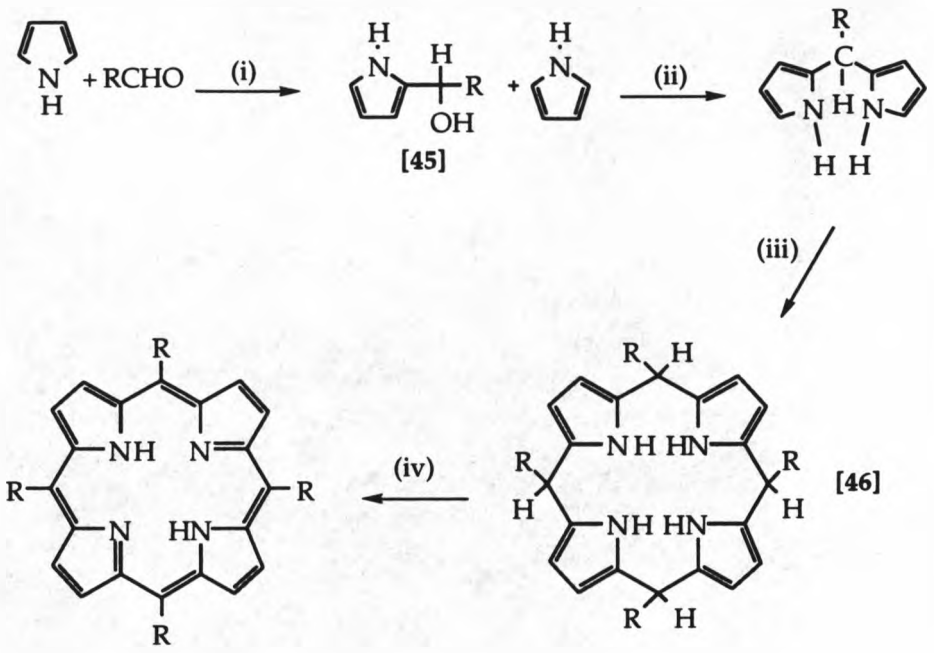
The importance of acidity, nature of the solvent, temperature, availability of oxygen and initial concentration of reagents was reported, as was the ease of purification for some porphyrins when using these new conditions.[143] It was proposed that formation of porphyrin proceeded through the four basic steps (i-iv) in Scheme 16:[144]

(i) initial formation of a carbinol **[45]**;

(ii) chain building by condensation of the carbinol with more pyrrole ;

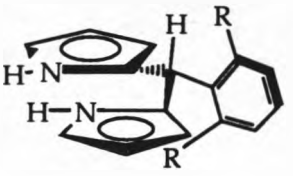
(iii) closure of the four-membered (pyrrollic) open-chain to form a porphyrinogen **[46]**;

(iv) oxidation (dehydrogenation) of the porphyrinogen to give the final porphyrin.



Scheme 16.

In 1985, separation of these "one-pot" syntheses into two separate stages was considered. The first stage aimed to synthesise only the porphyrinogen ring system [**46;** Scheme 16] and the second aimed to oxidise this up to the porphyrin stage.[145] The following year, research work was published in which this two-stage (or "two-pot") idea was developed.[146,147,148,149] The main objective was to synthesise a molecule such as 5,10,15,20-*tetrakis*(2',4',6'-trimethylphenyl)porphyrin as this is sterically a very demanding molecule because of the methyl groups in the *ortho* positions of the initial 2,4,6-trimethylbenzaldehyde. In the first chain step leading to porphyrinogen, one of the two methyl groups must face the incipient *meso*-proton, making the condensation step difficult. The other methyl group projects into the "groove" below the tetrahedral *meso*-carbon as depicted in Scheme 17. The ease of reaction depends on the size and shape of these incipient *meso*-groups.[149]

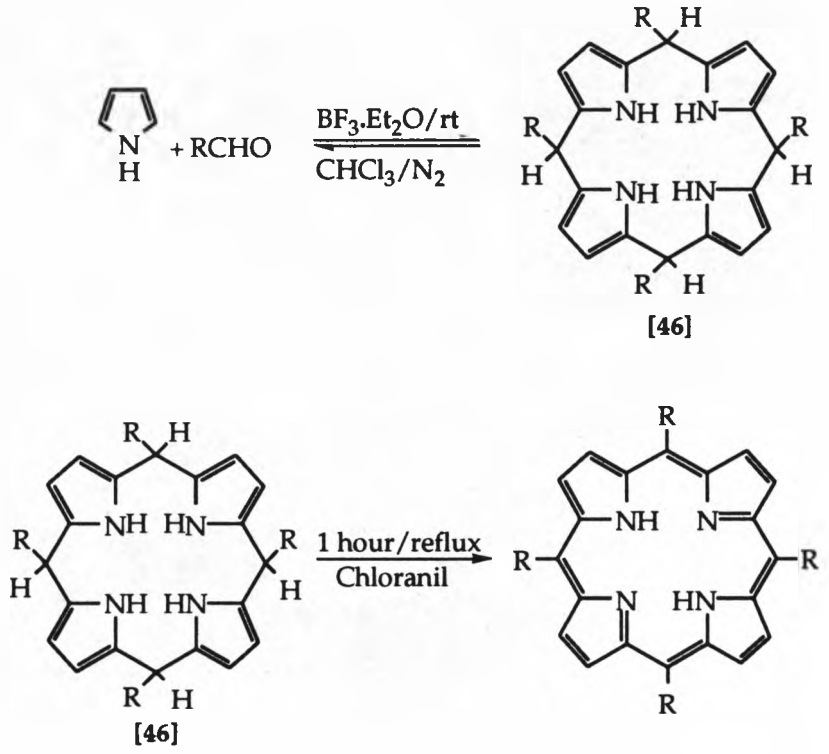


Scheme 17.

Previous attempts to synthesise this particular porphyrin had used forcing conditions to overcome the steric hindrance (170°C for 2-3 days, in the presence of metal salts) but yields were no more than 1-6%.[149] Aldehydes having similar *ortho*-groups suffer from the same limiting steric hindrances. The new "two-pot" approach allowed the preparation of porphyrins under very mild conditions, through catalysed condensation to the porphyrinogen stage.

To attain optimum yields, a long investigation was carried out by taking into account the dependence of the condensation step on the type of solvent, the presence of a co-catalyst (ethanol), the type of catalyst, the concentration of reagents and any steric effects of the reagents.[149] Amongst the catalysts tried, boron trifluoride etherate, $BF_3 \cdot Et_2O$ proved to be the best. It was found that chloroform gave better results than dichloromethane for all the aldehydes tested except for 2,6-dichlorobenzaldehyde and other benzaldehydes having electron-withdrawing substituents. The presence of ethanol in the chloroform was found to be the reason for the differences in reactivity of the two solvents. In fact, addition of the same percentage of ethanol to dichloromethane or taking it out of the chloroform resulted in similar results for the two solvents. The ethanol acts as a co-catalyst, with the boron trifluoride etherate. When only boron trifluoride etherate is present, the binding of aldehyde to boron trifluoride is too strong to allow reaction to occur. This effect is not observed with 2,6-dichlorobenzaldehyde because of the electronegativity of the chlorine atom which weakens aldehyde-boron

trifluoride binding.[149] The presence of ethanol stops the binding from being so efficient because it itself binds to the boron trifluoride by displacing ether.



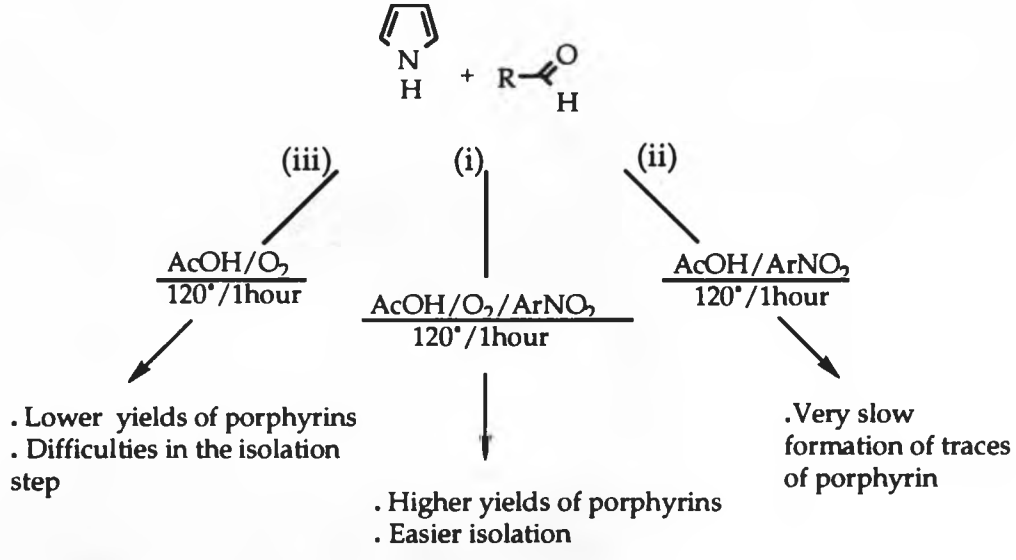
Scheme 18.

By using equimolar quantities of pyrrole and an aldehyde, RCHO, in chloroform with boron trifluoride etherate as catalyst under nitrogen at room temperature, porphyrinogens **[46]** were synthesised in a first condensation step. A second step was needed to oxidise the porphyrinogen to the porphyrin stage and, for this purpose, quinones such as 2,3,5,6-tetrachlorobenzoquinone were used. Yields reported for 5,10,15,20-*tetrakis*(2',4',6'-trimethoxyphenyl)porphyrin, the most investigated case, were around 30 to 40% although these were spectroscopic yields. When applying these same conditions to the synthesis of other porphyrins, the yields proved to be mostly good.[149] A separate research group not only confirmed the efficiency of this approach

but clarified a few more important factors, such as, the age of purchase and time of opening the bottle of boron trifluoride etherate catalyst, the amount of oxidant used in the second step, and the reaction temperature used in the second step.[150] Boron trifluoride etherate looses its catalytic activity over time, being reduced to only 50% of its initial activity after some 3 months from the time of opening of a fresh bottle. The optimum amount of oxidant, 2,3,5,6-tetrachlorobenzoquinone, was found to be around 0.33 equivalents. The optimum temperature required to avoid oxidative degradation of the porphyrin during the oxidation step must be only enough to allow a gentle reflux.[150] Although this "two-pot" method proved to be efficient, especially for the synthesis of porphyrins with *ortho* substituents its high cost in the oxidation step, when using expensive quinones and the isolation problems of separating some porphyrins from other products were very soon reported.[151] Several different metal salts have been used in place of quinones, but without success.[151]

Parallel to this "two-pot" approach, the previous "one-pot" method was still being investigated because of both its attractiveness in being cheaper to perform and the ease of isolation of products, which often crystallise directly from the reaction medium.[151] An improvement of this "one-pot" method was reported whereby a mixture of acetic acid and nitrobenzene could be used in the presence of air.[151] It was noticed that the presence of air together with nitrobenzene [reaction (i); Scheme 19] was essential for this improved method since anaerobic experiments with nitrobenzene [reaction (ii); Scheme 19], gave very slow formation of porphyrin and very poor yields. On the other hand, the presence of air alone gave lower yields than when used together with nitrobenzene; the isolation procedure was more difficult because most porphyrins did not crystallise directly from the reaction medium [reaction (iii); Scheme 19].[151] Further investigations with substituted nitrobenzenes[152] showed that

other nitro compounds could improve yields over those found for nitrobenzene itself and also helped crystallisation from the reaction medium. Hammet constants for various substituted nitrobenzenes appeared to correlate linearly with isolated yield of porphyrin. To explain these results further studies are being undertaken.[189] Using this new discovery of the effects of nitrobenzene derivatives in the synthesis of porphyrins, a larger number of 5,10,15,20-*tetrakis*arylporphyrins could be synthesised; their isolation being made easier by the direct crystallisation of the porphyrin from the reaction medium.



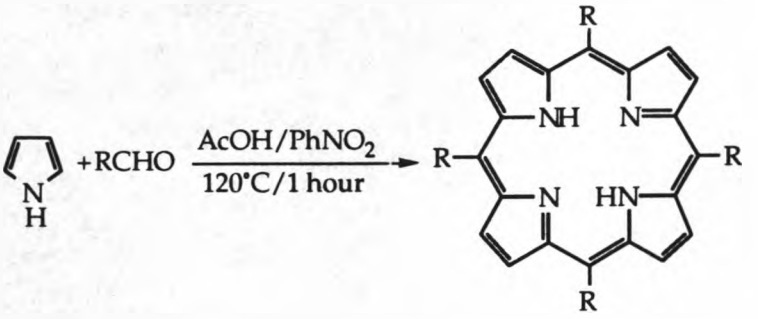
Scheme 19.

2.4. Synthesis of 5,10,15,20-*Tetrakis*arylporphyrins

2.4.1. The "One-Pot" Method

The advantages of ease of isolation when using the "one-pot" method was attractive for the present research and it was decided to

synthesise some *tetrakis*arylporphyrins using this "one-pot" method with nitrobenzene as an oxidative additive (Scheme 20). In all cases, equimolar amounts of pyrrole and the required aromatic aldehyde were added to a mixture of acetic acid and nitrobenzene, which was preheated to 120°C in the presence of air (Scheme 20). Table 1 shows the aldehydes used and yields of the corresponding porphyrins obtained.



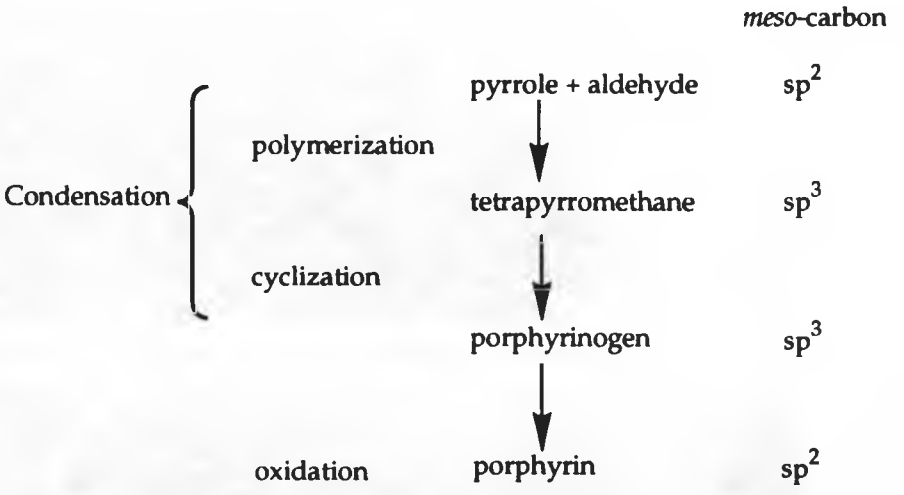
Scheme 20.

Table 1. Yields of porphyrins synthesised by the "one-pot" method

Starting Aldehyde	Porphyrin yield %
Benzaldehyde	20
4–Methoxybenzaldehyde	21
3–Methoxybenzaldehyde	18[b]
3,4-Dimethoxybenzaldehyde	18[a]
3,4-Methylenedioxybenzaldehyde	27[a]
4–Methylthiobenzaldehyde	36.6
4–Biphenylcarboxaldehyde	40
3,5-Di-*tert*–butyl-4-hydroxybenzaldehyde	43[a]
2,3,4,5,6-Pentafluorobenzaldehyde	13[b]
4–Chlorobenzaldehyde	37
3-Chlorobenzaldehyde	22
2,6-Dichlorobenzaldehyde	4

a - Steam distillation was required during work up
b - 4-Nitroaniline was used instead of nitrobenzene

When using 2,6-dichlorobenzaldehyde the yield of the corresponding porphyrin was only 4%. This was expected because the aldehyde has two chlorine atoms in the *ortho* positions which cause both kinetic and thermodynamic limitations to the condensation of aldehyde and pyrrole.[149] The two chlorine substituents cause the porphyrinogen intermediate to be so strained that its transition state energy of formation is much higher than usual.[151] During the synthesis, structural changes occur (Scheme 21), the incipient sp^2 *meso*-carbon going from sp^2 hybridization in the aldehyde to sp^3 during condensation to form the penultimate uncyclized tetrapyrromethane; this *meso*-carbon does not change its hybridization state on cyclisation to the porphyrinogen but the conformational effects of the aldehydic *ortho* substituents at this point are very important and they can prevent cyclisation from occurring efficiently. On the final oxidation step, the incipient *meso*-carbons on the porphyrinogen go to the actual sp^2 *meso*-state with relaxation into a planar porphyrin stucture (Scheme 21).[149]



Scheme 21.

The two *ortho* chlorine atoms entail steric hindrance to the formation of porphyrinogen because of the close proximity of one of the

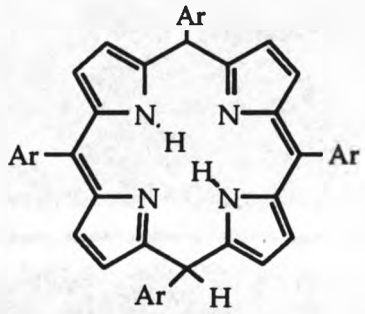
chlorines to the "*meso*"-proton in the porphyrinogen. Appropriate catalysis is needed with this aldehyde to overcome these structural effects.

With the other aldehydes listed in Table 1, the only one that could cause the same problems as the 2,6-dichlorobenzaldehyde would be 2,3,4,5-pentafluorobenzaldehyde because of the two fluorine atoms at the *ortho* positions. If the respective atomic radii of 0.99Å for Cl[153] and 0.64Å for F[153] are considered, then the fluorine would be expected to show smaller steric hindrance and therefore be less of a problem. Probably for these reasons, yields of porphyrins obtained from the two aldehydes are considerably different being 4% for the 2,6-dichlorobenzaldehyde as against 13% for the *penta*-fluorobenzaldehyde case.

With benzaldehydes such as the 2,3,4,5-pentafluoro and 3-methoxy substituted ones, the use of nitroaniline in place of nitrobenzene was imperative for obtaining yields better than the traces of porphyrin found when using nitrobenzene itself.

Studies concerning the influence of various nitrobenzene derivatives on these reactions are still under investigation and it is hoped they will explain some of the anomalous results. Nitrobenzene derivatives are known oxidants.[154,155,156,157] However, in these porphyrin syntheses the nitro additives appear only to be really effective in conjunction with oxygen. With only oxygen or nitrobenzene as oxidant alone, yields of porphyrin fall considerably. The redox potential of the nitrobenzene derivatives appear to correlate with porphyrin yields[152] and this might explain why nitroaniline proved successful in those cases in which nitrobenzene did not because the redox potential for nitroaniline in acidic conditions is greater than that of nitrobenzene.[189] A higher potential seems to be needed during the oxidation step of some porphyrins (Scheme 21). With 2,3,4,5-pentafluorobenzaldehyde and 3-methoxybenzaldehyde, there is not the *ortho* steric hindrance present as

with the *ortho* substituted aldehydes such as 2,6-dichlorobenzaldehyde. Two other possible explanations for general poor yields in "one-pot" porphyrin synthesis may be found in difficulties in the condensation step and/or in oxidations steps. The first is unlikely because starting materials are not recovered, only polymerisation products being formed thereby indicating that condensation always occurs. The second explanation (the existence of problems in the oxidation step) may be a real cause because nitroaniline appears to solve the problem. The passage of the sp^3 *"meso"* carbons in porphyrinogen to sp^2 *meso* in the porphyrin seems to be the difficult step for some porphyrins. The porphyrinogens from some aldehydes appear to be quite difficult to oxidise. Further, it could be that other intermediates between the porphyrinogen stage and porphyrin formation (such as the phlorin **[47]** which has been reported as being quite stable)[158,159] may be a problem. The activation energy needed to oxidise whatever intermediate (phlorin, chlorin) is causing the difficulty must be too high to be overcome by nitrobenzene but the greater oxidation potential of nitroaniline when under acidic conditions[189] is enough to solve the problem.



[47]

The possibility of getting a better yield using nitrobenzene instead of nitroaniline by changing other reaction parameters such as the ratio between carboxylic acid and nitrobenzene or temperature is not excluded.

Presumably these new conditions could be simply providing a better oxidising medium.

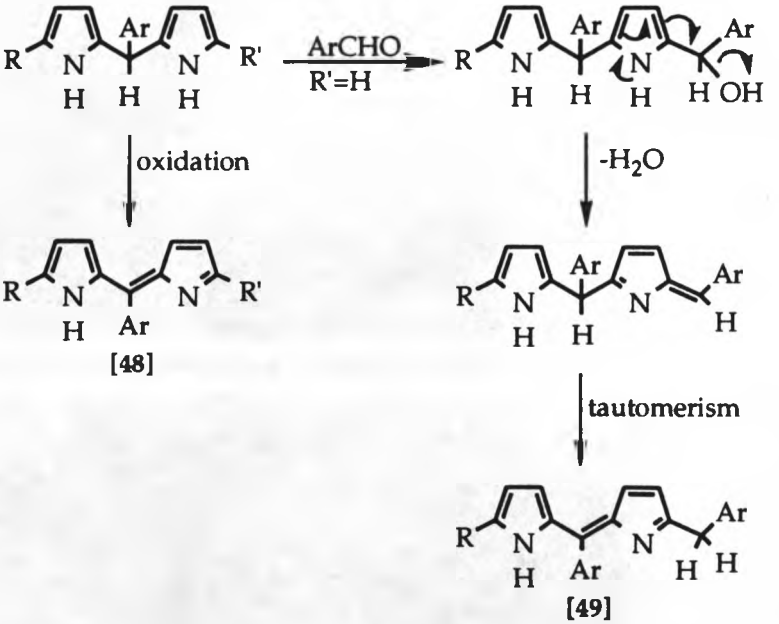
In respect to the ease of isolation of the product porphyrins, the benzaldehydes having the following substituents: 2,6-dichloro, 4-methylsulphide, 4-phenyl, 4-chloro, 3-chloro, hydrogen, and 4-methoxy, all gave porphyrin which crystallised out of the reaction medium and could be purified by washing well with methanol; there was little porphyrin remaining in the filtrate. Although these porphyrins could be recrystallized, for most practical purposes it was unnecessary because direct analysis of the crystals as obtained after methanol washing showed them to be pure and no chlorin could be detected by either uv/visible or ^{1}H-nmr spectroscopy.

With benzaldehydes having the substituents, 3,4-methylenedioxy, 3,4-dimethoxy and 3,5-di-*tert*-butyl-4-hydroxy, yields were quite good but nitrobenzene did not promote crystallisation direct from the reaction medium, thereby making their isolation more troublesome. In these cases, steam distillation was used to remove the nitrobenzene, followed by chromatography on alumina [grade II] followed by recrystallisation. Attempts to repeat these reactions using nitroaniline were not made although it could be desirable, for it might simplify the isolation step in that the nitroaniline could be extracted into strong acid thereby, avoiding the tedious removal of the nitrobenzene by steam distillation.

2.4.2. *The "Two-Pot" Method*

As an alternative to the "one-pot" procedure, it was decided to examine the use of the "two-pot" technique in order to improve some of the yields with aldehydes such as 2,6-dichlorobenzaldehyde and also to synthesise some new structures.[145,146,147,148,149] Following the literature

method already discussed in section 2.3, equimolar amounts of pyrrole and the requisite benzaldehyde were mixed in chloroform, which had been purged with nitrogen. To this solution was added fresh boron trifluoride etherate in a catalytic amount. The mixture was left to cyclize, under nitrogen, in the dark. The formation of porphyrinogen was monitored at regular intervals by removing small aliquots of the solution, oxidising each with excess of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and measuring the height of the resulting Soret band in the visible spectrum. The reaction was stopped when the height of the Soret peak reached a maximum. The syntheses were effected without the use of any triethyl orthoacetate or any other water scavenger, since the presence of the former sometimes stopped the cyclisation from occurring, possibly due to the formation of dipyrrin as the main product [**48**; Scheme 22]. Dipyrrins [**48, 49**] can be formed at any stage of the polymerisation as illustrated in Scheme 22. Their formation may be due to early oxidation of the growing open chain or by loss of water, followed by tautomerisation [**49**].



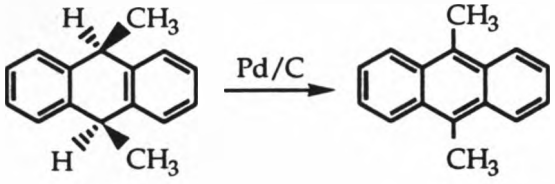
Scheme 22.

Although it is not known what effect triethyl orthoacetate had on these syntheses, it appears to have acted as a catalyst for the formation of dipyrrins. When used as a water scavenger, formation of porphyrin was always detected in the first 5 minutes of the condensation step but this was followed by complete disappearance of the Soret band and the appearance of a new, broad band at 450-500nm. This band is described in the literature as being due to dipyrrin species [**48, 49**; Scheme 22].[149]

In the syntheses described here, optimum reaction times to porphyrinogen were all about three hours. After the condensation step, the porphyrinogen was oxidised to porphyrin with chloranil which was added directly to the reaction solution; the mixture was then gently refluxed for one hour. Early in this work there were problems in the isolation step because of contamination of the product by the hydroquinone. Some yields of porphyrin, even after chromatography, were greater than theoretical. When the chromatographed materials were stirred with aqueous potassium hydroxide solution any existing hydroquinone which would be soluble in the potassium hydroxide aqueous phase, was removed and the yields decreased considerably to more like those expected. During these syntheses, the amount of quinone required for oxidation of porphyrinogen was kept within values considered ideal in other research publications, that is, the use of 0.33 equivalents.[150] For large-scale reactions, the use of quinones could become a limitation to the procedure because of the cost, and isolation difficulties, so it was necessary to find a more suitable oxidant. Investigation of the literature for possible oxidants which could be used in this synthesis was instigated. It was decided also to search for a new cheap oxidant, with the synthesis of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin being used as the model reaction.

2.4.2.1 Improvements to the "two-pot" oxidation step

Catalytic dehydrogenation of hydroaromatic compounds is a classic method of synthesis of polycyclic aromatic molecules from their perhydro precursors. One of the most generally used and satisfactory agents is the commercially available hydrogenation catalyst, palladium-on-charcoal, for which many examples can be found in the literature as, for instance, with the dehydrogenation of *cis*-9,10-dimethyl-9,10-dihydroanthracene **[50]** to give 9,10-dimethylanthracene **[51;** Scheme 23].[160]



[50] **[51]**

Scheme 23.

In an attempt to perform a similar oxidation of the porphyrinogen of 5,10,15,20-*tetrakis*(2',5'-dichlorophenyl)porphyrin with palladium-on-charcoal, the catalyst was added to a porphyrinogen solution prepared as before and left overnight, with strong agitation, at room temperature. No attempt was made to purify the traces of porphyrin indicated as having been formed by the height of the Soret band. Since the main objective was to simplify the isolation by improving the condensation step and not to turn the synthesis into a more troublesome method than it already proved to be, it was decided to try a different oxidant.

The next attempt was to attempt the oxidation with superoxide ion in the form of potassium superoxide. Superoxide can function either as an oxidising agent or as a reducing agent, as shown in reactions (i) and (ii) of Scheme 24.[161,162,163] As an oxidising agent [reaction (i); Scheme 24], the

superoxide ion picks up an electron and two protons to give hydrogen peroxide; this is its dominant reaction. When acting as a reductant, superoxide is weak.[164] Most of the reactions of superoxide are simple one-electron reductions [reaction (ii); Scheme 24] which occur with great rapidity.

$$O_2^{-\bullet} + 2H^+ + e^- \longrightarrow H_2O_2 \qquad \text{(i)}$$

$$O_2^{-\bullet} \longrightarrow O_2 + e^- \qquad \text{(ii)}$$

Scheme 24.

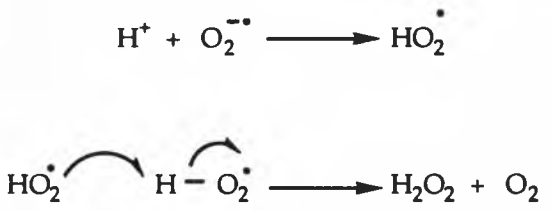
There are a few examples in the literature of the use of superoxide as an *oxidant,* as in the oxidation of ascorbic acid and the oxidation of NADH to NAD.[165] An example of its use as a *reductant* is the reduction of Copper(II) to Copper(I).[165] In the present system, it was needed to act as an oxidant, by dehydrogenating the porphyrinogen to porphyrin.

In initial reactions, four equivalents of potassium superoxide in water, with a phase transfer reagent (tetrabutylammonium perchlorate), were added directly to the porphyrinogen solution. The reaction was monitored by visible spectroscopy. After 2 hours no Soret band could be observed. This system appears not to work, possibly due to poor contact between the reagents. In later attempts, the solvent, dichloromethane, was removed from a small sample of porphyrinogen and a solution of potassium superoxide in acetic acid was added to the residue. After two hours at room temperature, the visible spectrum revealed a clear Soret band and reaction was complete. On repetition on a large scale, the large amount of potassium superoxide needed caused a violent reaction as soon as it was added to the acetic acid. Clearly, on the larger scale this exothermic reaction would be difficult to control. Scheme 25 shows the

likely cause of this reaction of protons with superoxide to evolve oxygen and form hydrogen peroxide at the same time.

Scheme 25.

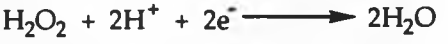
In fact it has been shown by electrochemical studies that the primary step with potassium superoxide involves abstraction of a proton from the substrate by the superoxide to give the hydroperoxide radical $HO_2^{\cdot}$ followed by dismutation to hydrogen peroxide and dioxygen (Scheme 26).[165]



Scheme 26.

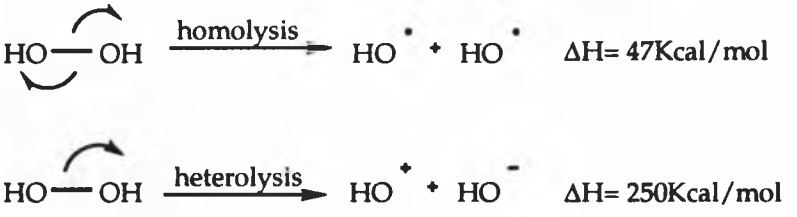
The reaction of potassium superoxide and acetic acid is highly exothermic making it dangerous to perform on a large scale. Obviously, the solvent was not the right choice for such an experiment but the experiments led to the idea that, because the reaction of superoxide with protons was very fast, probably the superoxide was not the principal oxidant of the porphyrinogen but was more likely to be the precursor of hydrogen peroxide, which was the principal oxidant. It was decided to examine the use of hydrogen peroxide alone for oxidizing the first stage porphyrinogen to porphyrin.

The hydrogen peroxide molecule is a powerful oxidant as can be seen from its redox potential of E= 1.76 volts (Scheme 27):



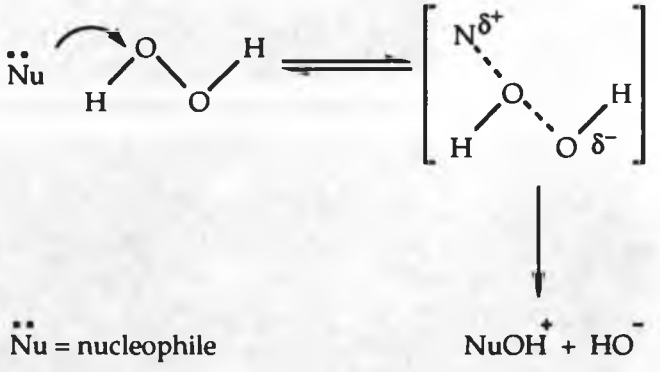
Scheme 27.

The hydrogen peroxide molecule can be cleaved, by a homolytic or heterolytic process (Scheme 28):[166]



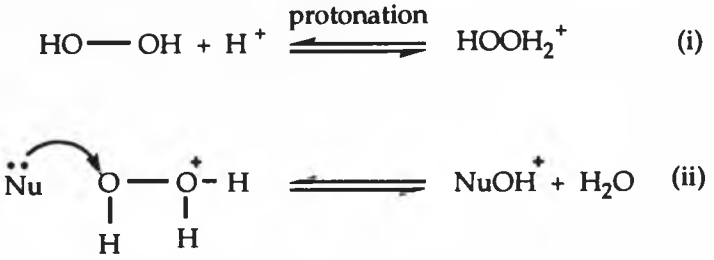
Scheme 28.

Heterolytic cleavage as a unimolecular process is highly disfavoured with respect to homolysis by more than 200kcal/mol due to the endothermic charge development associated with electron deficient oxygen formation (Scheme 28). On the other hand, heterolytic cleavage as part of a bimolecular process (Scheme 29) can be dominant:[166]



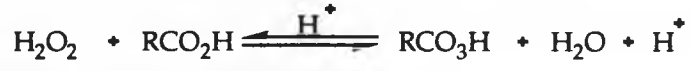
Scheme 29.

To act as an electrophile hydrogen peroxide must interact with a reductant having an available pair of electrons. The highest occupied molecular orbital (HOMO) of the nucleophile interacts with the lowest unoccupied molecular orbital (LUMO) of hydrogen peroxide (the sigma antibonding (σ^*) orbital of the O-O bond) to form a new bond.[166] This reaction can be catalysed by strong acid, which increases the rate of reaction with a nucleophile, [reactions (i) and (ii); Scheme 30].



Scheme 30.

Water as a leaving group is much better than HO^-. One of the most effective and frequently used ways of activating hydrogen peroxide for heterolytic cleavage is through the generation of peroxyacids. The reaction of carboxylic acids with aqueous hydrogen peroxide (30-90% w/v) in the presence of a strong acid catalyst gives a peroxycarboxylic acid (Scheme 31).[166]

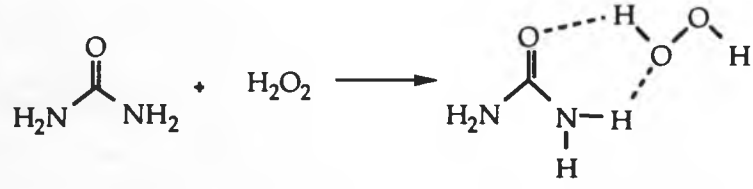


Scheme 31.

In the literature, it has been reported that hydrogen peroxide attacks the porphyrin ring in both *meso*- and β–positions.[167,168,169,170] However, the conditions under which this electrophilic attack occurs are very specific. In the reported cases, such oxidations appear only with metalloporphyrins in the presence of strong bases or with free base

porphyrins in the presence of strong acids. The metal complexes were reported to be more susceptible to electrophilic attack and this effect was explained as being due to dπ-pπ orbital overlap between the metal and the porphyrinic nitrogen atoms to stabilise an otherwise de-aromatised transition state.[168] It was also clear that attack occurring at the β– or *meso*-positions depends on the structure of the porphyrin and reaction conditions.[167,168,169,170] For present requirements, no metals were present and the porphyrinogen solution was not strongly acidic and, therefore, it was decided to test the use of hydrogen peroxide as an oxidant.

The first attempt used a hydrogen peroxide adduct that could dissolve easily in the solvent system. The advantage of the use of an adduct is its potential to release hydrogen peroxide in either an anhydrous or aqueous solution.[171] Amine oxides, amides, phosphine oxides and others compounds are reported to form adducts with hydrogen peroxide.[172,173,174,175] The most widely available stable hydrogen peroxide adduct is urea-hydrogen peroxide. In this, hydrogen bonding occurs between the peroxide oxygen and one of the urea hydrogen atoms (Scheme 32).



Scheme 32.

For the present experiments, the solvent was removed from the first stage porphyrinogen solution which had been neutralised previously with triethylamine, and a mixture of the urea/hydrogen peroxide adduct with dichloromethane was added to the porphyrinogen residue. The mixture was left at 55°C for two hours after which oxidation had

proceeded but was far from complete as shown by testing a sample with DDQ and comparing the height of the Soret band for the porphyrin after hydrogen peroxide and then after DDQ oxidation. The hydrogen peroxide method appeared not to be working efficiently. It was believed that contact between the hydrogen peroxide in the adduct and porphyrinogen in solution was not good enough for the reaction to occur efficiently, maybe because the urea adduct was only partially soluble in dichloromethane. The next attempt was to use free hydrogen peroxide directly by dissolving it in acetic acid. Dissolution of hydrogen peroxide in acetic acid might lead to reactions (i) and (ii) of Scheme 31 but, in the absence of strong acid, the equilibrium concentration of peroxyacetic acid would be low. Nevertheless, the hydrogen peroxide might react through formation of peroxyacid species or by providing HO· radicals.

As described above, the boron trifluoride remaining in the porphyrinogen solution was neutralised with triethylamine and the solvents were evaporated. A freshly prepared solution of aqueous hydrogen peroxide (35%w/w) in acetic acid was added to the porphyrinogen residue which dissolved completely. After one hour at room temperature, formation of porphyrin was complete as indicated by the height of the Soret band. Isolation of the product and purification by chromatography gave a 20% yield of pure 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, far better than any previous attempts at its synthesis. Attempts to repeat the experiment with other porphyrins did not work. Analysing the two reaction steps, it was found that, in the first step (condensation), formation of the porphyrinogen was occurring normally because oxidation of a small sample with DDQ gave porphyrin. Analysing the second step (oxidation) there was found to be a problem with the removal of the solvents from the first stage. The porphyrinogen of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin used for the trial

experiments is probably quite stable and survived removal of solvents and thus gave no problem. With other porphyrins, such as 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin, the porphyrinogen appeared to be degraded during removal of solvent, decreasing the yield of porphyrin obtainable by a considerable amount. In fact, oxidation with DDQ of the porphyrinogen residue obtained after removal of solvent from an attempted synthesis of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl) porphyrin revealed a considerable drop in yield compared with DDQ oxidation before removal of solvent, thus confirming the suspicion that the act of concentrating the porphyrinogen solution had led to its destruction.

To further confirm these results, it was decided to perform reactions without previously removing the solvent from the porphyrinogen stage, viz.,by addition of hydrogen peroxide in acetic acid to the neutralised porphyrinogen solution and then leaving it for one hour at room temperature. This procedure proved to be the most successful. The yields obtained using this new procedure are shown in table 2.

Table 2. Yields of 5,10,15,20-*tetrakis*arylporphyrins using the two-pot method with H_2O_2 as oxidant

Starting Aldehyde	Porphyrin Yield (%)
Benzaldehyde	14
4-Methoxybenzaldehyde	21
3,4-Dimethoxybenzaldehyde	23
3,4,5-Trimethoxybenzaldehyde	30
2,4,5-Trimethoxybenzaldehyde	17
3,4-Methylenedioxybenzaldehyde	20
4-Chlorobenzaldehyde	27
3-Chlorobenzaldehyde	19
2,6-Dichlorobenzaldehyde	20
2,3,4,5,6-Pentafluorobenzaldehyde	0
4-Biphenylcarboxaldehyde	12
4-Methylthiobenzaldehyde	39.5[a]

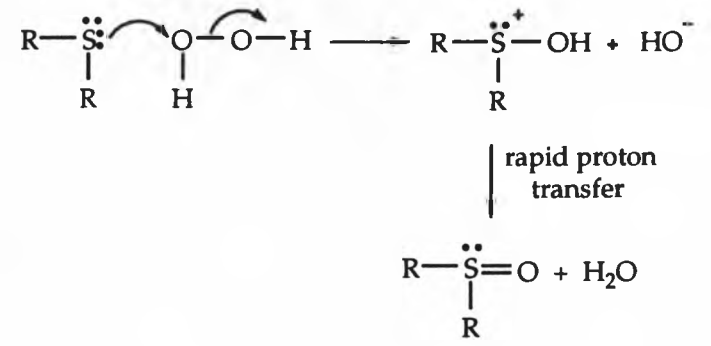
a - Isolated as the sulphone

Although almost all the above oxidations were efficient, even so, the synthesis of 5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluorophenyl) porphyrin using the two-step technique was not successful, giving no porphyrinic material. It is likely that this is mainly a question of obtaining the right conditions for condensation to porphyrinogen and not a problem with the oxidant. No attempts were made to find the right conditions for the synthesis of this porphyrin, using the "two-pot" technique because it was readily obtainable by the "one-pot" approach.

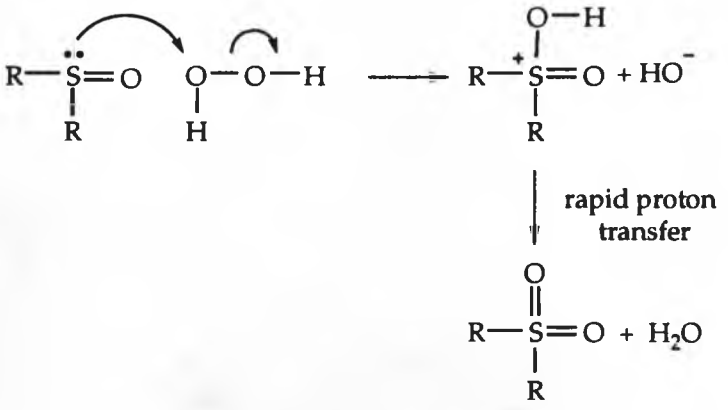
2.4.2.2. Synthesis of 5,10,15,20-*tetrakis*(4'-methylthiophenyl)porphyrin

In the synthesis of 5,10,15,20-*tetrakis*(4'-methylthiophenyl) porphyrin, using the "two-pot" procedure with hydrogen peroxide as the oxidant in the second step, it was of some concern that hydrogen peroxide

is known to oxidise sulphides to sulphoxides (Scheme 33) through nucleophilic attack of the sulphide by the oxygen of the peroxide, followed by rapid proton transfer to form the sulphoxide. Sulphones may also be formed by the same kind of nucleophilic attack a second time (Scheme 34) but this step is normally much slower than the first because a sulphoxide is a poorer nucleophile than a sulphide:[176]

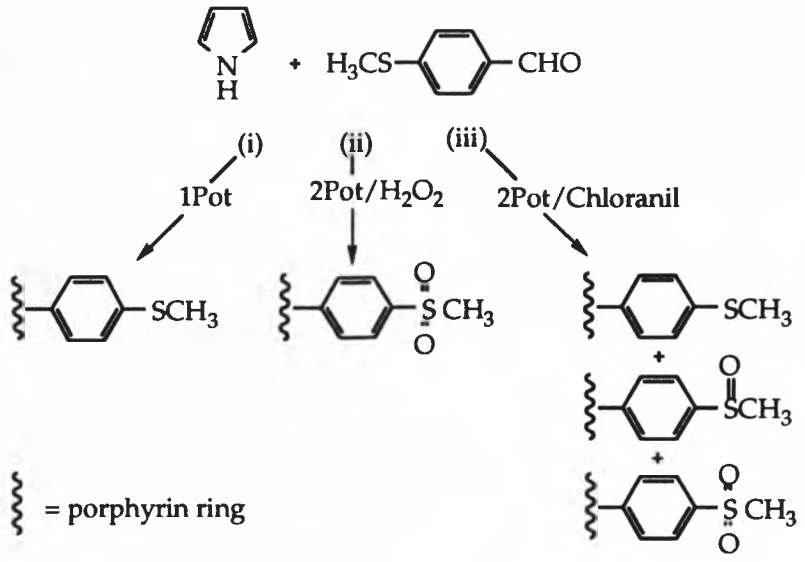


Scheme 33.



Scheme 34.

Therefore, it was decided to perform this reaction using either hydrogen peroxide or chloranil in the oxidation step; chloranil has a redox potential of $^{\circ}E$= 0.27volts, which is much lower than the 1.76volts of hydrogen peroxide. The reaction was also carried out with the "one-pot" procedure using nitrobenzene as oxidant (Table 1).



Scheme 35.

With the use of the "two-pot" method and hydrogen peroxide, a compound was obtained which proved to be pure 5,10,15,20-*tetrakis*(4'-methylsulphonylphenyl)porphyrin, confirmed through ^{1}H-nmr and mass spectra and microanalysis [reaction (ii); Scheme 35]. In the presence of hydrogen peroxide sulphides, are oxidised very slowly to give sulphoxides and eventually sulphones. The initially formed 5,10,15,20-tetrakis(4'-methylthiophenyl)porphyrin must be much more nucleophilic at sulphur than other sulphides such as methylthiobenzene, which reacts only slowly.

With the use of the "one-pot" method and nitrobenzene the product was found to be the required 5,10,15,20-*tetrakis*(4'-methylthiophenyl)porphyrin [reaction (i); Scheme 35]. The nitrobenzene was not able to effect further oxidation of the sulphide.

The compound obtained using the "two-pot" method with chloranil as the oxidizing agent proved to be a mixture of three compounds, the sulphone, and sulphoxide described above and some residual sulphide [reaction (iii); Scheme 35], as revealed by ^{1}H-nmr and

mass spectroscopy. After reacting this mixture with hydrogen peroxide, ^{1}H-nmr spectroscopy showed that, apart from the presence of very small amounts of residual sulphide and sulphoxide, the mixture had been transformed almost entirely to the sulphone obtained earlier during the reaction of porphyrinogen with hydrogen peroxide. Because the 5,10,15,20-*tetrakis*(4'-methylthiophenyl)porphyrin could be made in adequate yield by the one-pot method with nitrobenzene, no attempts were made to discover whether the reaction with hydrogen peroxide could be stopped before oxidation to sulphoxide or sulphone.

2.4.3. Combination of Two Methods of Synthesis

Parallel to the experiments with hydrogen peroxide as oxidant, another method was tried for the oxidation step that could combine the "two-pot" and the "one-pot" syntheses. The idea was to carry out the condensation step to porphyrinogen with reaction conditions similar to those of the "two-pot" method[146,147,148,149] but to oxidise the porphyrinogen to porphyrin using reaction conditions of the "one-pot" method, in order to take advantage of the ease of isolation of products when using this last approach.[151,152]

After the condensation step to porphyrinogen, the resulting solution was added dropwise *to* a mixture of nitrobenzene and acetic acid held at 120°C. During this *slow* addition, the solvent from the condensation step was distilled off continuously as it reached the hot mixture of nitrobenzene and acetic acid. At the end of the addition, the hot mixture was left overnight to cool to room temperature when, hopefully, the required porphyrin would precipitate out. Table 3 gives the results obtained with 8 different porphyrins, compared with the results obtained when using the "one-pot" and the "two-pot" reactions separately.

Table 3. Yields of *tetrakis*-arylporphyrins using: (a) "one-pot", (b) "two-pot" and, (c) combined methods

Starting Aldehyde	One-Pot [$PhNO_2$] Yield (%)	Two-Pot [H_2O_2] Yield (%)	Combined method [$RCO_2H/PhNO_2$] Yield[c] (%)
Benzaldehyde	18	14	6.2 (1.4)
4-Methoxybenzaldehyde	21	21	25 (11)
3,4-Dimethoxybenzaldehyde	18	23	25 (0)
3,4-Methylenedioxybenzaldehyde	27	20	18 (14)
4-Chlorobenzaldehyde	37.4	27	13 (4)
3-Chlorobenzaldehyde	30	19	22 (0)
2,6-Dichlorobenzaldehyde	4	20	5 (13)
4-Biphenylcarboxaldehyde	40	12	35 (0)
4-Methylthiobenzaldehyde	36.6	39.5[a]	b

a - Yield of the sulphone obtained, see discussion
b - A mixture of sulphide, sulphoxide and sulphone was obtained
c - Chlorin yields are shown in parenthesis

It was with disappointment that most of these porphyrins did not precipitate out and required the use of steam distillation to isolate them. Also, although yields were quite good, this separation step was an added problem. ^{1}H-nmr spectroscopic analysis of the porphyrins obtained in the combined method with acetic acid and nitrobenzene in the oxidation step, revealed the formation of relatively large quantities of the respective chlorin derivatives (Table 3). It appears that, for some porphyrins, the combined method is an efficient way of synthesising chlorins rather than porphyrins. Commonly, chlorins are made through reduction of porphyrin with diimide but this usually gives a mixture of chlorin, porphyrin and bacteriochlorin.[177] The combined procedure is particularly good for making the chlorin of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin for which only 5% of the porphyrin was

obtained as against 13% of the chlorin. More experiments need to be done in order to relate the factors involved but this was not relevant to the objectives of this present research and was not followed up.

2.4.4. Use of Statistical Methods to Improve Yields

Although yields of porphyrin had been greatly increased through use of the "two-pot" procedure, it was decided to attempt to improve yields from the "one-pot" procedure by optimising reaction conditions.

When investigating any reaction system, it is necessary to be aware of the number of variables that are applicable and which of them might be most important to the study for optimization of yields. Identification of possible variables is usually not too difficult but to know which are important is often more problematical. By using statistical methods (chemometrics) or simply by empirical studies, it is possible to identify the fundamental variables. Then, the target is to adjust the variables of the system until an ideal or optimum combination for best response yield is obtained. The problem lies in how many experiments to do. Usually the answer would be a lot! This is precisely where statistical methods such as the Simplex approach can be helpful.[178,179] A Simplex is a geometrical figure defined by a number of points in space equal to the number of dimensions of the space which defines the variables plus one.[178,179] The Simplex moves in a hyperspace defined by all the possible constraints of the system being studied.[178,179] For the present work, the objective was to force the Simplex to move in hyperspace to the region of optimum response (best yield) of the system. To move the Simplex across the hyperspace, it is necessary to follow certain defined rules which are explained in detail in Appendix I. This statistical approach is much less labour intensive for optimising yields than is the traditional approach of

designing a series of almost random experiments, hoping to hit the maximum.

For the present work with the "one-pot" method, the major variables were thought to be (a) the amount of carboxylic acid, (b) the amount of nitrobenzene and (c) the temperature of reaction. It was decided always to work under aerobic conditions in view of the known collective effect of oxygen and nitrobenzene, as discussed earlier. These variables implied a four dimensional Simplex (one for each parameter). The amounts of pyrrole and aldehyde were kept constant and equimolar. The Simplex approach was applied to three different porphyrins: 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin, 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, 5,10,15,20-*tetrakis*(4'-biphenyl)porphyrin. All three compounds normally crystallize from the reaction medium and the amount of porphyrin that did not do so could be estimated from the size of the Soret band. The crystalline and Soret yields were added to give a total yield. Tables 4, 5, and 6 show the results obtained in each set of experiments, together with the values used for the amounts of carboxylic acid, nitrobenzene and temperature (these were dictated by the Simplex as it developed). Acetic acid was not always used because of the high values required for the temperature as enforced by the movement of the Simplex. For example, for experiment P_5 of Table 4, a temperature of 150°C was required, well above the boiling point of acetic acid. Therefore, to attain these higher temperatures, a different carboxylic acid (valeric) was used with a five-carbon chain and boiling point of 185°C; the acidity of valeric acid was similar to that of acetic acid.

Table 4. Yields at each stage of the Simplex operations applied to the synthesis of 5,10,15,20-*tetrakis* (4'-methoxyphenyl)porphyrin[a]

Experiment Number	RCO_2H (ml)	$PhNO_2$ (ml)	Temperature (°C)	Yield (%)
P_1	45	5	141	59
P_2	35	15	150	54
P_3	45	15	120	33
P_4	25	20	145	57
P_5	35	30	150	52
P_6	50	12	148	55
P_7	31	18	148	57
P_8	41	12	143	54
P_9[c]	11	25	174	77
P_{10}[b]	12	30	160	57
P_{11}[d]	41	11	120	78

a - Time for all experiments was 1 hour
b - Simplex new direction
c - Simplex normal direction
d - Simplex contraction of P_8

During the movement of the Simplex for 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin (Table 4) it appeared that, at P_6, a plateau had been reached, since P_7, P_8 and P_{10} did not move the Simplex to any better response. However, by carrying out a vector contraction and then a vector extension (see Appendix I) to P_8 the Simplex moved to a better position on the hypersurface, as can be seen by an increase in yield. In P_9, the yield went up to 77% following the normal direction of P_8 and, in P_{11}, the yield reached 78%, by contracting P_8. When contracting P_8, the yield in P_{10} showed no great change. The experiments P_6-P_8 must have arrived at a "subsidiary" or "false" maximum below the true value. In conclusion, for this particular porphyrin, by use of the Simplex procedure, the yield was improved from 21% (Table 1) to a spectacular 78% (Table 4). It is worth noting that these same experimental conditions used for the synthesis of

5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin gave only traces of porphyrin. This is a general finding with all of the syntheses of the *tetrakis*arylporphyrins in this work, in that one set of optimum conditions for any one of them is not usually the optimum for the others and each synthesis needs to be examined for best yields.

Table 5. Yields at each stage of the Simplex operations for synthesis of 5,10,15,20-*tetrakis*(4'-biphenyl)porphyrin[a]

Experiment Number	RCO_2H (ml)	$PhNO_2$ (ml)	Temperature (°C)	Yield (%)
P_1	75	50	130	40
P_2	60	20	100	22
P_3	60	30	120	36
P_4	40	40	110	26
P_5	57	60	140	25
P_6	88	54	150	29
P_7	91	29	126	39
P_8	63	36	100	4.5
P_9	92	46	138	45
P_{10}	109	48	162	43
P_{11}[b]	84	42	129	46

a - Time for all experiments was 1 hour
b - Simplex contraction

With 5,10,15,20-*tetrakis*(4'-biphenyl)porphyrin the lowest yield obtained when using standard conditions was 40% (Table 1) but this could be improved to 46% (Table 5, P_{11}) through use of the Simplex method.

Table 6. Yields at each stage of the Simplex operations for the synthesis of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin[a]

Experiment Number	RCO_2H (ml)	$PhNO_2$ (ml)	Temperature (°C)	Yield (%)
P_1	75	50	120	37
P_2	60	20	100	26
P_3	60	30	130	42
P_4	40	40	110	28
P_5	56	60	140	42
P_6	88	53	150	33
P_7	61	46	160	34
P_8	30	37	136	54
P_9	36	39	111	33
P_{10}	21	61	128	14
P_{11}	36	67	159	15
P_{12}[b]	45	41	140	48
P_{13}[b]	52	43	141	56

a - Time for all experiments was 1 hour
b - Simplex contraction

With 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin, the yield could be improved from 37% when using standard conditions (Table 1) to 56% (P_{13}, Table 6) when using the Simplex. Again, the statistical method provided a significant improvement.

Finally, in Table 7, there is a comparison of the best yields obtained for these three porphyrins when using a standard set of experimental conditions against the yields obtained when using the Simplex statistical method. The Simplex approach proved to be extremely good for improving the yield of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, where an increase of 57% was observed. With the two other porphyrins, the increases were not so spectacular, being 19% for the 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin and 6% for the 5,10,15,20-*tetrakis*(4'-

byphenyl)porphyrin. In the three cases, more or less the same number of experiments was used. Depending on the first (random) set of experimental conditions (see appendix I), some porphyrins need more Simplex moves than others. It can be concluded that the statistical Simplex method helps to improve the yields of *tetrakis*arylporphyrins, sometimes impressively. The number of experiments needed to reach the best yields is really quite small and are easy to carry out.

Table 7. Comparison of the yields obtained for three different porphyrins starting from the aldehydes shown, when using standard conditions[a] and after application of the statistical Simplex method

Method	4-methoxy-benzaldehyde	4-chloro-benzaldehyde	4-biphenylcarboxaldehyde
RCOOH (75ml) $ArNO_2$ (50ml) T= 120°C	21% (Table 1)	37% (Table 1)	40%(Table1)
Simplex	78% (Table 4)	56% (Table 6)	46% (Table 5)

a - These "standard" conditions are indicated in column 1. The time for all reactions was 1hour as indicated in Table 1.

2.5. Conclusions

From the above results, it may be concluded that, in all three techniques used to synthesise porphyrins (the one-pot, the two-pot with hydrogen peroxide and the two-pot with acetic acid and nitrobenzene) there were always sensitive combinations of the reaction variables which seemed to depend particularly on the structure of the final porphyrin synthesised. Another observation from these syntheses is that the best conditions for the synthesis of one particular porphyrin structure are not

necessarily the best conditions for another. Having in mind these results and conclusions, it could be said that the success of these syntheses demands a search for a right balance between all factors involved plus a lot of care at the isolation and purification stage, and these must be individual for each porphyrin. The major factors leading to best yields are (i) an optimum yield of porphyrinogen and, (ii) its efficient oxidation to porphyrin. Deficient oxidation leads to chlorins being produced in greater or lesser amounts and these are often very difficult to separate from the desired porphyrin. The chlorins, although being dihydroporphyrins, are not easy to oxidise to the porphyrin stage. In the final analysis, there may not be much to choose between the various methods with regard to best yields for many porphyrins. In these cases, ease or convenience will dictate which method is used. For example, if the required pure porphyrin crystallises directly from the one-pot reaction medium in, say, 15% yield, that is an easier option than going through a two-step synthesis with attendant chromatography for final purification even to obtain, say, a 20% yield. In contrast, for a few hindered porphyrins such as the 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, the yield can improve dramatically by proper choice of reaction conditions. The work has discovered a cheap, clean oxidant in hydrogen peroxide for the second stage of a two-step synthesis. It is easier and much cheaper to use than the common DDQ, particularly on a large scale. Finally, it might be noted here that all of the yields reported are *isolated* ones unlike many reports in the literature which utilise the height of the Soret band as a measure of yield. From the experience gained here, yields based on a Soret band can be grossly at variance with actual yields and frequently prove over-optimistic by a large margin. This is probably because the Soret 'peak' represents not only the porphyrin required but also has contributions from isomers such as those shown in structures [36-42]. Also, the ε_{max} for the Soret band

appears to be measured infrequently but it is known from the present work that this varies, often considerably, from porphyrin to porphyrin. Spectroscopic yields based on measurements of the Soret band usually appear to relate to the ε_{max} for 5,10,15,20-*tetrakis*phenylporphyrin which has been reported widely in the literature.

Chapter Three

REDOX POTENTIALS OF COBALT *tetrakis*ARYLPORPHYRINS

3. REDOX POTENTIALS OF COBALT *tetrakis*ARYLPORPHYRINS

3.1 Introduction

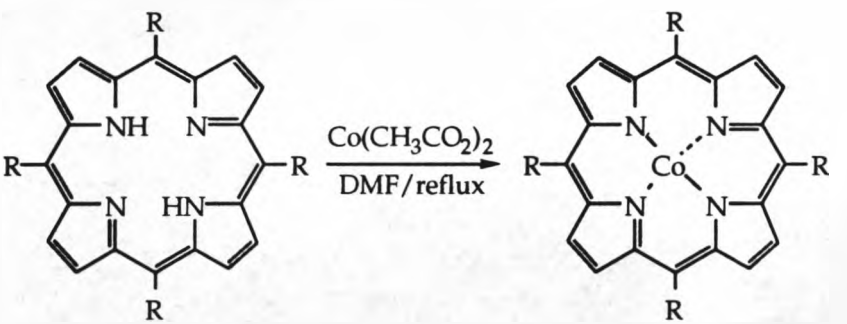
Much interest has been shown in the electrochemistry of porphyrins and metalloporphyrins from the standpoint of their redox properties which play a significant role in biological systems.[180,181,182] The interest for this present work into cobalt porphyrin complexes was to examine the redox stability of cobalt in a variety of porphyrin structures. The objective was to modify the redox behaviour of the cobalt complexes over a large range of potentials, through variation in the structures of the porphyrins. From these results it was hoped to be able to explain some of the catalytic activity of cobalt complexes, or at least to find some correlation between catalytic activity and redox potential. Electrochemical measurements on cobalt complexes of a range of 5,10,15,20-*tetrakis*arylporphyrins are presented and discussed in the next section.

3.2. Synthesis of Cobalt Complexes of 5,10,15,20-*tetrakis*Arylporphyrins

It has been reported that all metallations to give various types of *metallo*porphyrins can be classified into one of three general reaction types:[183] (i) reaction of a porphyrin with a metallic salt in an acidic medium; (ii) reaction of a porphyrin with a metallic salt in a basic medium; (iii) reaction of a porphyrin in a neutral medium with a specific organometallic compound.

It has been reported that analyses of all three methods reveal that reactions are slow and give low yields and, frequently, troublesome

purification. Most of the problems appear to be centred around the major difficulty of getting both the free base porphyrin and the metallic reagent simultaneously into the same solution under reactive conditions. In fact, most good solvents for porphyrins in their unionised forms are generally poor solvents for simple metallic ions and vice-versa. Focusing attention on this matter, published work has appeared on overcoming these problems.[183] The recommended best synthetic procedure consists of allowing the porphyrin and a divalent metal salt to react in refluxing dimethylformamide (DMF). At room temperature the solubility of most porphyrins is low but, at the reflux point, all the porphyrins tested were soluble at more than 1g/100ml.[183] Having this in mind it was decided to prepare the cobalt complexes of 5,10,15,20-*tetrakis*arylporphyrins by using this DMF technique with cobalt(II) acetate (Scheme 36).[183]



Scheme 36.

The 5,10,15,20-*tetrakis*arylporphyrins were dissolved in DMF and a requisite cobalt salt was added, the counter ion being usually acetate or chloride. The formation of the cobalt complexes was monitored by uv/visible spectroscopy. Just as with most metal complexes of this kind of compound, the cobalt complexes show different spectra from the free base and are very easy to identify. Figure 9 shows a comparison of the uv/visible spectrum of a free base porphyrin with that of the corresponding cobalt complex.

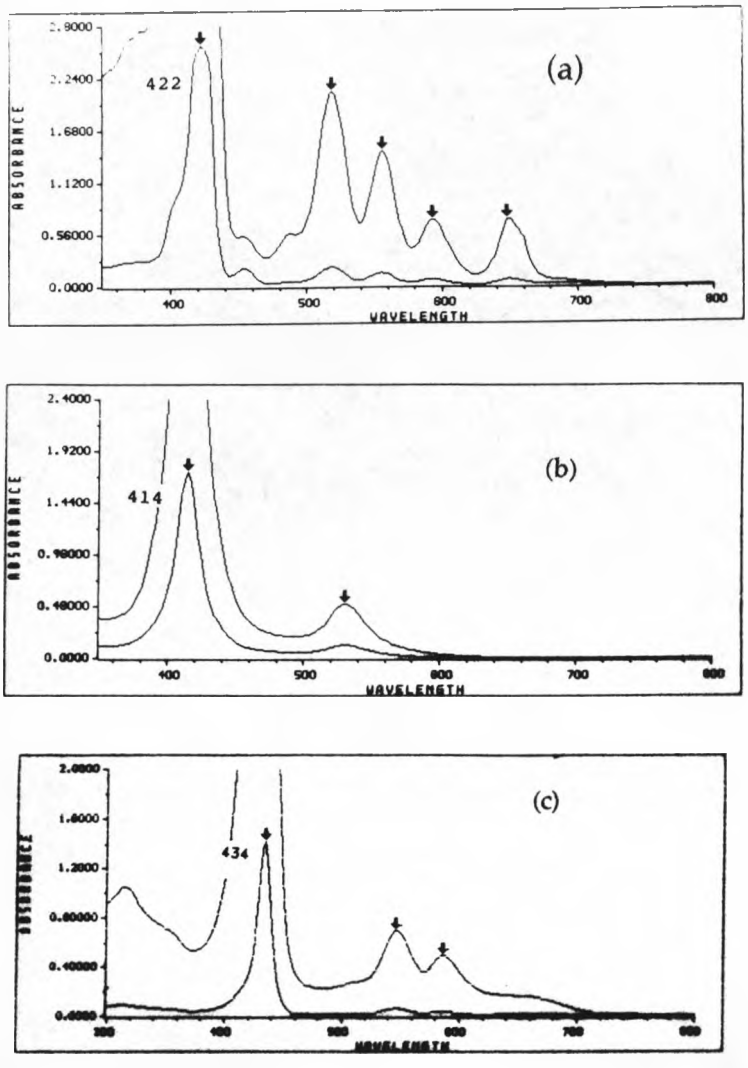


Figure 9. (a) Uv/visible spectrum of the free base porphyrin 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin. The Soret band appears at 422 nm and at longer wavelengths there are four Q bands, as indicated by arrows. (b) Uv/visible spectrum of the cobalt complex of the 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin showing the Soret band at 414 nm but only one Q band. This spectrum was taken after the isolation of the product, and not *during* metallation. (c) Uv/visible spectrum of the cobalt complex of the 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin during metallation. The Soret band appears at 434 nm and the Q band is split into two, indicative of a DMF/O_2/Co(III)porphyrin complex.[115] (The spectra were run at two different but unspecified concentration since only the λ_{max} values were important)

During these metallations, the Soret band shifts and the Q bands collapse from four to only one or two. As was discussed earlier in the

introduction to this thesis, the formation of a five co-ordinate complex of these cobalt complexes of porphyrins does not shift the Soret band but, reaction of a five co-ordinate complex with oxygen, does lead to a shift of the Soret band and the Q band splits into two.[115] During metallation this second effect was observed. After work up of the metalloporphyrins, a spectrum run in solvents such as chloroform and dichloromethane revealed a Soret band at shorter wavelength than the one observed during metallation and there was only one Q band instead of the two which had been detected before. This change in solvent to such as chloroform after removal of both DMF and dioxygen ligands, left the porphyrin/cobalt compound as a simpler planar tetradentate complex.

Most of the cobalt complexes synthesised here were formed within 5 to 8 hours. All of them were purified by column chromatography (silica gel or alumina oxide grade I). The yields were normally excellent and isolation easy.

Table 8 . Yields of Cobalt Complexes of 5,10,15,20-*Tetrakis*Arylporphyrins from corresponding free-base porphyrins

Cobalt Complex Aryl group[a]	Yield (%)	Cobalt Complex Aryl group[a]	Yield (%)
Phenyl	97	4-Biphenyl	87
4-Methoxyphenyl	89	4-Chlorophenyl	82
3-Methoxyphenyl	50	3-Chlorophenyl	82
3,4-Dimethoxyphenyl	62	2,6-Dichlorophenyl	73
2,4,5-Trimethoxyphenyl	41	2,3,4,5,6-Pentafluorphenyl	88
3,4,5-Trimethoxyphenyl	80	3,5-Di-tert-4-butylphenyl	43
3,4-Methylenedioxyphenyl	5.4	4-Methylthiophenyl	80

a - Aryl group in the 5,10,15,20-*tetrakis*arylporphyrin

Recrystallization is a very efficient method for the purification of the cobalt complexes but, for the purposes of cyclic voltammetry, it was not

adequate because only with very pure materials was it possible to obtain an acceptable cyclic voltagram. Therefore, chromatography was carried out and the yields given Table 8 correspond to those obtained *after* chromatography and crystallisation. The cobalt complex of 5,10,15,20-*tetrakis*(3',4'-methylenedioxyphenyl)porphyrin unusually was isolated consistently in very low yield . It was noticed that when carrying out the recrystallization, before chromatography, two different precipitates were formed, one very soluble in dichloromethane, the other quite insoluble. Uv/visible spectra obtained for both revealed that the first one was the expected cobalt(II) complex but the second one had a uv/visible spectrum similar to that taken during the metallation reaction and therefore was probably the six co-ordinated cobalt(III) complex, having dimethylformamide and dioxygen as the axial ligands. It is believed that such a low yield was due to loss of material during chromatography as a consequence of the difficulty of removal of dioxygen. However, neither change of column absorbent from silica gel to alumina oxide grade II, nor a change of solvent gave any improvement. As, voltammetry measurements require only a small amounts of pure compound and therefore chromatographic purification was continued despite the losses.

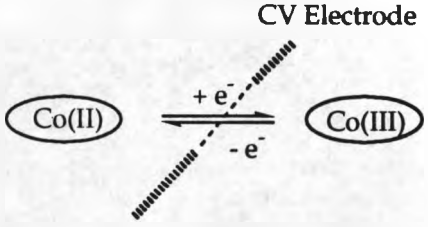
3.3 Redox Reactions and Cyclic Voltammetry

In a redox reaction involving metals and their cations, an electron from an orbital on the metal is transferred to the lowest unoccupied molecular orbital (LUMO) of the substrate or an electron from the highest occupied molecular orbital (HOMO) of a substrate is transferred to the metal. For a reductive process any one particular metal has a definite reducing power towards different functional groups. For example, it is

possible to reduce a carbonyl function in a molecule without reducing a C=C double bond in the same molecule. It has been said that "a given metal exerts a certain electron pressure towards a substrate but that the electron pressure is not always high enough to allow transfer of an electron to an empty orbital of sufficiently high energy". To overcome this energy difference a metal capable of exerting a higher electron pressure is needed. This can be achieved by changing the ligands around the metal[184] and, in this work, it was done by changing the nature of the 5,10,15,20-aryl groups in the porphyrin ring system.

To measure the reducing power of the resulting metallo complexes, the potential energy at which the electron transfer occurs, (the redox potential of the compound in question) was measured using cyclic voltammetry, (CV; see appendix II for more details about this technique). Briefly, the potential is measured at which an electron transfers to (or from) a metallated porphyrin from (or to) an electrode.

CV is very useful because it also helps to estimate the stability of the species produced in an electrode process. The potential at an electrode is varied linearly in most cases with time to a limit, followed by a reversal of the scan direction and a linear decrease of potential with time at the same scan rate. The applied potential changes are plotted against the simultaneous current flow at the electrode. The reverse reaction is immediately observed. Consider, the simple cobalt redox process shown in Scheme 37:



Scheme 37.

Depending on which electrode is being monitored, either the cobalt(II) is oxidised to cobalt(III) or vice versa. If a reduction (oxidation) is reversible the reverse scan will mirror the forward scan exactly . A simple example is shown by voltagram (a) in figure 10. If the reduction (oxidation) is irreversible, there is no mirroring in the reverse scan, which means the substrate in study is unstable on the time frame of the voltagram, [voltagram (b); figure 10]. It is quite common for a process that is reversible at low scan rates to became irreversible at higher ones after having passed through a region known as *quasi*-reversible at intermediates values. This transition from reversibility occurs when the relative rate of the electron transfer with respect to that of mass transport is insufficient to maintain a Nernstian equilibrium at the electrode surface.[185]

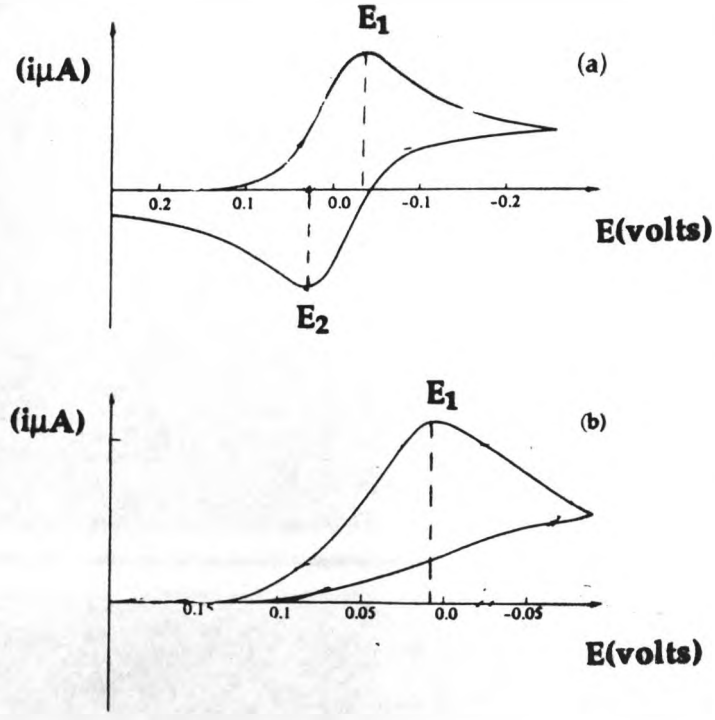
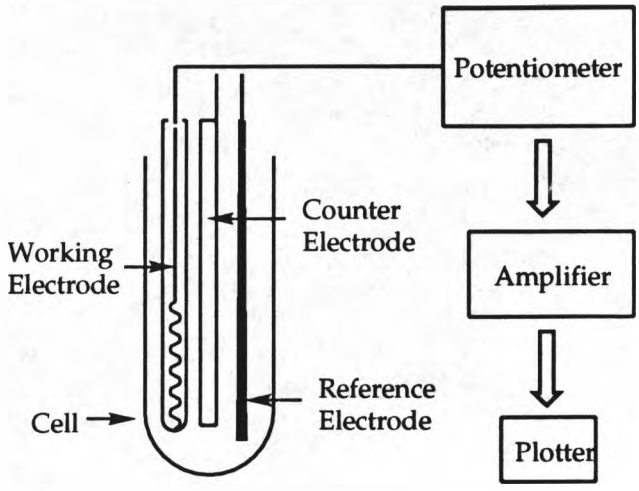


Figure 10. In (a) the cyclic variation in current flow of the foward scan from 0 to -0.25volts is mirrored by that for the reverse scan, showing that, on the time scale of the voltagram, the reduced (oxidized) substrate is stable. In (b), there is no such mirroring and the reduced (oxidized) substrate must be unstable on the time frame of the voltagram (i.e., has disappeared from the electrode surface).

The system illustrated in Scheme 38 was used in this present work. The cell comprised a reference electrode which was a silver wire coated with silver chloride, a working electrode where the redox reaction took place, and a counter electrode, that acted as a charge compensator.



Scheme 38.

The standard potential is the potential at equilibrium when the electrons on the electrode and those of the species in solution redistribute themselves among states on the electrode and on the electroactive solutes according to the usual principles of statistical thermodynamics. The Nernst equation expresses this relationship between the equilibrium constant and the standard redox potential, by the mathematical expression:

$$^{\circ}E_e=(RT/nF)\cdot(\ln K_{eq})$$

°E = standard redox potential at equilibrium
n = number of electrons involved in redox process (n= 1,2,3 etc)
T = temperature (Kelvin)
R = universal gas constant (8.31J/K/mole))
K_{eq} = equilibrium constant of the redox reaction being studied
F = faraday constant (9.65×10^4C/mol)

During CV measurements the measured potential is called the "half wave potential", $E_{1/2}$. Its value is calculated by taking the mid point between the two maxima shown in the voltagram spectrum figure 11. The maximum E_1 results from reduction (oxidation) of substrate at the electrode, the current rising to a maximum as the substrate is reduced (oxidised). After all the substrate has been reduced (oxidised), the current falls. On the reverse cycle, the current increases in the opposite direction as the reduced (oxidised) substrate is reoxidised (re-reduced). Again, the current falls as the substrate is used up. Therefore, if the substrate at the electrode surface is reduced (oxidised) and is stable and does not have time to diffuse away, then, on the reverse scan, the peak at E_2 will be the same height as that at E_1. If the reduced (oxidised) substrate is unstable or diffuses away then, by the time the reverse scan reaches E_2, the concentration of the reduced (oxidised) substrate will have been reduced and the peak at E_2 will be less than that at E_1. The scanning speed is normally such that there is no time for a significant amount of substrate to diffuse away from the electrode

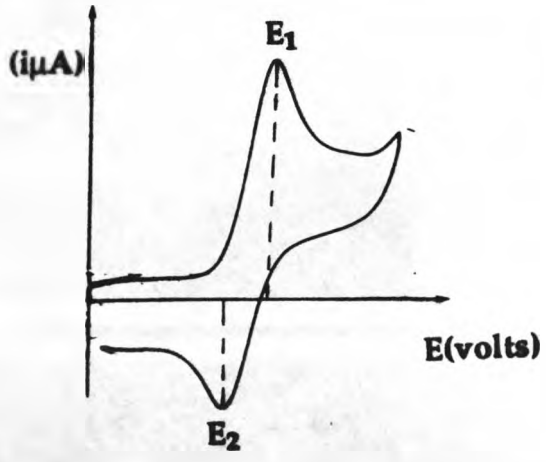


Figure 11. Voltagram of a typical reversible reaction; i(μA) is the current flowing to or from the electrode of potential E which may be positive or negative. The E_1 value is the maximum for the first (forward scanning) wave and E_2 is obtained from the reverse scan. The difference between E_1 and E_2 is due to the mass transport velocity. The half wave potential $E_{1/2} = (E_1 + E_2)/2$ is the mid-point between these two maxima. (See Appendix III for more details about the CV technique).

For reversible reactions, $E_{1/2}$ is virtually interchangeable with the classical polarographic redox value $E_{p1/2}$ because they are related through the diffusion coefficients (D_{ox}, D_{red}) of the oxidised and reduced substrate species (equation below). Because the diffusion coefficients are usually almost identical, $D_{ox}/D_{red} \simeq 1$ and $\log (D_{ox}/D_{red}) \simeq 0$. Therefore, $E_{1/2} \simeq E_{p1/2}$.

$$E_{1/2} = E_{p1/2} + A \log (D_{ox}/D_{red}), \text{ where A is a constant.}$$

$$\text{For } \log (D_{ox}/D_{red}) = 0, \text{ then } E_{1/2} = E_{p1/2}.$$

In these cases where the $E_{1/2}$ and $E_{p1/2}$ values are virtually interchangeable, the $E_{1/2}$ is also interchangeable with the thermodynamically significant $^{\circ}E_e$, the standard redox potential for the substrate oxidation/reduction equilibrium.[180]

During these electrochemical studies, the modern conventions regarding oxidation and reduction were used:

(i) all redox potentials correspond to reactions written towards the formation of the reduced products,

$$Ox + e^- \longrightarrow Re$$

(ii) the redox potential $^{\circ}E_e$ is positive for a spontaneous reaction and is negative for the reverse of a spontaneous reaction. It gives a measure of the driving force of a chemical reaction in that $\Delta G^{\circ} = -nF^{\circ}E_e$ where n is the number of electrons transferred during the reduction (oxidation) step and F is the Faraday constant (= 96,500 Coulombs/mole). Thus, if $^{\circ}E_e$ is positive ΔG° must be negative, viz., it represents an exothermic reaction,

(iii) all values are converted to a scale based on the standard hydrogen electrode (SHE), usually written as follows where a is the activity of the respective species:

$$Pt/H_2(a=1)/H^+ (a=1);\ ^{\circ}E=0.0V(SHE)$$

Conversion of measured values to the SHE scale were carried out by using the known potential of the reference electrode (Ag/Ag^+), which has a value of -0.22216 volts on the SHE scale.[186] Once the values, $E_{1/2}$, had been measured they could be related to the Gibbs free energy ($\Delta G°$) as discussed above.

The value of $\Delta G°$ was used to predict whether the reduction of cobalt(III) to cobalt(II) was favourable or unfavourable ($\Delta G°<0$ and $\Delta G°>0$ respectively) for the various cobalt/porphyrin complexes in butyronitrile.

3.4. CV Measurements

To carry out the cv measurements, an electrolyte solution of butyronitrile was made up to 0.1M in tetrabutylammonium perchlorate . The solvent had previously been passed through an alumina colunm to eliminate any possible contamination from traces of water that would affect the measurements. The cobalt complexes were all used at a concentration of 1mM and, like the solvent, they had all been purified previously by column chromatography. Once in the voltammetric cell, all samples were degassed with dry nitrogen for 10 minutes and a nitrogen atmosphere was maintained during each analytical measurement.

Studies of the redox potential of some cobalt porphyrin complexes have been reported.[110,180,187,182] However, most of the investigations were done with 5,10,15,20–*tetrakis*arylporphyrins in which the aryl group was 4-substituted. Furthermore, the oxidation and reduction of the porphyrin ligand itself were also of interest in those studies. During the measurements done in the present work, it was only of interest to

measure the redox behaviour of the cobalt porphyrin complex for the "metal" as in the reaction below:

$$Co(III)P + e^- \rightleftharpoons Co(II)P$$

P - porphyrin ligand

Therefore, no attempts were made to study and record the redox behaviour of the porphyrinic ligand itself.

Using the thermodynamic relationship between the measured potential and free energy, the Gibbs free energy (ΔG°) for the reaction above was calculated. Also, using the relationship between potential and equilibrium constant for the above reaction given by the Nernst equation, the equilibrium constant was calculated. The resulting values are listed in Table 9.

Table 9. Half wave potential, free energy and equilibrium constants for cobalt 5,10,15,20-*tetrakis*arylporphyrins corresponding to the process, $Co(III) + e^- \longrightarrow Co(II)$ a

Aryl groups in 5,10,15,20-tetrakisarylporphyrins of cobalt	$E_{1/2}$ (volts)	ΔG (Kcal/mole)	K_e ($\times 10^{11}$)
3-Methoxyphenyl	0.807	-77.86	476
2,3,4,5,6-Pentafluorophenyl	0.777	-74.97	148
3-Chlorophenyl	0.772	-74.49	122
2,6-Dichlorophenyl	0.767	-74.00	100
3,4,5-Trimethoxyphenyl	0.760	-73.33	76.1
3,4-Dimethoxyphenyl	0.732	-70.63	25.5
2,4,5-Trimethoxyphenyl	0.662	-63.87	1.66
4-Chlorophenyl	0.645	-62.23	0.855
Phenyl	0.637	-61.46	0.626
3,4-Methylenedioxyphenyl	0.617	-59.53	0.2868
4-Methoxyphenyl	0.612	-59.05	0.236
3,5–Di-*tert*-butyl-4-hydroxyphenyl	0.497	-47.95	0.00265

a - The values have all been related to the SHE

3.5. Analysis of Results of $E_{1/2}$ Measurements for the Co(III)/Co(II) System

As can be seen from Table 9, the values for the Gibbs free energy are all negative, which indicates that with all the cobalt complexes examined in this work, the conversion of cobalt(III) to cobalt(II) is exoergic. The equilibrium constants give more information about the *position* of equilibrium and this is useful later for understanding some oxidation reactions catalysed by the cobalt complexes.

Before analysing the system studied, it is important to clarify a few points related to electrochemistry.

Just as in general chemistry, electrochemistry occurs when the energetics are favourable. Potential in the electrostatic sense is the work required to bring a positive test charge from a point at infinity to the interior phase. That work can be raised or lowered by controlling of a very slight excess of charge in the phase by the use of some kind of power supply. It is obvious that this work is related to the energy required to bring an electron from the vacuum into the phase and therefore the potential controls the energy of that electron within the phase. At more negative potentials, reached by increasing the negative excess charge on an electrode, the electron attains relatively high energies. At more positive potentials, established with a less negative or a positive excess of charge, the electron attains low energies.

To explain the results given in Table 9, the change from cobalt(III) to cobalt(II) should be examined first.

As outlined in figure 12, when changing from cobalt(III) to cobalt(II) (a reduction), the electron density on cobalt increases with the extra electron going into a d_z^2 orbital. All the redox potentials, $E_{1/2}$, are positive which means that, to introduce an electron into the cobalt(III) ion, the electron energy must be reduced by increasing the potential energy on the

working electrode. When reaching the right potential, the energy balance favours the reduced form and electron transfer occurs since the electron starts to be more stable in the compound than on the electrode.

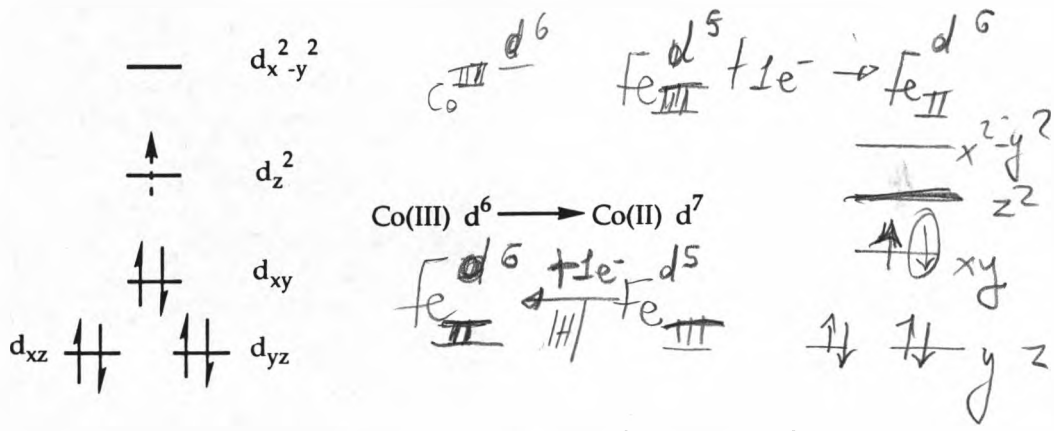


Figure 12. Schematic representation of the orbital energies of cobalt(III) [d^6] and cobalt(II) [d^7] when incorporated as part of a porphyrin (square planar) ring system.[108] The arrows represent electron filling of the orbitals. The electron in d_z^2 corresponds to the extra electron of cobalt(II) d^7, which absent in cobalt(III).

Cobalt(III) can be looked at in terms of a Lewis acid since it behaves like one. It has been shown that, because of the nature of the porphyrin ring system, electron donating or withdrawing substituents on the periphery of the molecule affect the basicity of the porphyrin nitrogens.[109]Therefore, the influence of such aryl substituents on the cobalt(III) must change its electron affinity, and also its Lewis acid character. Electron-withdrawing groups should increase the Lewis acid character of the cobalt(III), since it becomes easier to form a dative bond with a suitable nucleophile or ligand. At the same time, the electron affinity increases and, therefore, the electron energy does not need to be so high for electron transfer to occur, viz., the redox potential on cobalt should be more positive. Indeed, it can be seen from Table 9 that most of the porphyrins which have electronegative substituents have a more positive potential than the others such as the the cobalt complexes of

5,10,15,20-*tetrakis*(2,3,4,5,6-pentafluorophenyl)porphyrin, 5,10,15,20-*tetrakis*(2,6-dichlorophenyl)porphyrin and 5,10,15,20-*tetrakis*(3-chlorophenyl)porphyrin. There are exceptions that have to be explained in terms of the positions of the substituents on the aryl rings.

In contrast, as the nitrogen basicity of the porphyrin increases, there is a greater electron density on the cobalt d-orbitals and this provokes an increase in energy of the d-orbitals (figure 12). Therefore, it should be more difficult to introduce more electrons into the d_z^2 orbital.

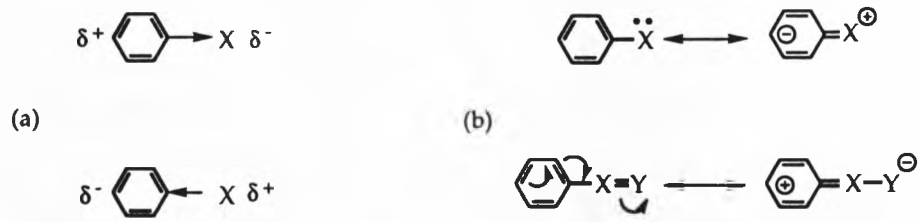
To facilitate analysis of the results presented in Table 9 it was decided to divide the cobalt porphyrin complexes into groups by taking into account the position of the substituents in the phenyl rings.

3.5.1. Cobalt porphyrin complexes with 4-substituted phenyl rings

For the porphyrins having 4-substituted phenyl rings, the measured $E_{1/2}$ potentials become less positive in the order, $OCH_3 < H < Cl$.

There are two main effects of the substituents that can act to control the redox potential, namely resonance and induction. Resonance (R) is the sharing or distribution of electron density through delocalization of substituent electrons into a π-electron system and induction (I) is the redistribution of electron density through a σ-system brought about by changes in electronegativity.

In a 4-substituted phenyl ring, the electronegativity of the substituent causes movement of electron density out of or into the ring, [structures (a); Scheme 39] by induction.



Scheme 39.

But if the substituent has a lone pair of electrons, the resonance effect can puts electron density back into or out of a phenyl ring (back-bonding) [structures (b); Scheme 39]. Therefore, the net electron density depends on both resonance and induction acting together.

For chlorine, induction is strong but resonance is weak. For methoxy, induction is not so strong but resonance is strong. Therefore, for methoxy, there will be a residual excess of negative charge in the phenyl ring which will appear mostly in the ortho and para positions. For chlorine, there is much less π-back bonding and therefore the residual excess of negative charge is much less. In both groups the excess of negative charge is going to increase the electron density at the porphyrin 5,10,15,20-positions. As a consequence, with methoxy the cobalt(III) Lewis acid character is more reduced than with chlorine. Hydrogen is slightly electron attractive (-I) compared with carbon. For hydrogen resonance is very weak and electron density is put back into the phenyl ring. In conclusion, methoxy decreases the Lewis acid character of cobalt(III) comparing with hydrogen, and chlorine increases it. The $E_{1/2}$ orders obtained agree with the discussed effects.

3.5.2. *Cobalt porphyrin complexes with 3-substituted phenyl rings*

With 3-substituted phenyl groups (3-methoxy and 3-chloro), the order for $E_{1/2}$ is reversed, $Cl<OCH_3$.

Both, 3-methoxy and 3-chloro are better able than 4-methoxy or 4-chloro to increase the cobalt(III) Lewis acid character, according to the results obtained for $E_{1/2}$. They must therefore give rise to a more positive excess charge in the 5,10,15,20-position of the porphyrin ring. The 3-substituted aryl groups leave, by resonance, an excess negative charge mainly at positions 2-,4- and 6- of the aryl rings. There is almost no resonance effect at the carbon bonded to the 5,10,15,20-positions of the porphyrin ring. So, mainly inductive effects count for the 3-substituted aryl rings. This inductive effect in both groups is responsible for the appearance of a residual excess of positive charge at the 5,10,15,20-positions of the porphyrin ring. This explains the relative orders of the 3-substituted aryl groups and the 4-substituted aryl groups. However the relative orders between themselves, 3-chloro and 3-methoxy, seems to contradict the orders for the relative strengths of the inductive effects. Indeed 3-chloro has a higher inductive effect than 3-methoxy, however 3-methoxy increases the cobalt(III) Lewis acid character more than 3-chloro. There are in the literature similar results, that although do not explain, they are a confirmation of the peculiarity observed.[188]

Considering the proton nmr of benzene and monosubstituted benzenes, which shifts are shown in table 10.

Table 10. Proton nmr shift (δ) of monosubstituted benzenes[188]

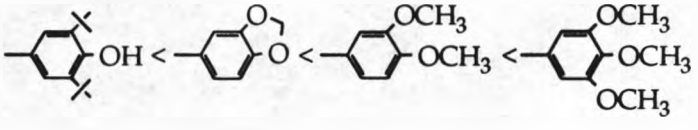
Substituent	2-Position	3-Position	4-Position
Hydrogen	7.27ppm	7.27ppm	7.27ppm
Chloro	7.28(0.01)[a]	7.21ppm(-0.06)[a]	7.19ppm(-0.08)[a]
Methoxy	6.81(-0.46)[a]	7.17ppm(-0.10)[a]	6.86ppm(-0.41)[a]

a - Difference between the proton nmr shift of the aromatic protons in comparison to benzene (in the stipulated positions).

For chlorobenzene both proton nmr at the 3- and 4-position of the monosubstituted aryl ring suffer only a small shift for negative values relative to the proton nmr of the benzene. This is expected since the resonance effects for chlorine are very weak and the inductive effects are stronger. However, resonance effects for methoxy are stronger than inductive effects. By resonance an excess residual negative charge appears mainly at the 2-, 4- and 6-positions. This effect makes the proton nmr at the 4-position shift to lower ppm in comparison with the proton nmr of benzene. The proton at the 3-position should be controlled mainly by inductive effects coming from the methoxy group. This shift should be smaller than the shift found for the protons at the 2- and 4-positions. However, the results show that the proton does suffer a negative shift but very similar to the chlorobenzene, as can be see in table 10.

3.5.3. Cobalt porphyrin complexes with both 3- and 4-substituted phenyl rings

For complexes that possess both, 3- and 4-substituents, the $E_{1/2}$ order obtained was:



By resonance methoxy puts electron density back into the aryl ring and so does hydroxy but with a larger effect. The methylenedioxy group should have a similar effect as methoxy.

The electronegativity of a hydroxy group removes electron density from the ring, but this effect is not as strong as the release of electron

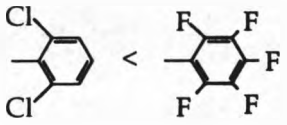
density due to resonance. Butyl groups are also electron releasing by induction, driving electron density into the phenyl ring system. Thus 3,5-di-tert-butyl-4-hydroxy-phenyl ring has the highest electron density and that appears mostly in the 2- and 6-positions. As a consequence, the cobalt(III) Lewis acid character is reduced and its $E_{1/2}$ is the smallest.

From the results discussed previously it was clear that 3-methoxy groups increase the cobalt(III) Lewis acid character. On the other hand, 4-methoxy has the opposite effect, since a strong π-back bonding and a small electron attraction, by induction, leave a residual excess of negative charge mostly in the ortho and para positions, close to the 5,10,15,20-positions of the porphyrin ring. It is seen that the same group has different effects on the cobalt(III) Lewis acid character, depending on the position in the phenyl ring. For the porphyrin with 3,4,5-trimethoxyphenyl substituents, the cobalt(III) Lewis acid character is increased more compared with the one with 3,4-dimethoxy substituents, where there is only one 3-methoxy substituent. This explains why the $E_{1/2}$ is greater for the cobalt complex of 5,10,15,20-*tetrakis*(3',4',5'-trimethoxyphenyl)porphyrin than for the cobalt complex of 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin.

According to the obtained redox potentials, the electron density is more increased in the cobalt centre of 5,10,15,20-*tetrakis*(3',4'-methylenedioxyphenyl)porphyrin than in 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin. In other words the Lewis acid character of cobalt(III) is more increased in the cobalt complex of 5,10,15,20-tetrakis(3',4'-dimethoxyphenyl)porphyrin.

3.5.4. Cobalt porphyrin complexes with 2- and 6-substituted phenyl rings

For complexes that possess 2- and 6-substituted phenyl rings, the order of $E_{1/2}$ obtained was:

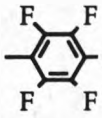


For fluorine and chlorine the inductive effect causes a movement of electrons out of the ring. This effect is larger for fluorine which is more electronegative than chlorine. The resonance effect of both fluorine and chlorine in the 2-, 4- and 6-positions feeds electron density back into the ring but this effect whilst small for fluorine is larger than for chlorine. From the results, the combined effect of five fluorines offset by the resonance effect of three fluorines is greater than the effect of the two chlorines in the 2- and 6-position.

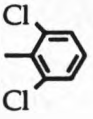
3.6. Conclusions

When comparing similar structures it is easier to explain the resonance and induction effects by invoking substituent effects on the cobalt centre, and thus to explain the order of observed $E_{1/2}$. However, when comparing very different structures, explanation becomes more difficult. The main reason being the strengths of the resonance and inductive effects of the different substituents which are difficult to quantify. When trying to do such a kind of comparison the main puzzling result is the unexpectedly very high value for the potential of the 5,10,15,20-*tetrakis*(3'-methoxyphenyl)porphyrin cobalt complex (Scheme 40).

$E_{1/2}$ = 0.807 volts ; ΔG = -77.86 ; K_e = 4.76 exp(13)



$E_{1/2}$ = 0.777 volts ; ΔG = -74.97 ; K_e = 1.48 exp(13)



$E_{1/2}$ = 0.767 volts ; ΔG = -74.00 ; K_e = 1.00 exp(13)

Scheme 40.

In fact when comparing its $E_{1/2}$ with values such as the 5,10,15,20-*tetrakis*(2',3',4',5',5',6'-*penta*fluoroyphenyl)porphyrin cobalt complex, that would be expected to be higher, or the 5,10,15,20-*tetrakis*(2'6'-dichlorophenyl)porphyrin cobalt complex that again would be expected to be higher, there was no explanation (Scheme 40).

Groups in 3-positions of phenyl rings very often represent an exception in respect to data interpretation.

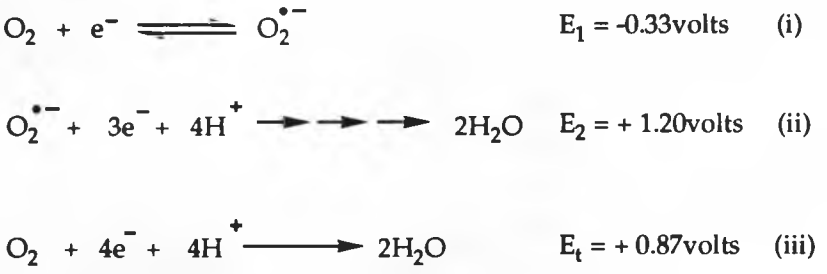
Chapter Four

USE OF THE COBALT COMPLEXES OF 5,10,15,20-*TETRAKIS*ARYL PORPHYRINS IN OXIDATION REACTIONS WITH DIOXYGEN

4. USE OF THE COBALT COMPLEXES OF 5,10,15,20-*TETRAKIS*ARYL PORPHYRINS IN OXIDATION REACTIONS WITH DIOXYGEN

4.1. Introduction and Objectives

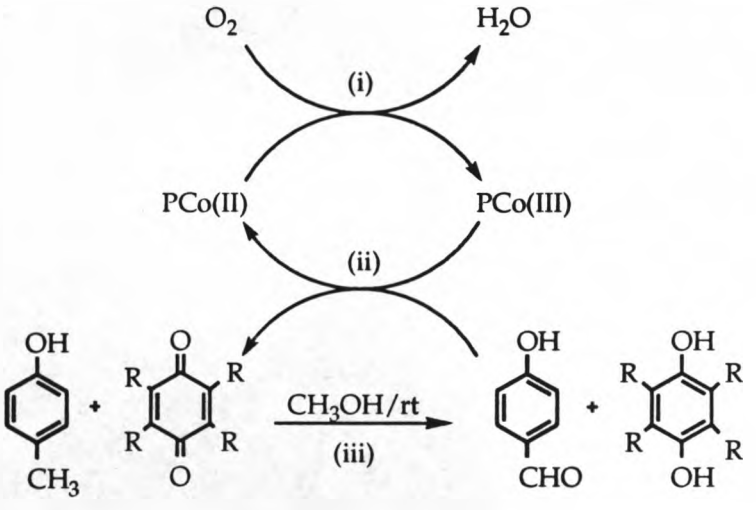
In appendix III it is explained why oxygen, being potentially such a powerful oxidant, is unable to react easily with most organic substrates. On the other hand, if suitably activated, oxygen becomes a powerful but relatively unselective oxidant, often attacking organic substrates in an uncontrolled manner. Dioxygen can be reduced in several steps, as shown in Scheme 41.[48,36]



Scheme 41.

As was discussed in the last chapter, by convention, the magnitude and sign of the potential of a half reaction, like those in Scheme 41 reflects the relative tendencies of the reactions to proceed from left to right but gives no indication of rate. In a first reversible, step oxygen can be reduced by one electron transfer process [reaction (i); Scheme 41] for which the redox potential has a negative value of -0.33 volts, viz., it is endoergic which makes its use as an oxidant limited.[48,36] This is one reason why oxygen does not destroy life on earth by reacting with all organic matter. Once this first step is overcome, the redox potential has a high and

positive value of +1.20 volts [reaction (ii); Scheme 41] making it strongly exoergic.[48,36] Thus, although the overall reaction has a positive redox potential, [reaction (iii); Scheme 41], the first step still needs to be overcome in order to take advantage of the available energy. It was the objective of this work to develop a system in which oxygen could be activated and selectively controlled. The use of cobalt complexes of porphyrins as good oxygen carriers has been presented during the introduction to this thesis. In order to take advantage of such oxidising capacity a system was visualised in which these compounds were used in oxidation reactions with dioxygen when normally the latter would not react by itself. Such a system and the objective of this research is presented in Scheme 42.

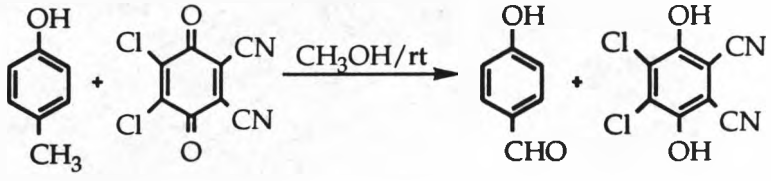


P-Porphyrin ligand

Scheme 42.

Here in a first step [reaction (i); Scheme 42] the oxygen binds with a cobalt(II) porphyrin with electron transfer to produce cobalt(III) porphyrin. The cobalt(III) porphyrin complex then reacts with a dihydroquinone to produce the respective quinone [reaction (ii); Scheme 42]. The quinone

produced is then expected to react with a substrate, oxidising it. In this example, the methyl group of a cresol substrate would be converted into aldehyde.[190] This last reaction given as an example [reaction (iii); Scheme 42] can be found in the literature, and is performed as illustrated by Scheme 43.[190]



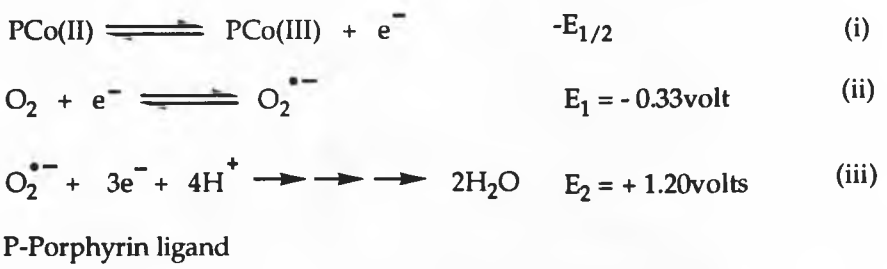
Scheme 43.

In this literature reaction (Scheme 43) expensive 2,3-dicyano-5,6-dichloro-benzoquinone, DDQ had to be used stoichiometrically. By using a system like the one presented in Scheme 42, the quinone would be used in lesser amount (catalytically), being reoxidised by the dioxygen/porphyrin system.

4.2. The Capacity of Cobalt/Porphyrin Complexes to Function as Oxygen Activators

Before trying any kind of oxidation reaction using the cobalt/porphyrin complexes made for this research, it was important to make sure they would be able to reversibly react with dioxygen. To test the capacity of the cobalt complexes to react with dioxygen, it was necessary to react them with dioxygen to change cobalt(II) into cobalt(III) and then to bring cobalt(III) back to cobalt(II) before repeating the cycle. Thus, the first question to answer before performing any experiments was whether the cobalt complexes could react with dioxygen in the first place? First the

thermochemistry of the reaction with dioxygen needed to be analysed, [reactions (i), (ii), (iii); Scheme 44]:



Scheme 44.

As indicated in Scheme 44, for each reaction taking place, there is a value for the redox potential (indicated as the reduction value as stipulated in Chapter three of this thesis). During the reaction of cobalt porphyrins with dioxygen, cobalt(II) transfer one electron to dioxygen to became cobalt(III) [reaction (i); Scheme 44]. Note how the value taken for the redox potential of the cobalt porphyrin is $-E_{1/2}$ and not $E_{1/2}$ because the reaction involved is the oxidation of cobalt(II) to cobalt(III). The dioxygen molecule is reduced in several steps to form water. For each molecule of dioxygen reduced to water, [reactions (ii) and (iii); Scheme 44] four electrons are needed. In the reduction of dioxygen to water, only the addition of the first electron has a negative value for the redox potential [reaction (ii); Scheme 44], viz., is endoergic. The overall reaction of cobalt with dioxygen has a reaction potential that is the sum (E_t) of the redox potentials of the half reactions involved (Scheme 45; compared with Scheme 44).

$E_t = -E_{1/2} - 0.33 + 1.20$

$E_t = -E_{1/2} + 0.87\text{volts}$

E_t is the overall reaction potential for $4Co(II) + 4H^+ + O_2 \rightleftharpoons 4Co(III) + 2H_2O$

Scheme 45.

According to thermodynamics, it is possible to infer how favourable or unfavourable a reaction may be by knowing the Gibbs free energy, ΔG°, of such a reaction. It is possible to calculate the Gibbs free energy from E_t since they are thermochemically related by equation (i) [Scheme 46], in which n is the number of electrons transferred and F is the Faraday constant.

$$\Delta G = -nFE_t \qquad \text{(i)}$$

$$\text{If} \quad E_t > 0 \text{ then } \Delta G < 0 \qquad \text{(ii)}$$

$$\text{But if } E_t < 0 \text{ then } \Delta G > 0 \qquad \text{(iii)}$$

Scheme 46.

As shown in equation (ii) of Scheme 46, if E_t is positive then ΔG will be negative and the reaction is favourable (exoergic). On the other hand, if E_t is negative, ΔG will be positive and the reaction is unfavourable (endoergic), (equation (ii) [Scheme 46]). For the present system, in which dioxygen and cobalt porphyrins are involved, E_t is positive when the $E_{1/2}$ value of any cobalt porphyrin complex is less than +0.87 volts and is negative value when $E_{1/2}$ is greater than +0.87 volts (Scheme 47).

$$\text{For} \quad E_{1/2} < 0.87\text{volts then } E_t > 0 \text{ and } \Delta G < 0$$

$$\text{and, for} \quad E_{1/2} > 0.87\text{volts then } E_t < 0 \text{ and } \Delta G > 0$$

Scheme 47.

From Table 9 in Chapter 3, it can be seen that all halfwave potentials for the cobalt porphyrins are less than +0.87 volts. It can be concluded that reactions of dioxygen with these cobalt porphyrin complexes are thermochemically favourable but not all equally so.

Such thermochemical analysis gives information about the capacity of any cobalt complex synthesised in this work to react with dioxygen.

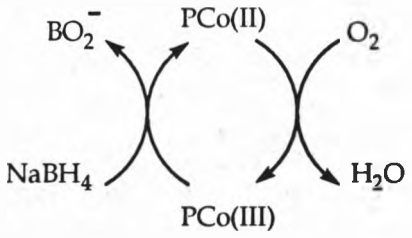
Extra information is needed concerning the reversibility of the dioxygen reaction.

When dioxygen reacts with cobalt(II) the new complex so formed can be viewed as a superoxide ion attached to cobalt(III), that is $Co(III)O_2^{\cdot-}$.[112] This came as a conclusion to research in which EPR studies showed that approximately 90% of the spin density of the unpaired electron on cobalt(II) could be calculated as being transferred to oxygen upon formation of the cobalt/dioxygen adduct. On this basis, the reaction of a cobalt porphyrin with dioxygen may be described as an electron transfer from cobalt(II) to the dioxygen molecule.[112] The strength of the bond between cobalt and the dioxygen will depend on the presence of any axial ligand, including the possibility of this being the solvent and on the structure of the porphyrinic ligand.[104,105,112] Having this in mind it was decided to use sodium borohydride to convert cobalt(III) into cobalt(II) (Scheme 48) when performing test reactions for reversible binding of dioxygen.

$$BO_2^- + 6H_2O + 8e^- \longrightarrow BH_4^- + 8HO^- \quad {}^{\bullet}E = -1.24\text{volts}$$

Scheme 48.

The large redox potential for sodium borohydride (Scheme 48) is sufficiently great to convert any porphyrin cobalt(III) complex back to the respective cobalt(II) complex. If the reduction should succeed then the cobalt/porphyrin complexes would be able to cycle between the two oxidation states of cobalt(II) and cobalt(III) on using dioxygen and sodium borohydride alternately. Scheme 49 illustrates the reactions that needed to be performed.



P-Porphyrin ligand

Scheme 49.

To monitor this kind of reaction, uv/visible spectroscopy was used. The uv/visible spectra of cobalt porphyrins show a shift in the Soret band according to the oxidation state of the cobalt. Usually, a cobalt(II) porphyrin has a Soret band at around 402nm and a cobalt(III) porphyrin at around 418nm. The exactitude of these values depends on the structure of the porphyrinic ligand and on ligand formation by solvent. Figure 13 gives an example.

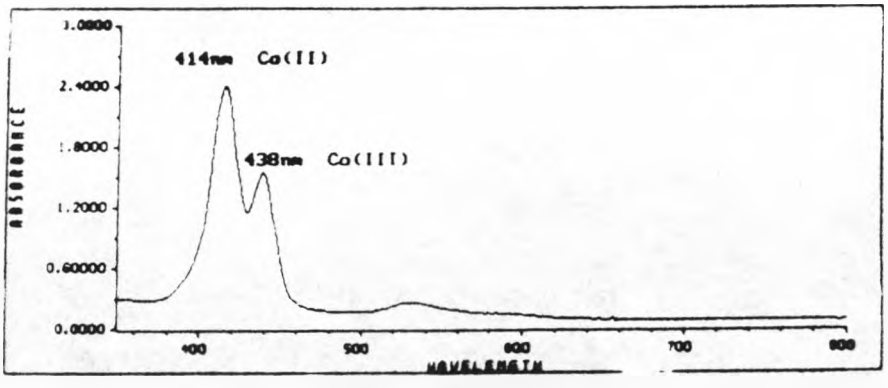
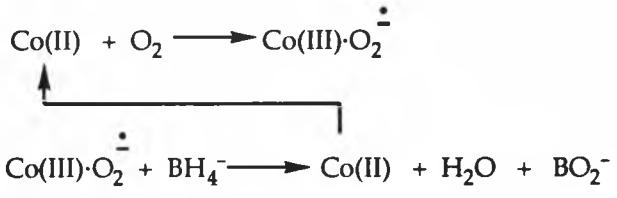


Figure 13. Example of a uv/visible spectrum of the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin in DCM/MeOH. The Soret band on the left at about 414nm, corresponds to cobalt with oxidation state of (+2). The Soret band on the right at about 438nm started to appear after the solution had been exposed to dioxygen. This band is typical of a cobalt/porphyrin complex in which cobalt is in its (+3) oxidation state.

The experiments were carried out by bubbling dioxygen for a few seconds into a small sample of a cobalt porphyrin complex dissolved in

methanol/dichloromethane. The uv/visible spectra of these samples were then measured. After this, a few milligrams of sodium borohydride was added to the sample, and the uv/visible spectra were measured again. This process was repeated for all the cobalt complexes at least 10 times.

With the cobalt complexes of such porphyrins as 5,10,15,20-*tetrakis*(4'-methylthiophenyl)porphyrin, it was not possible to make any measurements because of the low solubility of the cobalt complex in the solvent system, and no other reasonable solvent was found able to dissolve it. All the other cobalt porphyrin complexes responded positively to the cycling between the two oxidation states, (II) and (III), of the cobalt as illustrated in Scheme 50.

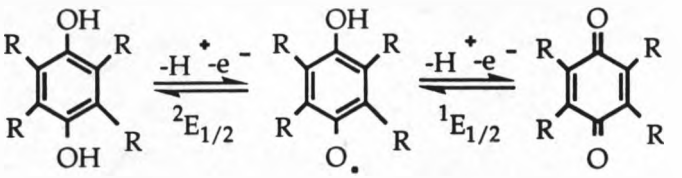


Scheme 50.

Having been able to prove the capacity of the cobalt complexes to act as oxygen "carriers", it was decided to go through to the next stage, the oxidations.

4.3. Thermochemical Study of the Reaction of Cobalt Complexes with Dihydroquinones

To build a system like the one presented in Scheme 42, it was decided to work with 1,4-dihydrobenzoquinone (H_2BQ), 2,3-dicyano-5,6-dichloro-1,4-dihydrobenzoquinone (H_2DDQ) and 2,3,4,5-tetrachloro-1,4-dihydrobenzoquinone (H_2TCQ).



Scheme 51.

The oxidation of dihydroquinones occurs in two steps (Scheme 51). In a first reversible step, the loss of an electron and a proton produces a semi-quinone HQ$^{\bullet}$ and, in a second step, the loss of a second electron and proton produces a quinone.[191,192] From the literature, the values of the redox potentials for each individual step for the quinones investigated here are shown in the table below. $^{1}E_{1/2}$ is the halfwave potential for the reduction of the quinone into the semiquinone, and $^{2}E_{1/2}$ is the halfwave potential for the second step reduction of the semiquinone into the dihydroquinone (Scheme 51).

Table 11. Half wave potentials of quinones in acetonitrile at 25°C[191]

Quinone	$^{1}E_{1/2}$ (SHE)[a]	$^{2}E_{1/2}$ (SHE)[b]
BQ	-0.27	-0.9
DDQ	+0.75	-0.06
TCQ	+0.25	-0.47

a - $^{1}E_{1/2}$ is the half-wave potential (measured against the standard hydrogen electrode) for conversion of quinone into semiquinone.
b - $^{2}E_{1/2}$ is the half-wave potential (measured against the standard hydrogen electrode) for conversion of semiquinone into dihydroquinone.

Note that, since the redox potential is, by convention, always referred to a reduction, the half wave potentials in Table 11 are relative to reduction in the second ($^{1}E_{1/2}$) and first ($^{2}E_{1/2}$) step of the reaction presented in Scheme 51, respectively. Following the lines of the previous

thermochemical analyses, the relevant equations involving cobalt porphyrin complexes and the dihydroquinones are shown in Scheme 52.

$$H_2Q \rightleftharpoons HQ^{\bullet} + e^- + H^+ \qquad -{}^2E_{1/2} \qquad \text{(i)}$$

$$HQ^{\bullet} \rightleftharpoons Q + e^- + H^+ \qquad -{}^1E_{1/2} \qquad \text{(ii)}$$

$$2PCo(III) + 2e^- \rightleftharpoons 2PCo(II) \qquad E_{1/2} \qquad \text{(iii)}$$

$$H_2Q + 2PCo(III) \rightleftharpoons Q + 2PCo(II) \qquad E_t = E_{1/2} - ({}^1E_{1/2} + {}^2E_{1/2}) \qquad \text{(iv)}$$

P - Porphyrin ligand
E_t - Overall redox potential

Scheme 52.

The oxidation of the dihydroquinones to quinones, [reactions (i), (ii); Scheme 52] by the cobalt porphyrin complexes [reaction (iii); Scheme 52] gives an overall reaction [reaction (iv); Scheme 52] with a redox potential which is the sum of the potentials involved [equation (iv); Scheme 52].

H_2BQ

$- ({}^1E_{1/2} + {}^2E_{1/2}) = 1.170$volts (Table 11)

$E_t = E_{1/2} + 1.170$volts

If, $E_{1/2} > -1.170$ then $E_t > 0$ and $\Delta G < 0$: Reactions Favourable

E_t - Overall redox potential

Scheme 53.

For the reaction involving H_2BQ (Scheme 53) to occur the redox potential ($E_{1/2}$) for the cobalt porphyrin complexes should be at least more positive than -1.170 volts, because of the magnitude of the value for the oxidation of the H_2BQ to the BQ, (+1.170 volts)(Scheme 53). All the cobalt

porphyrin complexes have positive redox potentials ($E_{1/2}$), which makes the Gibbs free energy negative for all reactions. Thus, with these dihydroquinones, all the reactions may be considered to be favourable (Scheme 53).

H_2TCQ

$-({}^1E_{1/2} + {}^2E_{1/2}) = 0.220$volts (Table 11)

$E_t = E_{1/2} + 0.220$volts

If, $E_{1/2} > -0.220$ then $E_t > 0$ and $\Delta G < 0$: Reactions Favourable

E_t - Overall redox potential

Scheme 54.

With reactions involving H_2TCQ (Scheme 54) similar results were observed. In these cases, the values for the redox potential of the cobalt porphyrin complexes ($E_{1/2}$) needed to be more positive than -0.220 volts, the value required for the oxidation of H_2TCQ to TCQ (Scheme 54). Again all $E_{1/2}$ values for the cobalt porphyrin complexes meet these requirements and so all reactions are considered thermochemically favourable (Scheme 54).

H_2DDQ

$-({}^1E_{1/2} + {}^2E_{1/2}) = -0.690$volts (Table 11)

$E_t = E_{1/2} + (-0.690)$volts

If, $E_{1/2} < +0.690$ then $E_t < 0$ and $\Delta G > 0$ Reactions Unfavourable

If, $E_{1/2} > +0.690$ then $E_t > 0$ and $\Delta G < 0$ Reactions Favourable

E_t - Overall redox potential

Scheme 55.

For H_2DDQ two different situations occur (Scheme 55). To get negative values for the Gibbs free energy and obtain a thermochemically favourable reaction a value more positive than +0.690, is needed for oxidation of H_2DDQ to DDQ (Scheme 55). Looking at the observed redox potentials of the cobalt porphyrin complexes two cases can be seen, one in which the Gibbs free energy becomes positive and the other in which it becomes negative (Table 12 and 13 respectively).

Table 12. Porphyrin cobalt complexes that make ΔG negative in reactions with H_2DDQ (according to Scheme 52)

Aryl group[a]	Redox Potential $E_{1/2}$ (volts)(SHE)
3-Methoxyphenyl	0.807
2,6-Dichlorophenyl	0.767
3-Chlorophenyl	0.772
3,4-Dimethoxyphenyl	0.732
2,3,4,5,6-Pentafluorophenyl	0.777

a - Aryl group in 5,10,15,20-*tetraki*sarylporphyrin cobalt complexes

Table 13. Porphyrin cobalt complexes that make ΔG positive in reactions with H_2DDQ (ccording to Scheme 52)

Aryl group[a]	Redox Potential $E_{1/2}$ (volts)(SHE)
4-Methoxyphenyl	0.612
Phenyl	0.637
3,4-Methylenedioxyphenyl	0.617
2,4,5-Trimethoxyphenyl	0.662
4-Chlorophenyl	0.645
3,5-Di-tert-butyl-4-hydroxyphenyl	0.497

a - Aryl group in 5,10,15,20-*tetraki*sarylporphyrin cobalt complexes

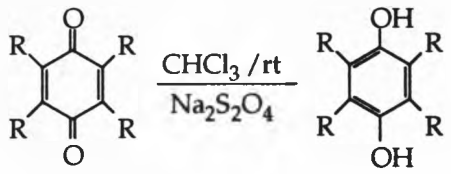
The cobalt porphyrin complexes in Table 13 have values that make the Gibbs free energy positive meaning that reactions with these cobalt porphyrin complexes and H_2DDQ are not thermochemically favourable. However, these calculations refer to a state of equilibrium. The half wave potentials of the cobalt porphyrin complexes and dihydroquinones are all referred to the equilibrium. In the laboratory, the equilibrium is not the starting situation. To calculate the real redox potential for a reaction at any time, the Nernst equation can be used (Chapter 3). Depending on the initial concentrations used in a particular reaction the Gibbs free energy can be positive or even negative if the reaction is not at equilibrium. Cobalt porphyrin complexes in Table 13 may also be able to convert H_2DDQ into DDQ if the concentrations are adjusted. Therefore, it was decided to carry on with all of the cobalt porphyrin complexes.

Since the thermochemical analyses of the two types of reactions involved in this cycle (cobalt porphyrin with dioxygen) and with different dihydroquinones have been done, the next step was to build a system to test its efficiency.

4.4. Study of the Efficiency of a Catalytic Cycle Involving Porphyrin Cobalt Complexes, Dioxygen and Dihydroquinones

4.4.1. Synthesis of dihydroquinones

The dihydroquinones H_2DDQ and H_2TCQ needed to be synthesised. The procedure from the literature is easy to perform, and Scheme 56 illustrates it.[193] H_2BQ was already available.



Scheme 56.

In this procedure the quinone is dissolved in chloroform, or chloroform/toluene, depending on the solubility of the quinone. Sodium hydrosulfite is dissolved in water and then added to the quinone solution. The dihydroquinone precipitates out from solution and can be isolated by filtration. Table 14 shows the yields obtained for the synthesis of the two dihydroquinones.

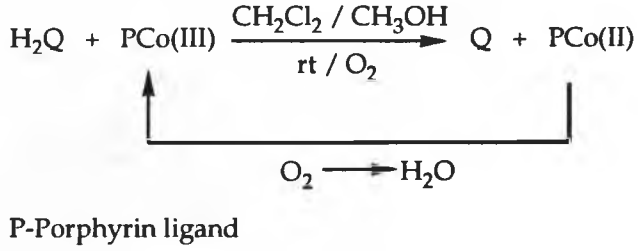
Table 14. Yields obtained for the synthesis of H_2DDQ and H_2TCQ

Dihydroquinone	Yield (%)
H_2DDQ	61
H_2TCQ	91

4.4.2. Choosing the conditions and building the cyclic system

The system of solvents examined for the reactions of the cobalt porphyrin complexes with dihydroquinones and dioxygen, was dichloromethane/methanol. Most of the cobalt porphyrin complexes are soluble in solvents such as dichloromethane. On the other hand, the dihydroquinones are soluble in more polar solvents such as methanol. By dissolving the cobalt porphyrin complexes in dichloromethane, and separately dissolving the dihydroquinone in a small amount of methanol it was possible to give the molecules the necessary conditions for reaction

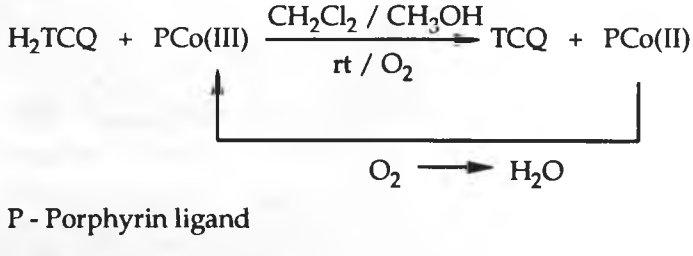
to occur. The reactions were performed in vessels open to the atmosphere and at room temperature (Scheme 57).



Scheme 57.

To begin with it was decided not to use any kind of extra axial ligand. Axial ligands have been described in the literature as being able to stabilise the bond between the cobalt porphyrin complex and dioxygen.[115] It was the objective of this work to have a labile system. So the use of ligands could stop the cycle between the cobalt oxidation states. In fact, as already discussed in the introduction to this thesis, the presence of some axial ligands in these compounds makes difficult the removal of dioxygen from the adducts.[104]

4.4.3. Study of the catalytic cycle with H_2TCQ



Scheme 58.

As Scheme 58 shows, these experiments were first performed with H_2TCQ by following the procedures already described. The control of the conversion of dihydroquinones to quinones was monitored by uv/visible

spectroscopy and TLC (Thin Layer Chromatography). The quinone, TCQ, has a band at 294nm that is absent in its dihydroquinone uv/visible spectrum and this allows for the monitoring of its formation during the reaction.

When performing these experiments it was observed that:

(i) most of the cobalt porphyrin complexes converted H_2TCQ into the quinone very quickly;

(ii) the cobalt porphyrin complexes of 5,10,15,20-tetrakis(2',6'-dichloro phenyl)porphyrin and 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl) porphyrin did not convert H_2TCQ into the respective quinone TCQ;

(iii) the cobalt porphyrin complexes being used catalytically to convert dihydroquinone into quinone were gradually destroyed during the reaction (disappearance of the Soret band);

(iv) uv/visible monitoring during the reaction revealed that the Soret band was centred on a cobalt(II) species at the beginning but this band would start to broaden and, after 24 hours all the cobalt complexes, except for 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl)porphyrin cobalt complexes, revealed a broad band centred on the cobalt(III) absorption band, as shown in figure 14;

(v) altering the solvent, to acetonitrile, where the cyano group can act as an axial ligand, did not alter the results, but decreased velocity of reaction.

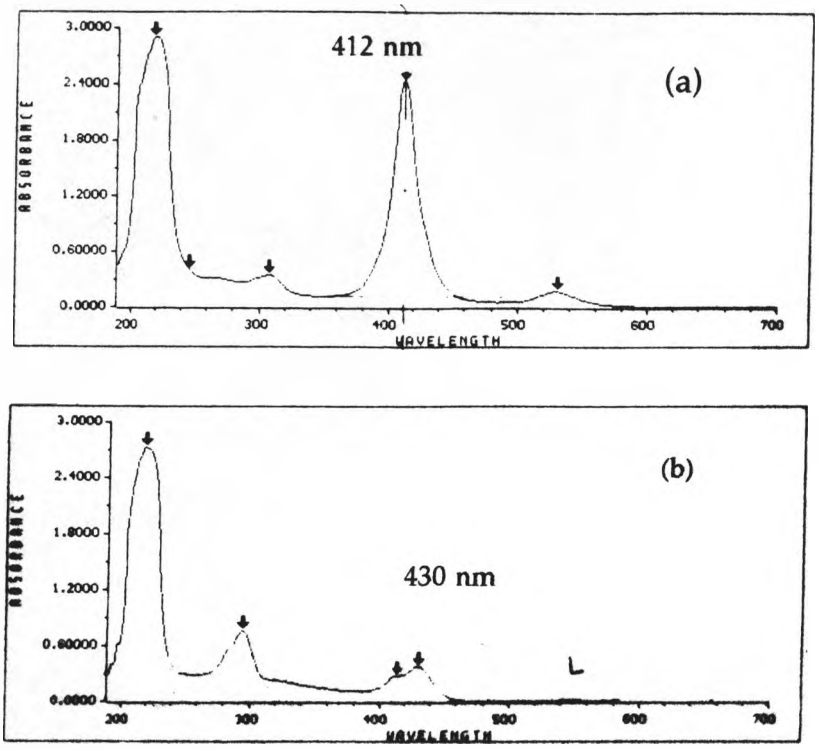


Figure 14. (a) uv/visible spectrum of a cobalt porphyrin complex, with the Soret band (taken at the beginning of a reaction) centred at 412nm, typical of a cobalt(II) complex. The band to the left of the Soret is due to the dihydroquinone and the band on the right of the Soret is a Q band of the cobalt porphyrin complex.

(b) uv/visible spectrum of the same cobalt porphyrin complex for which the Soret band (taken after 24 hours) is now centred at 430nm, typical of the cobalt(III) complex; the cobalt(II) band at 412nm is still visible. The Soret band shows a decrease in the intensity due to destruction of the porphyrin during the reaction with H_2TCQ and dioxygen. The band on the left at 300nm is typical of the TCQ absorption spectra.

To prove that the presence of dioxygen and metal were essential for the conversion of dihydroquinone into quinone, two different experiments were performed. These experiments were carried out only with two different cobalt porphyrin complexes. They were cobalt complexes of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',5'-di-tert-butyl-4'-hydroxyphenyl)porphyrin. The

reason for this choice was because the cobalt complexes of these porphyrins converted the dihydroquinone into quinone with differing median velocities. To prove that the presence of dioxygen was essential for the conversion of dihydroquinone to quinone to occur, the reaction shown in Scheme 58 was performed but in the absence of dioxygen. To perform the experiment an atmosphere of nitrogen was used. None of the cobalt porphyrin complexes was able to convert the dihydroquinone into the quinone. And in both cases no alterations of the values of the Soret bands was observed. To prove that the presence cobalt was essential, the reaction shown in Scheme 58 was carried out using the free base porphyrins of the cobalt complexes chosen. No conversion of dihydroquinone to quinone was found.

Performing experiments with imidazole as an axial ligand, two different cobalt porphyrin complexes were used. They were the cobalt porphyrin complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin because of its good reactivity in converting the dihydroquinone into the quinone, and the cobalt porphyrin complex of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin because under the experimental conditions used to perform the reaction illustrated in Scheme 58 this did not react. As expected, the use of imidazole as an axial ligand proved unsuccessful because no reaction was observed in its presence with both cobalt complexes. It is worth refering here the spectral changes observed due to the presence of imidazole. For the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, the Soret band was shifted from 416nm without imidazole to 432nm in the presence of it. The Q band was split into two bands, at 558nm and 600nm. The split into two bands is described in the literature as being due to the formation of a complex with dioxygen.[115] It is interesting that it was possible to see the split into two of the Q band, because in the literature the use of high pressures of dioxygen

is used for this effect to be observable.[115] Obviously the complex with dioxygen and the cobalt complex of this porphyrin in the presence of imidazole is very stable and easy to form. For the 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, the Soret band was shifted from 412nm to 436nm and the Q band from 536nm to 554nm. It was reported in the literature that the formation of a fifth ligand complex does not alter the wavelength of the Soret band, but only its intensity. The formation of a fifth ligand complex alters the value of the Q band to higher wavelengths. So the alteration here of the Soret band must be due to the formation of a sixth complex where the sixth ligand is dioxygen, as before. The possibility of the sixth ligand to be another imidazole molecule must be considered. However according to the literature the formation of it is less favourable than the formation of sixth ligand with dioxygen.[115]

The median velocity for these reactions was calculated by taking into account the solubility of the cobalt porphyrin complexes. In fact, some cobalt porphyrin complexes have very low solubility in this system and for these cases, the cobalt complex in solution was measured by the height of the Soret band by using the equation:

$$A = \varepsilon l c$$

where:

A - absorbance

ε -molar absorvity

l - cell width

c - concentration of the solution

To calculate the median velocity (V_m) for these reactions the equation below was used:

$$V_m = \frac{\text{moles substrate}}{\text{time}} \cdot \frac{1}{\text{moles catalyst}}$$

The table below shows the results.

Table 15. Median velocity for reactions between the cobalt porphyrin complexes with H_2TCQ and dioxygen

Aryl group[a]	Median velocity[b] (moles/min/mole catalyst)
Phenyl	0.95
4-Methoxyphenyl	0.95
3,4-Dimethoxyphenyl	0.95
3-Methoxyphenyl	0.63
3,4,5-Trimethoxyphenyl	0.38
2,4,5-Trimethoxyphenyl	0.63
3,4-Methylenedioxyphenyl	0.57
4-Chlorophenyl	0.133
3-Chlorophenyl	0.126
3,4-Di-tert-butoxy-4-hydroxyphenyl	9.0×10^{-3}
4-Biphenyl	0.06
4-Methylthiophenyl	not soluble
2,6-Dichlorophenyl	0.0
2,3,4,5,6-Pentafluorophenyl	0.0

a - Aryl group in 5,10,15,20-*tetrakis*arylporphyrin cobalt complexes
b - When the cobalt porphyrin complex was not soluble in the system, it was written "not soluble", and when reaction was not observed the velocity given was 0.0 moles per minute.

This system seems to work efficiently except for the fact that the cobalt porphyrin complexes were being destroyed during reaction and some of them did not react at all. To have a better idea about the efficiency and stability of the cobalt porphyrin complexes their turnover number was measured. Table 16 presents the values obtained.

Table 16. Turn over number for reaction between cobalt porphyrin complexes, H_2TCQ and dioxygen

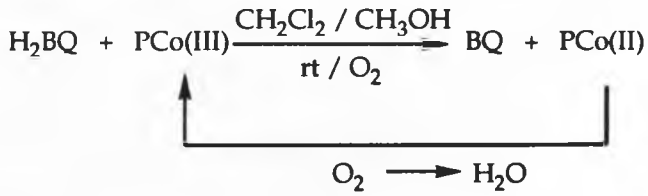
Aryl group[a]	Turnover Number
4-Chlorophenyl	92
3-chlorophenyl	102
2,6-Dichlorophenyl	no reaction
2,3,4,5,6-Pentafluorophenyl	no reaction
3,4-Methylenedioxyphenyl	64
3,5-Di-tert-buthoxy-4-hydroxyphenyl	82
4-Methylthiophenyl	not soluble
Phenyl	98
4-Methoxyphenyl	92
3-Methoxyphenyl	92
3,4-Dimethoxyphenyl	90
2,4,5-Trimethoxyphenyl	66
3,4,5-Trimethoxyphenyl	64
4-Biphenyl	70

a - Aryl group in the 5,10,15,20-*tetraki*sarylporphyrin cobalt complexes

It has to be said that the numbers obtained during these experiments were doubled since reaction of each cobalt porphyrin complex is the result of adding two electrons to dioxygen.

Usually, the turnover number of a successful catalyst is of the order of thousands or more. The cobalt porphyrin complexes used here have low turnover numbers. This was a main problem to be solved in this work.

4.4.4. Study of the catalytic cycle with H_2BQ



P - Porphyrin ligand

Scheme 59.

With this dihydroquinone (Scheme 59) the results observed show some differences, and some similarities to the previous ones:

(i) most of the cobalt porphyrin complexes were converting the dihydroquinone into the quinone, but with much longer reaction times;

(ii) some of the cobalt porphyrin complexes did not react at all, the same ones as in reactions with H_2TCQ, that is 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl)porphyrin cobalt complexes;

(iii) the cobalt porphyrin complexes were also being destroyed during these reactions except for the two that were not reacting at all;

(iv) the uv/visible spectrum revealed a Soret band always centred in the cobalt(II) wavelengths that after 24 hours would still be centred in the cobalt(II) wavelength and showing a shoulder or another Soret band at the cobalt(III) wavelength (figure 15). The cobalt complexes of 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl)porphyrin did not show any shoulder or band;

(v) changing the solvent to acetonitrile decreased the reaction velocity but did not alter the results.

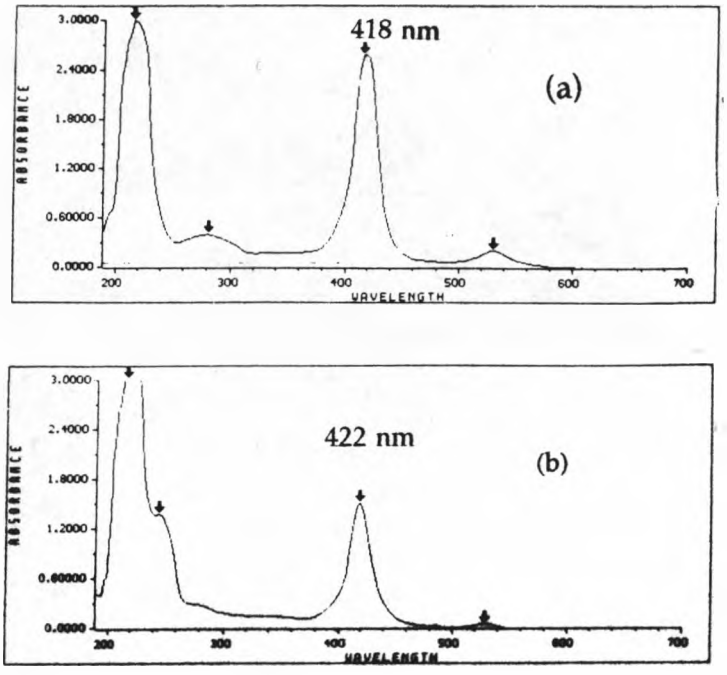


Figure 15. (a) uv/visible spectrum of a cobalt porphyrin complex taken at the beginning of the reaction with H_2BQ and dioxygen. The Soret band is centred at 418nm, the value corresponding to the cobalt(II) species. To the left are the bands characteristic of the H_2BQ and to the right the Q band of the cobalt porphyrin.

(b) uv/visible spectrum of the same cobalt porphyrin complex taken after 24 hours of a reaction with H_2BQ and dioxygen. In the example shown, the Soret near 422nm corresponds mainly to the cobalt(II) species.

To prove that the presence of dioxygen and metal were essential for the conversion of dihydroquinone into quinone, the same experiments performed for the reactions with H_2TCQ were carried out with H_2BQ. Again these experiments were carried out with only two porphyrin cobalt complexes. These were the cobalt complexes of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',5'-di-tert-butyl-4'-hydroxyphenyl)porphyrin. To prove that the presence of dioxygen was essential for the conversion of dihydroquinone to quinone, the reaction

shown in Scheme 59 was performed but in the absence of dioxygen. To perform the experiment an atmosphere of nitrogen was used as previously. Neither of the cobalt porphyrin complexes were able to convert the dihydroquinone into the quinone. And in both cases no alterations of the values of the Soret band was observed. To prove that the presence of cobalt was essential, the reaction shown in Scheme 59 was carried out using the free base porphyrins of the cobalt complexes chosen. No conversion of dihydroquinone to quinone was observed.

Performing experiments with imidazole as an axial ligand, two different cobalt porphyrin complexes were used. They were the cobalt complexes of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin. The reasons for the choice were the same as before for the reactions with H_2TCQ. As expected, the same results as with H_2TCQ were obtained.

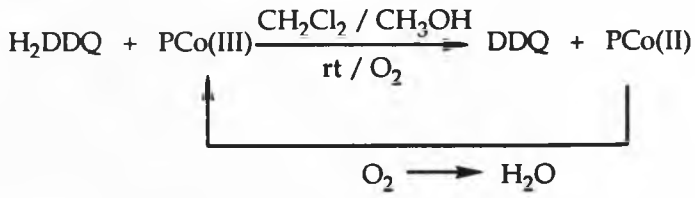
Most of the reactions with H_2BQ were not complete after 24 hours. Indeed, only five of the cobalt porphyrin complexes converted all of the dihydroquinone into quinone. Table 17 shows the median velocity calculated for the five cobalt complexes.

Table 17. Median velocity for reactions of cobalt porphyrin complexes with dihydrobenzoquinone and dioxygen

Aryl group[a]	Median velocity (moles/min/mole catalyst)
4-Methoxyphenyl	0.032
Phenyl	0.012
3,4-Dimethoxyphenyl	4.5×10^{-3}
2,4,5-Trimethoxyphenyl	4.5×10^{-3}
3,5-Di-tert-butyl-4-hydroxyphenyl	2.9×10^{-3}

a - Aryl group in 5,10,15,20-*tetrakis*arylporphyrin cobalt complexes

4.4.5. Study of the catalytic cycle with H_2DDQ



P - Porphyrin ligand

Scheme 60.

With this dihydroquinone (Scheme 60) results were quite different from the results obtained with the first two, H_2TCQ and H_2BQ:

(i) evidence for reaction was observed by tlc for all but 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluorophenyl)porphyrin cobalt porphyrin complexes ;

(ii) the cobalt porphyrin complexes were destroyed but not to the same degree as in the reactions with H_2TCQ or H_2BQ;

(iii) uv/visible monitoring revealed a Soret band always centred on the cobalt(II) species at the beginning of the reactions but, during the reaction an equilibrium situation of two Soret bands due to cobalt(II) and cobalt(III) was always observed. By the end of the monitoring period, at around 24 hours after starting the reactions, the Soret band for all of the cobalt porphyrin complexes, except for the cobalt complexes of 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl)porphyrin, had become broad and centred on cobalt(III), as shown for example in figure 16;

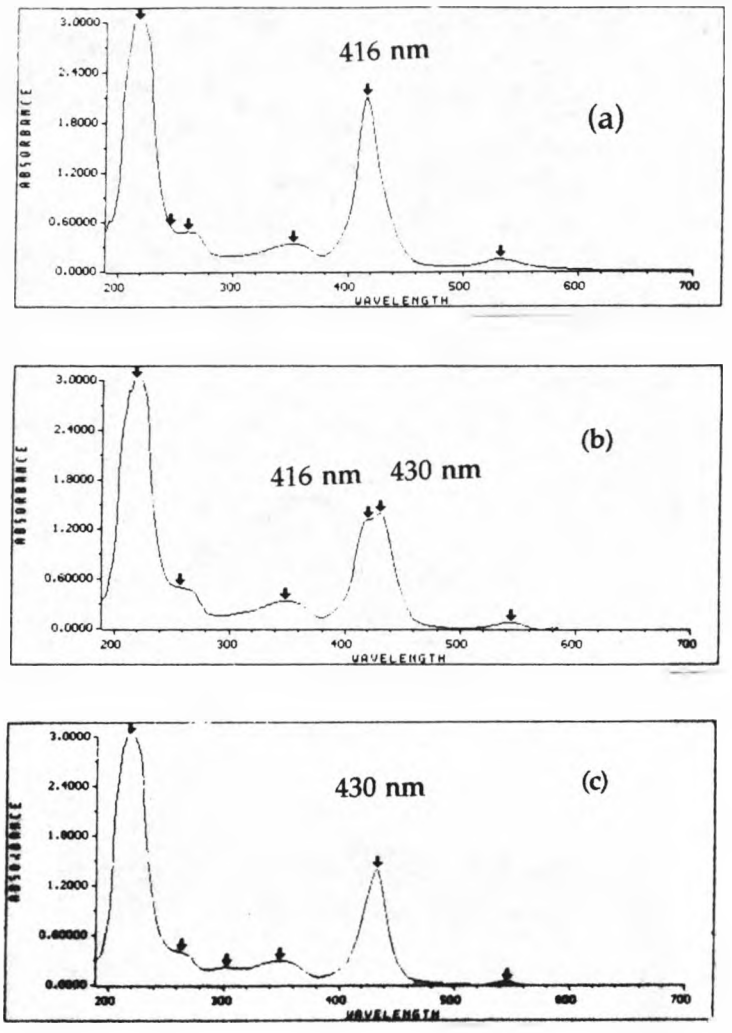


Figure 16. (a) uv/visible spectrum of a cobalt porphyrin complex taken at the beginning of a reaction with H_2DDQ. The Soret band appears at 416nm, a value typical for the Soret band of a cobalt(II) porphyrin complex. The band on the left is due to the H_2DDQ and the band on the right is a Q band of the cobalt porphyrin complex.

(b) uv/visible spectrum of the same cobalt porphyrin complex taken during reaction. The Soret band region shows a doublet for equilibrium between cobalt(II) and cobalt(III) species, with Soret bands at 416 and 430nm respectively.

(c) uv/visible spectrum taken at about 24 hours after initiation of reaction of H_2DDQ with dioxygen. The Soret band is centred at 430nm, corresponding to the cobalt(III) species, but its broad shape is indicative of the presence of some cobalt(II). On the left of the Soret band is the band characteristic of H_2DDQ, and on the right the Q band.

Interestingly, except for the cobalt porphyrin complexes of 5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluorophenyl)porphyrin and 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin which did not react at all, all the others showed evidence for the formation of DDQ after only 2 hours. However, after 24 hours, reaction monitoring showed only the same evidence for some reaction, viz., there had been no evolution in the formation of products. The amount of H_2DDQ converted into DDQ was not calculated since none could be detected in the uv/visible spectra. As a consequence of the results obtained for H_2DDQ, no median rates where calculated.

Studies for the importance of the presence of dioxygen and metal were investigated as before and as expected no reactions were observed.

The effect of imidazole as a ligand was investigated as previously. The same results were observed as before for the reactions involving H_2TCQ and H_2BQ dioxygen and the cobalt porphyrins complexes.

4.5. Discussion of Results and Mechanisms

4.5.1. The mechanism

As was discussed in the introduction of this thesis, porphyrin cobalt complexes bind dioxygen even without an axial ligand but, in the latter case, only to a very small extent. Some research goes even further in suggesting that the presence of an axial ligand is essential for the cobalt porphyrin to bind with dioxygen.[114] However, it has been reported also that removal of the oxygen as superoxide from the adduct formed with cobalt porphyrin complexes can be difficult when certain axial ligands are used.[104] In the system developed here, no formal axial ligand was used for

the reasons already stated, and spectroscopic data show an easy interconversion of cobalt(II) to cobalt(III) with subsequent conversion of dihydroquinone to quinone. Something is happening in these reactions that makes the absence of a ligand unimportant and perhaps this can help to explain some of the results obtained.

Step I

The first step in these reactions must be the reaction of a cobalt(II) porphyrin complex with dioxygen to produce cobalt(III). However, this does not occur in a simple single step. According to studies reported for protoporphyrin IX dimethyl ester the reaction of cobalt(II) porphyrin complex with dioxygen in methanolic solutions to produce cobalt(III) follows several steps (Scheme 61).[194,195,196]

$$PCo(II) + CH_3OH \rightleftharpoons [PCo(II)(CH_3OH)] \quad \text{(i)}$$

$$[PCo(II)(CH_3OH)] + O_2 \rightleftharpoons [PCo(II)(CH_3OH)(O_2)] \quad \text{(ii)}$$

$$[PCo(II)(CH_3OH)(O_2)] + CH_3OH \rightleftharpoons [PCo(II)(CH_3OH)(O_2H)]^+ + CH_3O^- \quad \text{(iii)}$$

$$[PCo(II)(CH_3OH)(O_2H)]^+ + CH_3OH \rightleftharpoons [PCo(III)(CH_3OH)_2]^+ + HO_2^\cdot \quad \text{(iv)}$$

$$[PCo(III)(CH_3OH)_2]^+ \rightleftharpoons [PCo(III)(CH_3O)(CH_3OH)] + H^+ \quad \text{(v)}$$

P-Porphyrin ligand

Scheme 61.

In a first step the cobalt(II) porphyrin complex is approached by a methanol molecule that acts as an axial ligand [reaction (i); Scheme 61]. Once "activated" the five co-ordinated cobalt(II) porphyrin complex binds dioxygen [reaction (ii); Scheme 61]. A proton from a methanol molecule is than released to bind to the species $[PCo(II)(CH_3OH)O_2]$ (strictly equivalent to a $Co(III)O_2^{-\bullet}$) in reaction (iii) of Scheme 61. The new $HO_2^\bullet$ radical

easily leaves the cobalt(III) porphyrin complex by exchange with a methanol molecule or a methoxy ion [reactions (iv); Scheme 61]. This research also revealed that solutions of cobalt(II) porphyrin complex in aprotic non co-ordinating solvents such as chloroform, methylene chloride and benzene, in the presence of air are very stable.[195] But in alcoholic solvents the cobalt(II) porphyrin solutions are only stable in the absence of oxygen. In the presence of air, the Soret and the Q bands were reported to shift with time as can be seen in figure 17.[195]

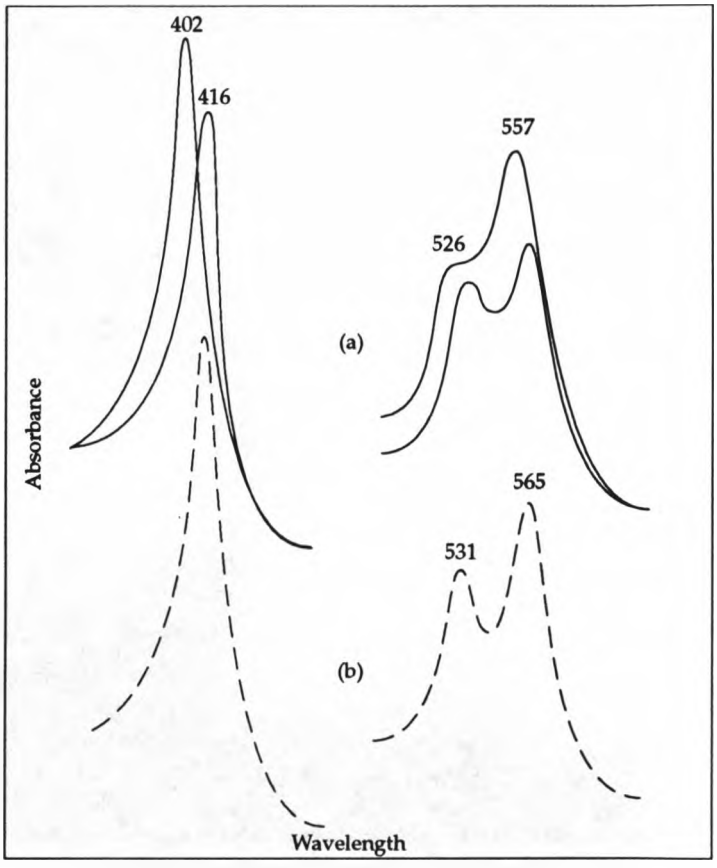


Figure 17. (a) Spectral changes in a solution of PCo(II) (Soret at 402nm and a Q band at 557nm) when dissolved in methanol and exposed to air. The Soret band shifts with time to give a new band at 416nm and a Q band split into two appearing at 526nm and 557nm corresponding to the species [Co(III)P(CH_3O)(CH_3OH)].[195] (b) Spectrum of a solution of [PCo(III)Cl] in methanol; upon dissolution in methanol, the complex releases its chloride yielding [PCo(III)(CH_3O)(CH_3OH)].[195]

As shown in figure 18, the complex [PCo(III)Cl] immediately releases its chloride on dissolution in methanol and equilibrates as in Scheme 62 to give a spectrum identical to the one obtained for methanol solutions of PCo(II).[195]

$$[PCo(III)Cl] \overset{Cl^-}{\rightleftharpoons} [PCo(III)(CH_3OH)_2]^+ \overset{H^+}{\rightleftharpoons}$$

$$[PCo(III)(CH_3O)(CH_3OH)] \overset{CH_3O^-}{\rightleftharpoons} [PCo(III)(CH_3O)_2]^-$$

P-Porphyrin ligand

Scheme 62.

A very important consequence of the use of a protic solvent like methanol, is prevention of the formation μ-peroxo-dimers, which would stop catalytic activity. In fact, the presence of protons was reported to help to eliminate superoxide [reactions (iii) and (iv); Scheme 61], by producing $HO_2^{\bullet}$ which is easy to eliminate.

Step II

The next step in these reactions appears to be electron transfer from the dihydroquinone to [PCo(III)(CH_3O)(CH_3OH)] or any of the species indicated in reaction (v) (Scheme 61). The mechanism in Scheme 63 is proposed. As the dihydroquinone gives electrons to the cobalt(III) porphyrin complex, it needs to get close enough for the reaction to occur. In other words, it needs to act as a ligand by replacing methanol or methoxide in the species [PCo(III)(CH_3O)(CH_3OH)] [reaction (i); Scheme 63]. As methanol is a better leaving group this is presumably the one being replaced.[195]

$$[PCo(III)(CH_3O)(CH_3OH)] + H_2Q \rightleftharpoons [PCo(III)(CH_3O)(H_2Q)] + CH_3OH \quad (i)$$

$$[PCo(III)(CH_3O)(H_2Q)] \rightleftharpoons [PCo(II)(HQ)] + CH_3OH \quad (ii)$$

$$[PCo(II)(HQ)] \rightleftharpoons PCo(II) + HQ^{-\bullet} \quad (iii)$$

P-Porphyrin ligand

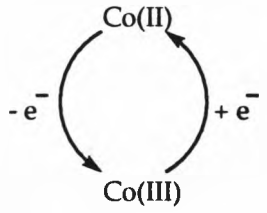
Scheme 63.

Other research has shown that replacement of methanol in [Co(III)(CH_3O)(CH_3OH)] by other ligands is a competitive process and depends on the electron-donating ability of the ligands. However, the order of reactivity of the ligands as reported was somewhat puzzling because it was expected that the most basic ligand should react at the fastest rate; just the opposite effect was found.[195] It appears that methoxide in the [Co(III)(CH_3O)(CH_3OH)] species strongly increases the electron density at the trans-axial positions, and favours entry of less basic ligands.[195] π-Back bonding was reported to be an important interaction and so the better the capacity of the ligand to establish this kind of π-back bonding the easier the replacement of methanol. These reactions appear to follow an S_N1 mechanism, in which π-back bonding stabilises the transition state.[195] Once replaced by dihydroquinone, electron transfer to the cobalt(III) porphyrin complex occurs [reaction (ii); Scheme 63] and a methoxide ligand is released. The newly formed cobalt(II) porphyrin complex is finally recovered to start a new cycle [reaction (iii); Scheme 63]. Following this discussion and considering the dihydroquinones used in this work, it would be expected that, where π-back bonding is more efficient, then that dihydroquinone would react faster.

4.5.2. The results

4.5.2.1. Factors involved

No linear relationship between the redox potential of the cobalt porphyrin complexes and reaction velocity was found. However, after analysis of the results, it appears that lower $E_{1/2}$ potentials give the best results, possibly because they imply a less stable cobalt(II) porphyrin complex and, as a consequence, this results in a more labile system in which cobalt(II) and cobalt(III) are easily interconvertible (Scheme 64).



Scheme 64.

This does not always happens as can be seen by the fact that the redox potential order does not follow the order of median velocity. In such cases, what has to be taken into account is the porphyrin structure and the facility for the dihydroquinone to get close enough to the metal centre for an electron to be transferred [reaction (i); Scheme 63]. This was particularly well shown by the example of the cobalt complex of 5,10,15,20-*tetrakis*(3',5'-di-tert-butyl-4'-hydroxyphenyl)porphyrin. The redox potential of this cobalt complex is the lowest found in this work but its median velocity was one of the lowest. It is believed that this can be explained by the steric effect of the bulky t-butyl groups that make the approach of the dihydroquinones to the metal centre difficult. Finally, the structure of the

different dihydroquinones must also be taken into account since they have different basicities and π-back bonding capacities.

4.5.2.2. Comparison of the three dihydroquinones

Consider H_2BQ for which slow reactions are found. Analysis of the uv/visible spectra for reactions with this dihydroquinone reveals that the cobalt(II) porphyrin complex is the major species observed. This means that reaction with dioxygen to form cobalt(III) is being slowed or prevented. As oxidation of this dihydroquinone is observable, it is acceptable to say that reactions of [PCo(III)(CH_3O)(CH_3OH)] species with H_2BQ occurs. However, the cobalt(III) species were never detected, which leads to the conclusion that reaction with H_2BQ is fast but the reaction of the cobalt(II) species with dioxygen is not. These observations do not apply to H_2DDQ or H_2TCQ for which cobalt(III) species were detected spectroscopically. This last observation means that the dihydroquinone (H_2BQ) is directly responsible for inability to detect cobalt(III) spectroscopically. When considering reactions involving H_2BQ as in reaction (ii) [Scheme 63] where the intermediate [PCo(II)HQ] was proposed, it appears that this species is stable enough to be detected in the uv/visible spectrum and to slow down the reaction. In fact, being a smaller molecule compared with H_2TCQ and H_2DDQ, the approach to the metal centre is facilitated. On the other hand, H_2BQ is the most basic of the three dihydroquinones used but its π-back bonding capacity balances this disadvantage and the replacement of methanol occurs fast. Once replaced, the basicity stabilises the new complex.

With H_2TCQ, faster reactions were observed. The uv/visible spectra for these reactions show most of the time, as mentioned before, the

presence of cobalt(III) porphyrin species suggesting easy electron transfer from cobalt(II) to dioxygen. On the other hand, the conversion of dihydroquinone to quinone is also fast, as can be concluded by the results obtained for the median velocity of these reactions (Table 15), which means that electron transfer from the dihydroquinone to the metal centre is not a problem. However, this must be the rate controlling step of the reaction, because cobalt(III) species were detected at all times and not cobalt(II). In agreement with the discussion of mechanism for these reactions (Scheme 63), the electronegative chlorine atom must make the dihydroquinone less basic (more acidic) which favours the replacement of methanol in reaction (i) of Scheme 63 to produce [PCo(III)HQ(CH_3O)]. The size of the chlorine atoms are thought to make the approach of this dihydroquinone to the metal centre more difficult, allowing for the detection of cobalt(III) species spectroscopically.

Finally, with H_2DDQ for which evidence of reaction was found. Here the uv/visible spectrum shows an equally balanced equilibrium between cobalt(II) and cobalt(III) species, with a tendency for an increase in the amount of cobalt(III) with time. Nevertheless, reactions with this dihydroquinone are not efficient as measured by the medium velocity. The chlorine and the cyano groups make this dihydroquinone less basic and it should be a good ligand in accord for replacing methanol but, again, the size of both makes approach to the metal centre more difficult. In this case, an equilibrium of both cobalt(II) and cobalt(III) species was observable but there was no great conversion to quinone. This result leads to the conclusion that both steps, electron transfer from cobalt(II) to dioxygen and from H_2DDQ to cobalt(III), are difficult and slow. In conclusion, the size of its substituents makes the approach of H_2DDQ to the metal centre slow enough that cobalt(III) species can be detected but, once inserted as a ligand,

the resulting cobalt(III) complex is stable enough to stop reaction with dioxygen. From the results obtained after 24 hours, it can be said that the approach to the metal centre is the rate controlling factor and the amount of cobalt(III) was starting to become greater than the amount of cobalt(II).

4.5.2.3. Cobalt complexes with which no reaction could be observed

The cobalt complexes of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-*tetrakis*(2',3',4',5',6'-*penta*fluorophenyl)porphyrin are considered separately from the above discussion. As was observed, these two porphyrins show uv/visible spectra in which only cobalt(II) species are observed. If cobalt(III) is ever formed it is not apparent for any of the three dihydroquinones. They did react in the sodium borohydride/dioxygen test. It is believed that these cobalt complexes reacted because pure dioxygen was being bubbled through the reaction mixture giving a high concentration of dioxygen and shifting the equilibrium towards the formation of $Co(III)O_2^{\bullet-}$. In the reaction with dihydroquinones, the available dioxygen is not enough to de-locate the equilibrium towards formation of $Co(III)O_2^{\bullet-}$. The free energies for electron transfer from cobalt(III) to cobalt(II) are negative for these two metalloporphyrins, which means that formation of cobalt(II) is the more favourable. This happens with all the cobalt porphyrin complexes used in this work but, the equilibrium constant calculated from the Nernst equation for these reactions (Table 9 of Chapter 3), shows that the largest values of redox potential were recorded in the order 3-methoxyphenyl>2,3,4,5,6-pentafluorophenyl>3-chlorophenyl>2,6-dichlorophenyl. With 2,3,4,5,6-pentafluorophenyl and 2,6-dichlorophenyl, the groups in the ortho positions make the phenyl rings adopt a position close to 90° to the plane of the porphyrin ring so as to avoid interaction between

the orbitals of the ortho group and the β-protons. This protects the metal centre by making the approach of other molecules more difficult. Taken together, the equilibrium constant and the steric effect explain the results obtained.

4.5.2.4. Discussion of the median velocities obtained for each set of reaction with the different dihydroquinones

Reaction with H_2TCQ

All the redox potentials for the cobalt porphyrin complexes have positive values (Table 9). The redox potentials measured ($E_{1/2}$; Table 9) refer to the reduction of cobalt(III) to cobalt(II) porphyrin complexes. They give a measure of the relative stability of cobalt(II) and cobalt(III). Being positive means that under standard conditions the cobalt(II) porphyrin complex will be formed in preference to the cobalt(III) porphyrin complex.

For the cobalt porphyrin complexes having 3- or 4-substituted phenyl rings the calculated median velocity decreases in the order: phenyl = 4-methoxyphenyl > 3-methoxyphenyl > 4-chlorophenyl > 3-chlorophenyl > 4-biphenyl (Table 15). Here the increase of the median velocity correlates with the decrease of the respective redox potentials. The highest velocities were found for the cobalt porphyrin complexes with the lowest redox potentials. These orders were expected since the lowest redox potentials imply an increased stability of the cobalt(III) porphyrin complex. This increased stability of cobalt(III) porphyrin complex makes the system cobalt(II)/cobalt(III) more labile and as a consequence increases the median velocity for the reaction involved with H_2TCQ and dioxygen. The 5,10,15,20-*tetrakis*(3'-methoxyphenyl)porphyrin cobalt complex, however, does not correlate with the redox potential. This cobalt complex shows a

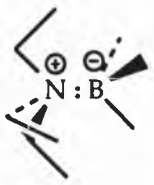
redox potential ($E_{1/2}$; Table 9), already discussed in Chapter three, as being exceptionally high. Although no explanation was given another example was referred to where this group behaves in a similarly exceptional manner.

For the porphyrin having 3- and 4-substituents in the phenyl rings, the order for the median velocity calculated was 3,4-dimethoxyphenyl > 3,4,5-trimethoxyphenyl > 2,4,5-trimethoxyphenyl > 3,4-methylenedioxyphenyl > 3,4-di-*tert*-butyl-4-hydroxyphenyl. The order for the redox potential obtained was 3,4-di-*tert*-butyl-4-hydroxyphenyl < 3,4-methylenedioxyphenyl < 2,4,5-trimethoxyphenyl < 3,4-dimethoxyphenyl < 3,4,5-trimethoxyphenyl. There is no correlation between the redox potential and the median velocity for this group of cobalt porphyrin complexes. For porphyrins with bulky substituents the approach of H_2TCQ to the metal centre is made difficult, which cannot always be overcome by a favourable low redox potential. Although 5,10,15,20-*tetrakis*arylporphyrins can have their aryl groups in the same plane as the porphyrin ring, it is more probable that they will be in a position close to 90°C. In such a position the substituents offer more steric hindrance to the approach of other species to the metal centre.

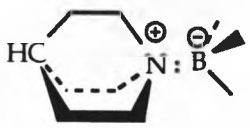
Molecular complex formation is often readily detected by the appearance of an intense "charge transfer" band in the ultraviolet or visible spectrum.[197] However, such bands have been difficult to detect for 1:1 porphyrin complexes with quinones. The complex is reported to be very weak, and only a slight broadening and drop in the intensity of the porphyrin absorptions bands are detected.[197] It was reported that the planes of the porphyrin and the quinone are approximately parallel in the complex and the oxygen atoms of the quinone are not co-ordinated to the metal ion of metallated porphyrins.[197] The interaction must occur between the porphyrin ring and the quinoid ring.[197] In particular the

cobalt complex of 5,10,15,20-*tetrakis*(4-biphenyl)porphyrin where the π-system of the biphenyl substituents can be in the same plane as the porphyrin ring a complex with the quinone ring is highly probable. And although the redox potential of the cobalt complex of 5,10,15,20-*tetrakis*(4-biphenyl)porphyrin was not measured for the reasons already mentioned in Chapter 3 (*loc. cit.*) the low median velocity in the reaction with H_2TCQ can be understood in terms of the formation of a porphyrin:quinone complex.

For the cobalt complexes of 5,10,15,20-*tetrakis*(3',4'-methylenedioxyphenyl)porphyrin a higher median velocity than that of 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin would be expected because its the redox potential is much lower (Table 9). It is believed the reason for the median velocities to be just the opposite of that expected is the rigid structure of the aryl substituent in 5,10,15,20-tetrakis(3',4'-methylenodioxyphenyl)porphyrin. For the aryl substituent 3,4-dimethoxyphenyl the methoxy groups can move within certain limits. This movement is enough to allow the approach of other species to the metal centre namely dioxygen. For the aryl substituent 3,4-methylenodioxyphenyl the methylenedioxy bridge keeps the two oxygen atoms in a more rigid position. This rigid structure might help to make the approach to the metal center more difficult. There are other examples in the literature where the presence of a rigid structure had similar effect.[198] An example is that of complex **[52]** formed between triethylamine and trimethyl boron. This complex dissociates extremely readily.[198] On the other hand, the complex **[53]** formed between trimethyl boron and quinuclidine, which can be viewed as having three ethyl groups on the nitrogen that are "held back", is very stable.[198]



[52]



[53]

The difference in the stability is not due to differences in electron availability at the nitrogen atom, since both amines differ very little in their base strength.[198] The uptake of relatively bulky groups such as trimethyl boron is more difficult when a rigid structure prevents the approach at the nitrogen.[198]

Reaction with H_2BQ

The median velocities obtained for the reaction of the porphyrin cobalt complexes with dioxygen and H_2BQ are presented in Table 17. Only five cobalt complexes had complete reactions (100% conversion of H_2BQ into BQ) before 24hours. For the five cobalt complexes the order obtained for decreasing median velocity was 4-methoxyphenyl > phenyl > 3,4-dimethoxyphenyl = 2,4,5-trimethoxyphenyl > 3,5-di-tert-butyl-4-hydroxyphenyl. For the respective increase in redox potentials the order was 3,5-di-tert-butyl-4-hydroxyphenyl < 4-methoxyphenyl < phenyl < 2,4,5-trimethoxyphenyl < 3,4-dimethoxyphenyl. Reactions with 5,10,15,20-*tetrakis*(3,5-di-*tert*-butyl-4-hydroxyphenyl)porphyrin cobalt complex were already discussed as being controlled by steric hindrance. So again it is not a surprise to see that for the cobalt porphyrin cobalt complex with such substituent, shows the lowest median velocity. It should be noted however that although the median velocity is very low, the low redox potential of 5,10,15,20-*tetrakis*(3,5-di-*tert*-butyl-4-hydroxyphenyl)porphyrin cobalt complex is indicative of a increased stability of cobalt(III). This

explains why, in spite of the low median velocity, 5,10,15,20-*tetrakis*(3,5-di-*tert*-butyl-4-hydroxyphenyl)porphyrin cobalt complex still converts all H_2BQ to BQ in less than 24 hours reaction. For the cobalt porphyrin complexes having the groups 3,4-dimethoxyphenyl and 2,4,5-trimethoxyphenyl the same value for the median velocity was obtained. From the respective values for the redox potentials the cobalt complex with the groups 2,4,5-trimethoxyphenyl should have a higher median velocity. However the steric hindrance is high due to the methoxy group in the 2-position of the phenyl ring slowing down the reaction. All the other cobalt porphyrin complexes whose median velocities were not measured must form a very stable complex with the dihydroquinone as already discussed.

Reaction with H_2DDQ

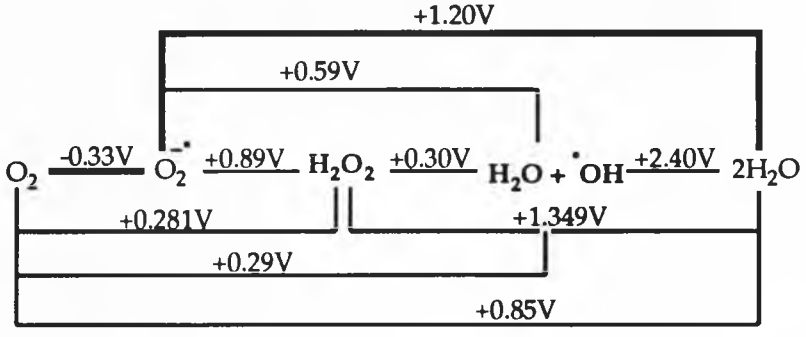
With H_2DDQ the median velocities were not calculated for the reason already mentioned. Therefore no discussion about their relative values will be done.

4.6. Investigation of the Destruction of the Cobalt Porphyrin Complexes During the Oxidation Reactions

4.6.1. The species involved in the destruction of the metalloporphyrins

The reactions of cobalt porphyrin complexes with H_2TCQ and dioxygen were quite successful except for the fact that the cobalt complexes were slowly destroyed at the same time.

Analysing the reactions involved in the conversion of dioxygen to water and considering the reaction conditions used, it is found that the formation of very reactive species such as superoxide or hydroxy radicals can occur (Scheme 65).[199] In fact, it is believed that during these reactions, formation of hydrogen peroxide and hydroxyl radicals occurs in successive steps for which donation of electrons and protons are involved (Scheme 66).



Scheme 65.

$$[PCo(II)(CH_3OH)(O_2)] + CH_3OH \rightleftharpoons [PCo(II)(CH_3OH)(O_2H)]^+ + CH_3O^- \quad (i)$$

$$[PCo(II)(CH_3OH)(O_2H)]^+ + CH_3OH \rightleftharpoons [PCo(III)(CH_3OH)_2]^+ + HO_2^{\bullet} \quad (ii)$$

$$HO_2^{\bullet} + e^- \rightleftharpoons HO_2^- \quad (iii)$$

$$HO_2^- + H^+ \rightleftharpoons H_2O_2 \quad (iv)$$

$$H_2O_2 + e^- \rightleftharpoons HO^{\bullet} + HO^- \quad (v)$$

P-Porphyrin ligand

Scheme 66.

The cobalt(II) porphyrin complex which has a methanol as a fifth co-ordinated ligand, binds dioxygen and a proton can be transferred from a methanol molecule to protonate the new species, $Co(III)O_2^{-\cdot}$, as represented in Scheme 66 by $[PCo(II)(CH_3OH)(HO_2)]^+$ [reaction (i); Scheme

66]. The radical $HO_2^{\bullet}$ is than easily released as already discussed, [reaction (ii); Scheme 66]. This hydroperoxide radical $HO_2^{\bullet}$ can receive an electron to form HO_2^{-} which is then protonated to give hydrogen peroxide [reactions (iii) and (iv); Scheme 66]. Hydrogen peroxide easily breaks homolyticaly to give hydroxyl radicals [reaction (v); Scheme 66]. Superoxide and hydroxyl or hydroperoxide radicals are very reactive.

4.6.2. The species formed on destruction of porphyrin

Hydrogen peroxide and hydroxyl radicals are known to be able to attack metalloporphyrins, as discussed previously in Chapter 2 of this thesis.[167,170] According to the literature, these two species can attack metalloporphyrins at two different positions, as figure 18 illustrates, the *meso*- or the β-positions of the porphyrin ring, leading to degradation of the porphyrin by producing such compounds as (a) or (b) (figure 18); these are unable to act as catalysts.

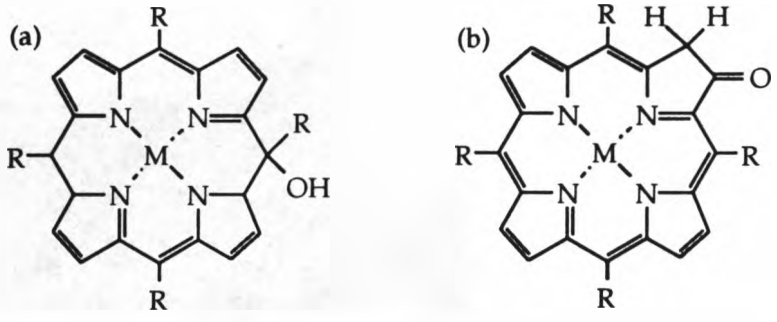


Figure 18. (a) attack at the *meso*-positions of a metalloporphyrin by H_2O_2 or $HO^{\bullet}$.[169] (b) attack at a β-position of a metalloporphyrin by H_2O_2 or $HO^{\bullet}$.[167]

It has been reported that the 5,10,15,20-positions in metalloporphyrins are susceptible to electrophilic attack.[169] It was also reported that metalloporphyrins of Mn(II), Fe(II) and Co(II), in which an easily accessible higher oxidation state is available to the metal ion, suffer

electrophilic attack whereas complexes of Fe(III), Co(III), Ni(II), Cu(II) and Zn(II) only suffer attack to a minor degree.[169] Taking this into consideration, it is believed that the fate of the cobalt porphyrin complexes in reactions with dioxygen and dihydroquinones is to suffer attack by the reactive species being formed (superoxide, hydroperoxide radical, hydroperoxide anion or hydrogen peroxide).

Because evidence has not been found for cobalt porphyrin complexes being destroyed in reactions involving 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluoro phenyl)porphyrin cobalt complexes, it was concluded that, in the absence of reaction, the reactive species were not being formed. In fact, repeating some of the reactions in the absence of dihydroquinone, it was found that no porphyrin degradation products were formed.

4.6.3. The formation of an active species in the destruction of the porphyrins

To prove the formation of active species such as hydrogen peroxide it was decided to use H_2TCQ in a reaction with the cobalt porphyrin complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin; two different experiments were carried out (Schemes 67 and 68).

$$H_2TCQ + PCo(III) \xrightarrow[rt\ /\ N_2]{CH_2Cl_2\ /\ CH_3OH} \text{No } H_2O_2 \text{ Detected}$$

P-Porphyrin ligand

Scheme 67.

In a first experiment (Scheme 67), the porphyrin cobalt complex was reacted with H_2TCQ using the already reported experimental conditions,

but under nitrogen. A sample of this solution was extracted into water but a test for hydrogen peroxide proved negative. This test was done with an indicator strip that changes to a blue colour when hydrogen peroxide is present (Merck product).

$$H_2TCQ + PCo(III) \xrightarrow[rt\ /O_2]{CH_2Cl_2\ /\ CH_3OH} \text{Detection of } H_2O_2$$

P-Porphyrin ligand

Scheme 68.

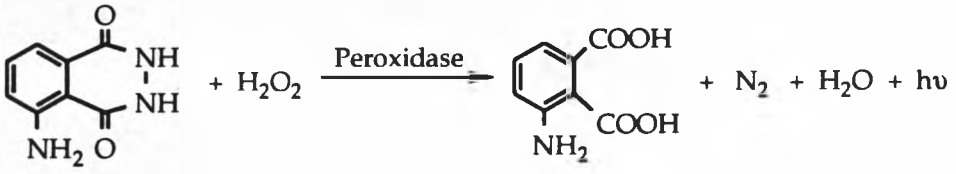
In a second experiment the reaction was exposed to air as illustrated in Scheme 68. In this experiment the test for hydrogen peroxide was positive.

Although this test for hydrogen peroxide is quite valid, an analytical technique was required to confirm this result specifically for hydrogen peroxide. The analytical technique chosen to prove the formation of hydrogen peroxide was chemiluminescense. Chemiluminescence arises when a chemical reaction produces an electronically excited state, which emits light as it returns to its ground state.[200] Such reactions are common in biological systems where the phenomenon is called bioluminescence.[200] In the latter part of the 19th century it was found that rather simple organic compounds (non-biological) could give rise to chemiluminescence.[200,201] Today, many chemiluminescent systems are known, biological as well as non-biological.[200]

For analytical applications in the liquid state, a few different luminescent species are of particular importance, luminol and lucigenin, and siloxanes. Methods based on these particular compounds have already achieved wide application because analysis is rapid and very high sensitivities are possible.[200] For the purposes of this work, a system

utilizing luminol was used. The light produced was measured in a spectrofluorimeter. The systems tested were those illustrated in schemes 67 and 68.

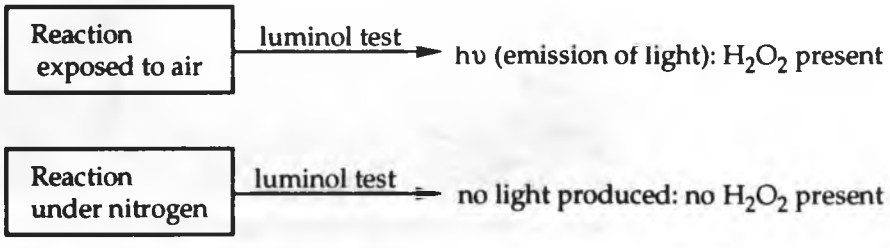
The luminol system makes use of the fact that it [5-amino-2,3-dihydro-1,4-phthalazinedione; **54**] is oxidised to a carboxylic acid by hydrogen peroxide with emission of a quantum of light when catalysed by a peroxidase (Scheme 69).[202,203]



[54]

Scheme 69.

Using horseradish peroxidase and luminol, solutions of the reactions carried out under nitrogen, or exposed to the atmosphere (Schemes 67 and 68) were tested. In both cases, any hydrogen peroxide being produced was extracted into water and then analysed for. Results are shown in Scheme 70:



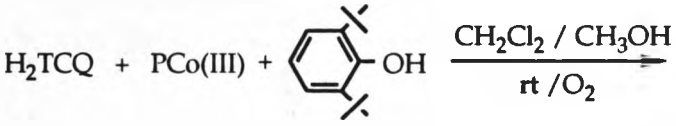
Scheme 70.

In the reaction done in air, hydrogen peroxide was produced but not in the reaction under nitrogen, in which neither was conversion of dihydroquinone to quinone observed.

At this stage of the work it seemed desirable to find a way of preventing the attack of hydrogen peroxide on the porphyrin or to synthesise a porphyrin which was stable to such oxidative attack.

4.6.4. Attempts to stop the attack on porphyrins by hydrogen peroxide

To avoid the attack from hydrogen peroxide, a system with a radical scavenger, 2,6-di-tert-butyl-phenol, was built (Scheme 71). As discussed earlier it is believed, that the first species to be formed on the way to the formation of hydrogen peroxide are the radicals superoxide $O_2^{-\bullet}$ or hydroperoxide radical $HO_2^{\bullet}$ [reaction (iii); Scheme 66]. Therefore, it was expected that a radical scavenger should trap this species before they could attack the cobalt porphyrin.



P-Porphyrin ligand

Scheme 71.

When carrying out this reaction (Scheme 71), degradation of the cobalt complexes was still observed and a luminescence test showed the formation of hydrogen peroxide once more. It was observed that in the presence of 2,6-di-tert-butyl-phenol the cobalt porphyrin complex was being destroyed faster than when in its absence. Also in the chemiluminescence test the amount of light detected was of higher intensity when 2,6-di-tert-butyl-phenol was present. Figure 19 illustrates the graphics obtained in the chemiluminescence tests for a reaction done in the presence of 2,6-di-tert-butyl-phenol [graphic (a); figure 19] and in its absence [graphic (b); figure 19].

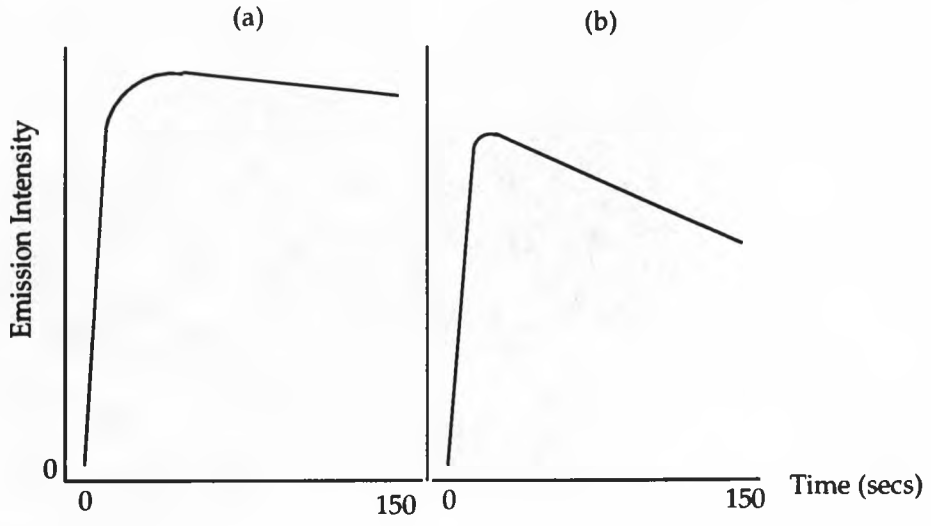
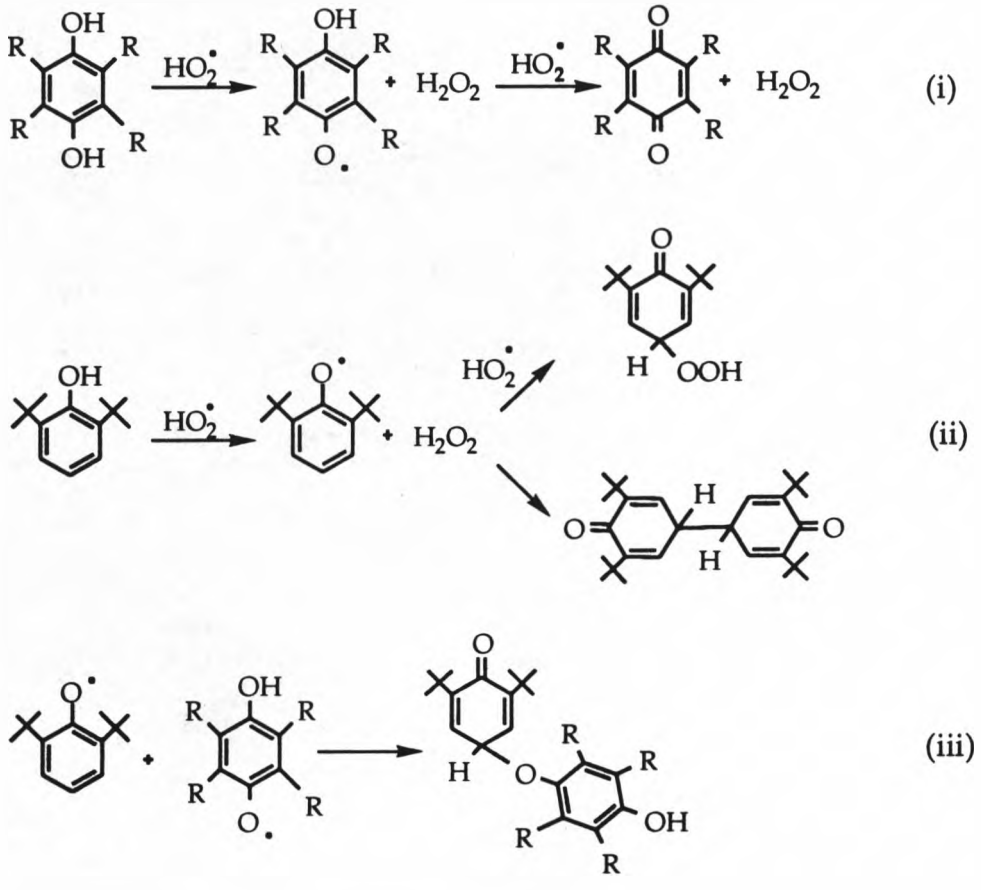


Figure 19. Detection of hydrogen peroxide produced by luminescence. Luminescence is detected in reactions of luminol [57] with hydrogen peroxide in the presence of a peroxidase. (a) - Corresponds to the hydrogen peroxide detection during the reaction of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin with H_2TCQ and dioxygen in the presence of a radical scavenger. During the 150 seconds of the experiment the intensity of the light emission did not decrease substantially. (b) - Corresponds to the hydrogen peroxide detected during the reaction of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin with H_2TCQ and dioxygen. The intensity of the light emission does not reach as high a value as in (a) and decreases faster during the 150 seconds of the experiment.

In the literature it was reported that chemiluminescence experiments with luminol would give a yield of 3-aminophthalic acid (Scheme 69), the product of reaction of luminol with hydrogen peroxide, proportional to the quantum yield of chemiluminescence.[204] Accordingly it can be said that in (a) of figure 19 the emission of light should correspond to a higher amount of 3-aminophthalic acid being formed than in (b). So in (a) the amount of hydrogen peroxide being detected is higher than in (b).

The presence of 2,6-di-tert-butyl-phenol might be acting as a "protector" for hydrogen peroxide. Scheme 72 illustrates how such "protection" might occur. Dihydroquinones are able to react with

hydroperoxide radical being produced [reaction (ii); Scheme 66] during reaction of cobalt porphyrin complexes with dioxygen.



Scheme 72.

In reaction (i) [Scheme 72] is illustrated how the hydroperoxide radical can react with the dihydroquinone to produce quinone and hydrogen peroxide.[205] Reaction (ii) [Scheme 72] illustrates what can happen to 2,6-di-tert-butyl-phenol when in the presence of hydroperoxide radicals. In a first step, 2,6-di-tert-butyl-phenol reacts with hydroperoxide radical to actually produce hydrogen peroxide. Then two possible reactions can occur with the phenoxide radical. In one the phenoxide radical combines with hydroperoxide radical and in the other with another phenoxide radical.[205] Because 2,6-di-tert-butyl-phenol phenoxide radical is not a hindered molecule at the 4-position, coupling with another

phenoxide radical can occur.[205] In reaction (iii) [Scheme 72] the possibility of the phenoxide radical reacting with a semiquinone is proposed. If combination of phenoxide and semiquinone occurred, then hydroperoxide radical would be left to react with the cobalt porphyrin complexes. This would explain why in the presence of 2,6-di-tert-butyl-phenol there was a higher amount of hydrogen peroxide being detected than when without 2,6-di-tert-butyl-phenol.

In a second attempt to avoid attack from hydrogen peroxide or other active radicals on the porphyrin cobalt complex, a small amount of palladium-on-charcoal was added to the reaction mixture. Palladium-on-charcoal is commonly used to destroy hydrogen peroxide at the end of reactions in which it has been utilised. Palladium(0) reduces hydrogen peroxide by producing hydroxyl anions that do not attack the metalloporphyrin. This reagent also proved to be ineffective.

No attempts were made to alter the structure of the porphyrin in order to make it resistant to attack. From the literature presented in the introduction to this thesis, it is believed that 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin cobalt complex, would be a good candidate for solving this problem. In such a case, another problem starts concernning, how to find a way to make the cobalt complex of such a porphyrin reactive enough. Due to lack of time no more research was done in this direction.

4.6.5. Attempts to identify the position of attack by hydrogen peroxide in cobalt porphyrin complexes

The cobalt porphyrin complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin was dissolved in a mixture of dichloromethane/methanol and allowed to react with an aqueous solution of hydrogen peroxide (70%w/w) at room temperature. After

work up, and removal of the solvents 'in vacuo', a yellow solid was obtained. The uv/visible spectrum of the yellow solid showed two broad bands, at 326 and 402nm, the second band being less intensive. ^{1}H-nmr provides evidence for the incorporation of three OH groups at the 5,10,15,20-positions of the porphyrin ring, and for the loss of the cobalt. No further investigation was carried out.

4.7. Conclusions

Although no oxidation of a methyl group to aldehyde was tried with the catalytic cycle developed, the work did prove its potential for oxidation of hydroquinones. Best results were obtained for cobalt complexes of porphyrin having the lowest redox potentials. There were exceptions, such as with the cobalt complex of 5,10,15,20-*tetrakis*(3'-methoxyphenyl)porphyrin, for which a high redox potential is accompanied by good catalytic activity. In summary, it cannot be said that the redox potential controls the overall catalytic activity, but it does give a very good idea about the probabilities of a cobalt porphyrin complex acting as a catalyst.

TCQ is very widely used as an oxidant and, for this reason, the results with it and the porphyrin cobalt complexes were very promising. On the other hand, it would be desirable to obtain similar results for DDQ, since this is a stronger oxidant than TCQ, and is also very much used.

Another aspect of this system that limits it is the destruction of the cobalt complexes by the hydrogen peroxide that is produced. If a polymer was attached to the cobalt complex, attack by hydrogen peroxide might be

prevented as in cytochrome P450 where a protein is wrapped around the metalloporphyrin. Also, the cobalt complexes of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin and 5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluorophenyl)porphyrin having the ortho-positions of the phenyl rings substituted are believed to give some protection from attack by hydrogen peroxide and merit more investigation.

Summary of results

During this research project, several new porphyrins were synthesised. The method of their synthesis was improved either by changing reaction conditions (in the "two-pot" method), or by using statistical methods, such as the Simplex approach (in the "one-pot" method). The new reaction conditions for the "two-pot" method are very mild, allowing improvements in yields and making purification and isolation of porphyrins easier. The reaction conditions used for the "one-pot" method not only improved the yields obtained when using older "one-pot" reaction conditions but also made isolation easier by the precipitation of the product porphyrins directly from the reaction medium for most porphyrins. In this work, the use of the Simplex method showed that reaction conditions can be optimised in order to achieve much better yields. Metallation of all porphyrins was effected successfully.

The redox potentials of the cobalt metallated porphyrins was measured using cyclic voltammetry. A correlation between substituent effect and the redox potential of the metallated porphyrins was investigated. In most cases, it was possible to correlate the redox potential with the structure of the porphyrin.

Using the cobaltoporphyrins in a catalytic system with dioxygen and dihydroquinones, it was found that the catalytic activity shown by the system cobalt(II)/cobalt(III) correlates with the redox potential for most of the porphyrins. This catalytic activity was found to be very sensitive to the porphyrin substituent.

It has been shown that, under the right conditions, oxygen does oxidise cobalt(II) to cobalt(III) and some dihydroquinones do change cobalt(III) back to cobalt(II). A very sensitive catalytic system was

developed whereby dioxygen was used in a controlled and delicate manner, just as in biological systems.

Chapter Five

EXPERIMENTAL

5. EXPERIMENTAL

5.1. Instrumentation and Experimental Techniques

(a) All nuclear magnetic resonance (NMR) spectra are for ^1H and were recorded on a Bruker WM2000 (200MHz) spectrometer. Deuteriochloroform and deuteriodimethylsulphoxide were used as solvents with tetramethylsilane (TMS) as the internal reference. Spectra were recorded on the δ scale and signals were recorded in the form of a chemical shift measured in ppm.

(b) All mass spectra (MS) were recorded on a VG7070E spectrometer using fast atom bombardment (FAB) mode, with 3-nitrobenzylalcohol as the matrix and xenon as the fast atom.

(c) Thin layer chromatography (tlc) was performed using Merck type precoated silica plates.

(d) Column chromatography was carried out using either Merck Silica gel 60 or Fluka neutral alumina (type 507 C) Brockman grade I. Alumina grade II was prepared by adding 3% of water to the alumina grade I and stirring until homogeneous. The prepared alumina was then allowed to cool to room temperature before use. The alumina used for the purification of solvents for cyclic voltammetry measurements, was from ICN Alumina N Super 1 Biomedicals.

(e) UV/visible (ultra-violet/visible) spectra were recorded using a Hewlett Packard 8452A diode array spectrometer, usually in dichloromethane or chloroform as solvent.

(f) Luminescence analyses were carried out using a Perkin-Elmer MPF-43, Fluorescence Spectrophotometer.

(g) Cyclic voltammetry (CV) measurements were carried using a potentiostat/galvanostat EG&G Princeton Applied Research Model 173.

5.2. Purification of Solvents

(a) Dichloromethane and chloroform were refluxed over potassium carbonate and then distilled before use.

(b) Potassium carbonate was dried in an oven overnight prior to use.

(c) Butyronitrile was passed through a column of alumina before use.

5.3. Reagents

(a) Pyrrole was distilled before use.

(b) BF_3.Etherate was used from a newly opened bottle. This was always replaced after about three months, even if only partially used.

(c) All other reagents were used as received.

(d) Nitrogen and dioxygen were from BOC (British Oxygen Company).

5.4. Abbreviations

In this section the term 'in vacuo' refers to the removal of solvents under reduced pressure using a rotary evaporator and a vacuum line.

5.5. Synthesis of the 5,10,15,20-*Tetrakis*aryl Porphyrins

To synthesise 5,10,15,20-*tetrakis*arylporphyrins three general methods were used (A, B, C).

Method A

Pyrrole (1 x 10^{-2} mole) was added dropwise to a solution of an aromatic aldehyde (1 x 10^{-2} mole) in acetic acid (75 ml) and nitrobenzene (50 ml) which had been preheated to 120°C. After addition of pyrrole, this temperature was maintained for 1 hour and then the solution was allowed to cool to room temperature and left to stand overnight. Porphyrin crystals that precipitated out of solution were filtered off, washed with methanol and dried in a desiccator. For the porphyrins that did not precipitate out of solution, steam distillation was used to remove all of the nitrobenzene. The residue was dissolved in chloroform or dichloromethane which was washed with an aqueous solution of sodium hydrogen carbonate (2 x 100 ml), washed with distilled water (100 ml), and dried over anhydrous sodium or magnesium sulphate. Finally, this solution was filtered and the solvent removed from the filtrate 'in vacuo'.

Most of the porphyrins that precipitated out of solution did not require further purification before general use. For any that did together with those that did not precipitate directly on cooling the reaction mixture, column chromatography was used on alumina (grade II) or silica gel with dichloromethane, chloroform, dichloromethane/chloroform or ethyl acetate as the elution solvents. Finally, recrystallisation of the porphyrins was effected from a mixture of petroleum ether (b.p. 40/60°C) and dichloromethane.

Method B

A mixture of pyrrole (5×10^{-3} mole) and an aromatic aldehyde (5×10^{-3} mole) in distilled chloroform (500 ml) was purged with nitrogen for 10 minutes at room temperature. Boron trifluoride etherate (5×10^{-4} mole) was then added to this solution which was left to stand in the dark at room temperature and under a nitrogen atmosphere. Small test samples (25 µl) of this solution were removed at regular intervals and the amount of porphyrinogen which had formed was monitored by oxidising the sample with an excess of a solution of DDQ in toluene (50 µl; 0.01M). The resulting solution containing porphyrin corresponding to the porphyrinogen was diluted with a solution of dichloromethane (4 ml) to which had previously been added some triethylamine (a few drops of triethylamine to 200 ml dichloromethane). The visible spectra of the oxidised samples were obtained by measuring the height of the Soret band. When the Soret band had reached a maximum, usually after 3 to 4 hours this indicated an optimum yield of porphyrinogen. At this stage, a slight excess of triethylamine (70 µl) was added to deactivate any remaining boron trifluoride. A freshly prepared solution of aqueous hydrogen peroxide (1.5-2 g; 35% w/w) dissolved in acetic acid (100 ml; 98-100%) was then added and the new mixture was left at room temperature for 1 hour exposed to the atmosphere and to light. The solvent was removed 'in vacuo' and the residue was dissolved in chloroform, washed twice with an aqueous solution of sodium hydrogen carbonate (200 ml) and finally with water (200 ml). The organic layer was dried over anhydrous magnesium or sodium sulphate, filtered and the solvent removed 'in vacuo'. Purification of the resulting solid was effected by chromatography on alumina grade II or silica gel with dichloromethane, chloroform, dichloromethane/chloroform or ethyl acetate as elution solvents. Finally,

recrystallisation of the porphyrins was carried out from a mixture of petroleum ether (b.p. 40/60°C) and dichloromethane.

Method C

Pyrrole (5×10^{-3}mole) and the requisite aromatic aldehyde (5×10^{-3} mole) were dissolved in distilled chloroform (500 ml) which was then purged with nitrogen for 10 minutes. Boron trifluoride etherate (5×10^{-4}mole) was added to this solution and the mixture was left to stand in the dark at room temperature. Small test samples (25 µl) were removed at regular intervals and oxidised with a solution of DDQ in toluene (50 µl; 0.01 M). As previously described in Method B, this was diluted with a previously prepared solution of dichloromethane (4ml) and triethylamine and the visible spectrum was run for each sample. The reaction was considered complete when no further increase in the hight of the Soret band was observed (usually 3 to 4 hours). At this stage, a slight excess of triethylamine (70 µl) was added to deactivate the remaining boron trifluoride and this neutralised porphyrinogen solution was added slowly and dropwise to a pre-heated (120°C) mixture of acetic acid and nitrobenzene. The rate of addition was such that the chloroform solvent from the porphyrinogen solution distilled out as almost fast as it was added.

After all of the chloroform solution had been added, the reaction temperature was maintained at 120°C for 1hour further. The reaction mixture was allowed to cool then to room temperature overnight. Often, the required porphyrin crystallised directly from the reaction medium and could be simply filtered off, washed with methanol and dried. Otherwise, steam-distillation was required to remove the excess of nitrobenzene. In this case, the residue from steam distillation was dissolved in chloroform or dichloromethane which was then washed with an aqueous solution of

sodium hydrogen carbonate (2 x 200ml), with distilled water (200 ml) and finally dried over anhydrous magnesium or sodium sulphate. This solution was filtered, the solvent removed 'in vacuo', and the residue was chromatographed on a column of alumina grade II or silica gel, using dichloromethane, chloroform, dichloromethane/chloroform or ethyl acetate as the elution solvent. Finally, recrystallisation of the porphyrins was carried out using a mixture of petroleum ether (b. p. 40/60°C) and dichloromethane.

5.5.1. Synthesis of 5,10,15,20-tetrakisphenylporphyrin

By method A. Using benzaldehyde, this porphyrin was obtained directly from the reaction mixture as purple crystals in 20% yield. The crystals were washed with cold methanol and dried under vacuum at high 100°C. Found: C, 85.41; H, 4.98; N, 8.83; $C_{44}H_{30}N_4$ calc. for C, 85.96; H, 4.92; N, 9.12 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.66), 516(4.56), 550(4.23), 590(4.08) and 646nm(3.99); m.s. (FAB)[M+H$^+$], m/z 615; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.82(2H, s, NH), 7.67-7.72(12H, m, ArH), 8.07-8.19(8H, m, ArH), 8.79(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) with dichloromethane as the eluent and recrystallisation of the solid from the first band from the column with dichloromethane/petroleum ether (b.p. 40/60°C), the yield required porphyrin was isolated in 14%. Found: C, 85.97; H, 4.91; N, 9.07; $C_{44}H_{30}N_4$ calc. for C, 85.96; H, 4.92; N, 9.12 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.66), 516(4.56), 550(4.23), 590(4.08) and 646nm(3.99); m.s. (FAB)[M+H$^+$], m/z 615; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.82(2H, s, NH), 7.69-7.72(12H, m, ArH), 8.15-8.19(8H, m, ArH), 8.79(8H, s, βH).

By method C. Crystallisation of product from the reaction mixture did not occur so steam-distillation was required. Chromatography of the residue from steam-distillation was performed on alumina (grade II) with dichloromethane as the eluent. The first band from the column was collected, the solvent removed 'in vacuo' and the residue solid was recrystallised in dichloromethane/petroleum ether (b.p. 40/60°C), to give a 7.6% yield of which 6.2% was porphyrin and 1.4% was the corresponding chlorin (^{1}H-nmr and visible spectrum). Found: C, 85.86; H, 5.00; N, 8.44; $C_{44}H_{30}N_4$ calc. for C, 85.96; H, 4.92; N, 9.12 %; m.s. (FAB)[M+H$^+$], m/z 615; ^{1}H-nmr (200MHz)($CDCl_3$)(mixture): δ, -2.79(2H, s, NH), -1.46(2H, s, NH), 7.60-7.81(12H, m, ArH), 8.07-8.20(10H, m, βH and ArH), 8.39(4H, s, βH), 8.53-8.55(2H, d, βH), 8.82(8H, s, βH).

5.5.2. Synthesis of 5,10,15,20-tetrakis(4'-chlorophenyl)porphyrin

By method A. Using 4-chlorobenzaldehyde the porphyrin was obtained directly from the reaction mixture as purple crystals in 33% yield. The crystals were filtered off, washed with methanol and dried under vacuum at 100°C. Found: C, 70.16; H, 3.43; N, 7.45; $C_{44}H_{26}N_4Cl_4$ calc. for C, 70.23; H, 3.45; N, 7.45 %; λ_{max}($CHCl_3$)(logε), 420(5.61), 516(4.48), 550(4.17), 590(4.04) and 646nm(3.93); m.s. (FAB)[M+H$^+$], m/z 753; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.8(2H, s, NH), 7.71-7.76(8H, d, ArH), 8.10-8.11(8H, d, ArH), 8.83(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) with chloroform as the eluent and recrystallisation of the material from the first band from the column with dichloromethane/petroleum ether (b.p. 40/60°C), the yield was 27%. Found: C, 70.38; H, 3.86; N, 6.94;

$C_{44}H_{26}N_4Cl_4$ calc. for C, 70.2; H, 3.45; N, 7.45 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 420(5.61), 516(4.48), 550(4.17), 590(4.04) and 646nm(3.93); m.s. (FAB)[M+H$^+$], m/z 753; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.8(2H, s, NH), 7.71-7.76(8H, d, ArH), 8.10-8.11(8H, d, ArH), 8.83(8H, s, βH).

By method C. The porphyrin did not precipitate from the reaction mixture which had to be steam distilled to remove the nitrobenzene. Chromatography on alumina (grade II) with dichloromethane as the eluent and recrystallisation with dichloromethane/petroleum ether (b.p. 40/60°C) of the solid from the first band off the column afforded a 17% yield of which 13% was porphyrin and 4% was the corresponding chlorin. m.s. (FAB)(mixture)[M+H$^+$], m/z 753; ^{1}H-nmr (200MHz)($CDCl_3$)(mixture): δ, -2.8(2H, s, NH), -1.5(2H, s, NH), 7.64-8.39(24H, m, ArH and βH), 8.83(10H, s, βH).

5.5.3. Synthesis of 5,10,15,20-tetrakis(3'-chlorophenyl)porphyrin

By method A. Using 3-chlorobenzaldehyde the porphyrin was obtained directly from the reaction mixture in 21.6% yield as purple crystals which were washed with methanol and dried under vacuum. Because this porphyrin is not very soluble in deuterated chloroform or other deuterated solvents, to be able to analyse by nmr spectroscopy, the dication was produced. Trifluoroacetic acid was added (few drops) to a mixture of porphyrin and chloroform, turning the porphyrin immediately soluble. The dication was then isolated by removing the solvents and drying the material 'in vacuo'. Found: C, 70.17; H, 3.46; N, 7.46; $C_{44}H_{26}N_4Cl_4$ requires C, 70.24; H, 3.46; N, 7.45 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.62), 514(4.47), 548(4.09), 588(4.04) and 646nm(3.82); m.s. (FAB)[M+H$^+$],

m/z 752; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.76(4H, s, NH), 7.85-7.92(8H, m, ArH), 8.39(4H, d, ArH), 8.55(4H, s, ArH), 8.72(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) with dichloromethane as the eluent, and recrystallisation of the material from the first eluted band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), the yield was 19%. Found: C, 69.39; H, 3.39; N, 7.38; $C_{44}H_{26}N_4Cl_4$ requires C, 70.24; H, 3.45; N, 7.45 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.62), 514(4.47), 548(4.09), 588(4.04) and 646nm(3.82); m.s. (FAB)[M+H$^+$], m/z 752; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.76(4H, s, NH), 7.85-7.92(8H, m, ArH), 8.39(4H, d, ArH), 8.55(4H, s, ArH), 8.72(8H, s, βH).

By method C. The porphyrin did not precipitate and steam-distilation was required to remove excess of nitrobenzene. Chromatography was performed on alumina (grade II) with dichloromethane as the eluent and recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), afforded a 30% yield and without contamination by chlorin (^{1}H-nmr; visible spectroscopy). Found: C, 70.17; H, 3.45; N, 7.46; $C_{44}H_{26}N_4Cl_4$ requires C, 70.24; H, 3.45; N, 7.45 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.62), 514(4.47), 548(4.09), 588(4.04) and 646nm(3.82); m.s. (FAB)[M+H$^+$], m/z 752; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.76(4H, s, NH), 7.85-7.92(8H, m, ArH), 8.39(4H, d, ArH), 8.55(4H, s, ArH), 8.72(8H, s, βH).

5.5.4. Synthesis of 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin

By method A. The porphyrin was obtained directly from the reaction mixture as a 6% yield of purple crystals which were washed with

methanol and dried under vacuum. Found: C, 59.25; H, 2.46; N, 6.30; $C_{44}H_{22}N_4Cl_8$ calc. for C, 59.27; H, 2.47; N, 6.28 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.47), 512(4.51), 588(4.08), and 656nm(3.55); m.s. (FAB)[M+H$^+$], m/z 891; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.59(2H, s, NH), 7.60-7.77(12H, m, ArH), 8.62(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) or silica gel with chloroform as the eluent and recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), a yield of 20% was obtained. Found: C, 59.26; H, 2.47; N, 6.28; $C_{44}H_{22}N_4Cl_8$ calc. for C, 59.27; H, 2.47; N, 6.28 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.47), 512(4.51), 588(4.08), and 656nm(3.55); m.s. (FAB)[M+H$^+$], m/z 891; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.59(2H, s, NH), 7.60-7.77(12H, m, ArH), 8.62(8H, s, βH).

By method C. The porphyrin was obtained directly from the reaction mixture as purple crystals which were washed with methanol and dried under vacuum to give a 20% yield of which 6% was porphyrin and 14% was the corresponding chlorin (1H-nmr; visible spectroscopy). m.s. (FAB)[M+H$^+$], m/z 891; ^{1}H-nmr (200MHz)($CDCl_3$)(porphyrin): δ, -2.59(2H, s, NH), 7.60-7.77(12H, m, ArH), 8.62(8H, s, βH); ^{1}H-nmr (200MHz)($CDCl_3$)(chlorin): δ, -1.31(2H, s, NH), 7.60-7.77(12H, m, ArH), 8.06-8.09(2H, d, βH), 8.25(4H, s, βH), 8.43-8.46(2H, d, βH), 8.65(2H, s, βH).

5.5.5. Synthesis of 5,10,15,20-tetrakis(4'-methoxyphenyl)porphyrin

By method A. Using 4-methoxybenzaldehyde the required porphyrin was obtained directly from the reaction mixture as purple crystals in 21% yield which were washed with methanol and dried under

vacuum. Found C, 78.43; H, 5.15; N, 7.61; $C_{48}H_{38}N_4O_4$ calc. for C, 78.36; H, 5.17; N, 7.61 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 422(5.59), 518(4.34), 556(4.19), 594(4.05) and 652nm(4.06); m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.76(2H, s, NH), 4.09(12H, s ,CH_3), 7.26-7.30(8H, d, ArH), 8.10-8.14(8H, d, ArH), 8.85(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) or silica gel with chloroform as the eluent and recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), a yield of 21 % was obtained. Found: C, 78.40; H, 5.65; N, 6.93; $C_{48}H_{38}N_4O_4$ calc. for C, 78.36; H, 5.17; N, 7.61 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 422(5.59), 518(4.34), 556(4.19), 594(4.05) and 652nm(4.06); m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.76(2H, s, NH), 4.09(12H, s ,CH_3), 7.26-7.30(8H, d, ArH), 8.10-8.14(8H, d, ArH), 8.85(8H, s, βH).

By method C. The porphyrin did not precipitate from the reaction mixture steam-distilation was required to remove the excess of nitrobenzene. Chromatography was performed on alumina (grade II) or silica gel with chloroform as the eluent. After recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), the yield was 36% of which 25% was porphyrin and 11% was the corresponding chlorin (^{1}H-nmr; visible spectroscopy). m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$) (porphyrin): δ, -2.76(2H, s, NH), 4.09(12H, s ,CH_3), 7.26-7.30(8H, d, ArH), 8.10-8.14(8H, d, ArH), 8.85(8H, s, βH); ^{1}H-nmr (200MHz)($CDCl_3$)(chlorin): δ, -1.5(2H, s, NH), 4.01-4.15(12H, m ,CH_3), 7.22-7.25(8H, d, ArH), 8.10-8.14(8H, d, ArH), 7.74-7.78(2H, d, βH), 7.98-8.03(2H, d, βH), 8.43(4H, s, βH), 8.86(2H, s, βH).

5.5.6. Synthesis of 5,10,15,20-tetrakis(3',4'-dimethoxyphenyl)porphyrin

By method A. Using 3,4-dimethoxybenzaldehyde the required porphyrin did not precipitate out of solution. After steam-distillation to remove the nitrobenzene followed by chromatography on alumina (grade II) or silica gel with chloroform as the eluent and recrystallisation in dichloromethane/petroleum ether(b.p. 40/60°C) an 18% yield of purple crystals was obtained. Found: C, 73.12; H, 5.43; N, 6.50; $C_{52}H_{46}N_4O_8$ requires C, 73.00; H, 5.40; N, 6.60 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.53), 520(4.38), 556(4.29), 594(4.03) and 650nm(4.04); m.s. (FAB)[M+H$^+$], m/z 855; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.75(2H, s, NH), 3.98(12H, s ,CH_3), 4.17(12H, s, CH_3), 7.25-7.26(4H, d, ArH), 7.73-7.74(4H, d, ArH), 7.78(4H, s, ArH), 8.90(8H, s, βH).

By method B. After performing chromatography on alumina (grade II) or silica gel with chloroform as the eluent and recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), the yield was 23 %. Found: C, 73.06; H, 5.48; N, 6.33; $C_{52}H_{46}N_4O_8$ requires C, 73.00; H, 5.40; N, 6.60 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.53), 520(4.38), 556(4.29), 594(4.03) and 650nm(4.04); m.s. (FAB)[M+H$^+$], m/z 855; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.75(2H, s, NH), 3.98(12H, s, CH_3), 4.17(12H, s, CH_3), 7.25-7.26(4H, d, ArH), 7.73-7.74(4H, d, ArH), 7.78(4H, s, ArH), 8.90(8H, s, βH).

By method C. The porphyrin did not precipitate and steam-distillation was required to remove the excess of nitrobenzene. Chromatography was performed on alumina (grade II) or silica gel with chloroform as the eluent. Recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), gave 25% of purple crystals with no contamination by chlorin

(^{1}H-nmr; visible spectroscopy). Found: C, 73.06; H, 5.48; N, 6.33; $C_{52}H_{46}N_4O_8$ requires C, 73.00; H, 5.40; N, 6.60 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.53), 520(4.38), 556(4.29), 594(4.03) and 650nm(4.04); m.s. (FAB)[M+H$^+$], m/z 855; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.75(2H, s, NH), 3.98(12H, s ,CH_3), 4.17(12H, s, CH_3), 7.25-7.26(4H, d, ArH), 7.73-7.74(4H, d, ArH), 7.78(4H, s, ArH), 8.90(8H, s, βH).

5.5.7. Synthesis of 5,10,15,20-tetrakis(3',4'-methylenedioxyphenyl) porphyrin

By method A. Using 3,4-methylenedioxybenzaldehyde the required porphyrin was isolated after steam-distillation to remove the excess of nitrobenzene. The residue was chromatographed on alumina (grade II) or silica gel and dichloromethane (or chloroform) as the eluent. The first band was collected and the solvent removed. The residual porphyrin was recrystallised from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C) to obtain a 27% yield of purple crystals. Found: C, 72.87; H, 3.83; N, 7.06; $C_{48}H_{36}N_4O_8$ requires C, 72.91; H, 3.79; N, 7.09 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.58), 518(4.39), 554(4.14), 592(3.92) and 650nm(3.90); m.s. (FAB)[M+H$^+$], m/z 791; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.85(2H, s, NH), 6.21(8H, s, CH_2), 7.12-7.16(4H, d, ArH), 7.59-7.63(4H, d, ArH), 7.67(4H, s, ArH), 8.87(8H, s, βH).

By method B. The yield obtained after chromatography on alumina (grade II) or silica gel and dichloromethane (or chloroform) as the eluent and recrystallisation using a mixture of dichloromethane/petroleum ether (b.p. 40/60°C) was 20%. Found: C, 72.92; H, 3.82; N, 7.06; $C_{48}H_{36}N_4O_8$ requires C, 72.91; H, 3.79; N, 7.09 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.58), 518(4.39), 554(4.14), 592(3.92) and 650nm(3.90); m.s. (FAB)[M+H$^+$], m/z 791; ^{1}H-nmr

(200MHz)($CDCl_3$): δ, -2.85(2H, s, NH), 6.21(8H, s, CH_2), 7.12-7.16(4H, d, ArH), 7.59-7.63(4H, d, ArH), 7.67(4H, s, ArH), 8.87(8H, s, βH).

By method C. The porphyrin did not precipitate out of solution so steam-distillation was required to remove the excess of nitrobenzene. Chromatography was performed on alumina (grade II) or silica gel with chloroform as eluent. Recrystallisation of the material from the first band from the column in dichloromethane/petroleum ether (b.p. 40/60°C), gave a 32% yield of purple crystals of which 18% was porphyrin and 14% was the corresponding chlorin (^{1}H-nmr; visible spectrocopy). Found: C, 72.80; H, 3.80; N, 7.00; $C_{48}H_{36}N_4O_8$ requires C, 72.91; H, 3.79; N, 7.09 %; m.s. (FAB)[M+H$^+$], m/z 791; ^{1}H-nmr (200MHz)($CDCl_3$)(porphyrin): δ, -2.85(2H, s, NH), 6.21(8H, s, CH_2), 7.12-7.16(4H, d, ArH), 7.59-7.63(4H, d, ArH), 7.67(4H, d, ArH), 8.87(8H, s, βH); ^{1}H-nmr (200MHz)($CDCl_3$)(chlorin): δ, -1.57(2H, s, NH), 6.21(8H, s, CH_2), 7.12-7.16(4H, d, ArH), 7.59-7.63(4H, d, ArH), 7.67(4H, s, ArH), 8.18-8.20(2H, d, βH), 8.43(4H, s, βH), 8.57-8.59(2H, d, βH), 8.84(2H, s, βH).

5.5.8. Synthesis of 5,10,15,20-tetrakis(4'-biphenyl)porphyrin

By method A. Using 4-biphenylcarboxaldehyde the required porphyrin was obtained directly by crystallisation from the reaction medium. The crystals were well washed with methanol and dried under vacuum at 100°C to give a 40% yield. Because this porphyrin is not very soluble in deuterated chloroform or other deuterated solvents, to be able to analyse by nmr spectroscopy, the dication was produced. Trifluoroacetic acid was added (few drops) to a mixture of porphyrin and chloroform, turning the porphyrin immediately soluble. The dication was then isolated by removing the solvents and drying the material 'in vacuo'.

Found: C, 88.55; H, 5.07; N, 5.97; $C_{68}H_{46}N_4$ requires for C, 88.88; H, 5.01; N, 6.10 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.63), 518(4.62), 554(4.41), 590(4.19) and 650nm(4.20); m.s. (FAB)(for the dication)[M-H$^+$], m/z 919; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.0605(4H, s, NH), 7.55-7.75(12H, m, ArH), 8.03-8.07(8H, d, ArH), 8.31-8.36(8H, d, ArH), 8.75-8.79(8H, d, ArH), 8.79(8H, s, βH).

By method B. The yield was 12% after chromatography on alumina (grade II) or silica gel and dichloromethane (or chloroform) as the eluent and recrystallisation from a mixture of dichloromethane/petroleum (b.p. 40/60°C). Found: C, 88.58; H, 4.96; N, 5.93; $C_{68}H_{46}N_4$ requires C, 88.80; H, 5.01; N, 6.10 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.63), 518(4.62), 554(4.41), 590(4.19) and 650nm(4.20); m.s. (FAB)(for the dication)[M-H$^+$], m/z 919; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.0605(4H, s, NH), 7.55-7.75(12H, m, ArH), 8.03-8.07(8H, d, ArH), 8.31-8.36(8H, d, ArH), 8.75-8.79(8H, d, ArH), 8.79(8H, s, βH).

By method C. The porphyrin was obtained by direct crystallisation from the reaction mixture as purple crystals that were washed with methanol and dried under vacuum to afford a 40% yield with no contamination by chlorin. Found: C, 88.74; H, 5.05; N, 6.07; $C_{68}H_{46}N_4O_8$ requires C, 88.80; H, 5.01; N, 6.10 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.63), 518(4.62), 554(4.41), 590(4.19) and 650nm(4.20); m.s. (FAB)(Dication)[M-H$^+$], m/z 919; ^{1}H-nmr (200MHz)($CDCl_3$)(for the dication): δ, -0.0605(4H, s, NH), 7.55-7.75(12H, m, PhH), 8.03-8.07(8H, d, ArH), 8.31-8.36(8H, d, ArH), 8.75-8.79(8H, d, ArH), 8.79(8H, s, βH).

5.5.9. Synthesis of 5,10,15,20-tetrakis(3'-methoxyphenyl)porphyrin

By method A. The use of nitroaniline (2.07g; 0.015mole) was required instead of nitrobenzene . The required porphyrin was isolated by chromatography on alumina (grade II) and dichloromethane as the eluent. The first band was collected and the solvent was evaporated off. The residual dark material was recrystallised from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C) to afford a 19% yield of the required porphyrin. Found: C, 78.56; H, 5.17; N, 7.62; $C_{48}H_{38}N_4O_4$ calc. for C, 78.47; H, 5.18; N, 7.63 %; $\lambda_{max}(CHCl_3)$(relative %), 418(100), 514(8.9), 548(3.6), 588(3) and 646nm(2.2); m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.85(2H, s, NH), 3.93(12H, s, CH_3), 7.26-7.29(4H, d, ArH), 7.55-7.63(4H, t, ArH), 7.74-7.78(4H, d, ArH), 8.83(8H, s, βH).

5.5.10 Synthesis of 5,10,15,20-tetrakis(4'-hydroxyl-3',5'-di-tert-butylphenyl) porphyrin

By method A. Using 3,5-di-tert-4-hydroxybenzaldehyde the required porphyrin did not precipitate out of solution and steam-distillation was required to remove the nitrobenzene. The residue from steam-destillation was chromatographed on alumina (grade II) with dichloromethane as eluent. The first band was collected and the solvent was evaporated off to leave a dark residue which was recrystallised from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C) to give a 19% yield of porphyrin as purple crystals. Found: C, 81.04; H, 8.43; N, 4.96; $C_{76}H_{94}N_4O_4$ calc. for C, 80.85; H, 8.33; N, 4.96 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 426(5.53), 522(4.42), 560(4.33), 594(4.05) and 652nm(3.96); m.s. (FAB)[M+H$^+$], m/z 1128; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.65(2H, s, NH), 1.62(36H, s ,CH_3), 5.51(4H, s, OH), 8.04(8H, s, ArH), 8.93(8H, s, βH).

5.5.11. Synthesis of 5,10,15,20-tetrakis(3',4',5'-trimethoxyphenyl)porphyrin

By method B. Using 3,4,5-trimethoxybenzaldehyde the required porphyrin was chromatographed on alumina (grade II) with ethyl acetate as eluent. The solid obtained from the first band out of the column was recrystallised from a mixture of dichloromethane and petroleum ether (b.p. 40/60°C) 30% yield. Found: C, 68.23; H, 5.65; N, 5.32; $C_{56}H_{54}N_4O_{12}$ requires C, 68.85; H, 5.58; N, 5.75 %; $\lambda_{max}(CHCl_3)(\log \varepsilon)$, 424(5.45), 516(4.25), 552(3.97), 592(3.87), 648nm(3.75); m.s. (FAB)[M+H$^+$], m/z 975; ^{1}H-nmr (200MHz)($CDCl_3$) δ, -2.88(2H, s, NH), 4.03(24H, s, CH_3), 4.08(12H, s, CH_3), 7.37(8H, s, ArH), 8.97(8H, s, βH).

5.5.12. Synthesis of 5,10,15,20-tetrakis(2',4',5'-trimethoxyphenyl)porphyrin

By method B. Using 3,4,5-trimethoxybenzaldehyde the required porphyrin was chromatographed on alumina (grade II) with ethyl acetate as eluent. The solid obtained from the first band out of the column was recrystallised from a mixture of dichloromethane and petroleum ether (b.p. 40/60°C) in 17% yield. Found: C, 68.22; H, 5.65; N, 5.32; $C_{56}H_{54}N_4O_{12}$ requires C, 68.80; H, 5.68; N, 5.75 %; $\lambda_{max}(CHCl_3)(\log \varepsilon)$, 424(5.20), 516(4.14), 550(3.95), 588(3.93), 644nm(3.51); m.s. (FAB)[M+H$^+$], m/z 976.

5.5.13. Synthesis of 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl) porphyrin

By method A. Using 2,3,4,5,6-pentafluorobenzaldehyde the required porphyrin crystallised out of the reaction mixture. The crystals were washed with methanol and dried to give a 13% yield of the required porphyrin. Found: C, 53.90; H 1.09; N, 5.50; $C_{44}H_{10}N_4F_{20}$ calc. for C, 54.21;

H, 1.03; N, 5.75 %; $\lambda_{max}(CHCl_3)$(relative %), 412(100), 506(7.6), 584(2.5), 638(0.4) and 656nm(0.6); m.s. (FAB)[M+H$^+$], m/z 975; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.96(2H, s, NH), 8.87(8H, s, βH).

By method B. The required porphyrinogen was not formed during the condensation step and no porphyrin could be isolated.

5.5.14. Synthesis of 5,10,15,20-tetrakis(4'-methylthiophenyl)porphyrin

By method A. Using 4-methylthiobenzaldehyde, the required porphyrin was obtained directly by crystallisation from the reaction medium. The crystals were washed well with methanol and dried under vacuum at 100°C to give a 37% yield. Found: C, 72.03; H, 4.76; N, 7.02; $C_{48}H_{38}N_4S_4$ requires C, 72.18; H, 4.76; N, 7.02 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.54), 520(4.22), 556(4.07), 594(3.69) and 650nm(3.71); m.s. (FAB)[M+H$^+$], m/z 799; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.84(2H, s, NH), 2.70(12H, s, CH_3), 7.56-7.60(8H, d, ArH), 8.06-8.09(8H, d, ArH), 8.82(8H, s, βH).

By method B. The required porphyrin was chromatographed on alumina (grade II) using dichloromethane as the eluent. The solid from the first band out of the column was recrystallised from a mixture of dichloromethane and petroleum ether (b.p. 40/60°C); the crystals were collected and dried to give a 40% yield of 5,10,15,20-*tetrakis*(4'-methylthiosulphonylphenyl)porphyrin. Found: C, 62.72; H, 4.57; N, 5.66; $C_{48}H_{38}N_4S_8$ requires C, 62.20; H, 4.10; N, 6.04 %; $\lambda_{max}(CHCl_3)$(relative %), 420(100), 514(7.35), 550(4.01), 590(2.94) and 646nm(2.00); m.s. (FAB)[M+H$^+$], m/z 880; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.79(2H, s, NH), 3.06(12H, s, CH_3), 8.03-8.07(8H, d, ArH), 8.36-8.39(8H, d, ArH), 8.83(8H, s, βH).

Method B was repeated again but this time using chloranil to perform the second oxidative step of the reaction instead of hydrogen peroxide. In this case, chloranil (0.9g; 0.00375mole) was added to the solution after the first condensation step. This new solution was refluxed for one hour. The solvents were evaporated off and the residue was washed with methanol before chromatography on alumina (grade II) with dichloromethane as eluent. Removal of the solvent from the first band out of the column and recrystallisation of the material with dichloromethane/petroleum ether (b.p. 40/60°C) gave a 27% yield of a mixture of porphyrins with sulphide, sulphoxide and sulphone groups attached to the meso-phenyl rings (^{1}H-nmr; visible spectroscopy). $\lambda_{max}(CHCl_3)$(mixture)(relative %), 424(100), 518(6.25), 556(4.51), 594(2.17) and 650nm(2.17); m.s. (FAB)[M+H$^+$], m/z (mixture), 800, 816 and 832; ^{1}H-nmr (200MHz)($CDCl_3$)(mixture): δ, -2.79(2H, s, NH), 2.70(12H, s, CH_3), 2.72(12H, s, CH_3), 3.07(12H, s, CH_3), 7.60-8.41(16H, m, ArH), 8.36-8.39(8H, d, ArH), 8.83-8.87(8H, m, βH).

5.5.15. Oxidation experiment on the mixture obtained during synthesis of 5,10,15,20-tetrakis (4'-methylthiophenyl)porphyrin when using Method B with chloranil as the oxidant

The mixture obtained from the above synthesis of 5,10,15,20-*tetrakis*(4'-methylthiophenyl)porphyrin (using method B with chloranil instead of hydrogen peroxide) was dissolved in a mixture of dichloromethane/methanol (70/30 ml) and was heated to reflux. At this point, a solution of aqueous hydrogen peroxide (70%; w/w; 1.5-2.0g) was added and the mixture was left to stand at room temperature. After 12 hours, the solution was washed several times with distilled water (3 x 50 ml) and dried (Na_2SO_4) ^{1}H-nmr revealed a mixture of sulphide,

sulphoxide and sulphone groups was still present but, this time, the nmr spectrum resembled more that of the porphyrin having 4-sulphonyl groups obtained when using method B with hydrogen peroxide as oxidant (see above). Thus, oxidation to the sulphone stage did occur but not completely during the time of the experiment. ^{1}H - n m r (200MHz)($CDCl_3$)(mixture): δ, -2.87(2H, s, NH), 2.74(12H, s, CH_3), 3.02(12H, s, CH_3), 3.07(12H, s, CH_3), 8.00-8.04(8H, d, ArH), 8.32-8.35(8H, d, ArH), 8.73(8H, s, βH), 8.76(8H, s, βH), 8.78(8H, s, βH).

5.5.16. Attempts to Synthesise 5,10,15,20-tetrakisarylporphyrins using a "two-pot" technique in the presence of a water-scavenger during condensation

A solution of pyrrole (1.0×10^{-3}mole), triethylorthoacetate (0.5×10^{-3} mole) and an aromatic aldehyde (1.0×10^{-3}mole) in distilled chloroform (100 ml) was purged with nitrogen for 10 minutes at room temperature. Boron trifluoride etherate (1.0×10^{-4}mole) was added to this solution which was left in the dark at room temperature and under nitrogen. As described previously, test samples (25 µl) were removed at regular intervals and were oxidised with a solution of DDQ in toluene (50 µl; 0.01M) which was first diluted with a solution of dichloromethane (4 ml), containing a little of triethylamine. The visible spectrum of this solution was obtained. During this monitoring process, it was noticed always that the Soret band appeared in the first 5-10 minutes of reaction, the solution showing a very light pink colour as in a normal successful synthesis. However, further monitoring showed that the Soret band disappeared completely but there was a new, very broad band at 450-500 nm identified from literature[149] as being due to a formation of dipyrrin . These changes were accompanied by a change in the colour of the solution to a very light

green. No attempts were made to isolate the materials. Porphyrins for which syntheses were attempted using this method were 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, 5,10,15,20-*tetrakis*phenylporphyrin and 5,10,15,20-tetrakis(4'-methoxyphenyl)porphyrin. All gave the same results.

5.6. Attempts to synthesise 5,10,15,20-*tetrakis*arylporphyrins in a "two-pot" method using 2,3,5,6-tetrachloro-1,4-benzoquinone (TCQ) as the oxidant in the second step

A mixture of pyrrole (5×10^{-3}mole) and an aromatic aldehyde (5×10^{-3}mole) in distilled chloroform (500 ml) was purged with nitrogen for 10minutes. BF_3.etherate (5×10^{-4}mole) was added to this solution which was left to stand in the dark at room temperature under nitrogen. Test samples (25 µl) were removed at regular intervals and the amount of porphyrinogen formed was monitored by oxidising the sample with a solution of DDQ in toluene (50 µl; 0.01M) containing triethylamine (described in Section 5.5 in Method B). The visible spectrum of this solution was obtained. When the Soret band no longer increased in height, TCQ (3.75×10^{-3}mole) was added at once to the porphyrinogen solution and the new mixture was left under reflux for 1 hour. The solvent was removed 'in vacuo' and the residue was dissolved in chloroform, dichloromethane or ethyl acetate and then chromatographed on alumina (grade II) or silica gel to give 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin in apparent 58% yield after chromatography due to contamination from reduced chloranil. This made recrystallisation impossible. Washing the contaminated material with an aqueous solution of KOH (saturated; 3 x 50 ml) removed the reduced chloranil and

gave a true yield of 7% of 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin. Found: C, 73.12; H, 5.43; N, 6.50; $C_{52}H_{46}N_4O_8$ requires C, 73.00; H, 5.40; N, 6.60 %; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.53), 520(4.38), 556(4.29), 594(4.03) and 650nm(4.04); m.s. (FAB)[M+H$^+$], m/z 855; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.75(2H, s, NH), 3.98(12H, s, CH_3), 4.17(12H, s, CH_3), 7.25-7.26(4H, d, ArH), 7.73-7.74(4H, d, ArH), 7.78(4H, s, ArH), 8.90(8H, s, βH).

A similar result was obtained in the synthesis of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, in that a yield of 64% after chromatography went down to 9% after treatment with aqueous KOH. Found: C, 78.40; H, 5.15; N, 7.61; $C_{48}H_{38}N_4O_4$ calc. for C, 78.36; H, 5.17; N, 7.61; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 422(5.59), 518(4.34), 556(4.19), 594(4.05) and 652nm(4.06); m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.76(2H, s, NH), 4.09(12H, s ,CH_3), 7.26-7.30(8H, d, ArH), 8.10-8.14(8H, d, ArH), 8.85(8H, s, βH).

5.7. Attempts to synthesise 5,10,15,20-*tetrakis*arylporphyrins using the "two-pot" method but with palladium-on-charcoal as a dehydrogenating agent of porphyrinogen

The synthesis of porphyrinogen was carried out by following the procedures described in Section 5.6. The porphyrin used for this experiment was 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl) porphyrin. For the oxidation of the first-stage porphyrinogen, palladium-on-charcoal (200 mg; 10%) was added directly to the solution (500 ml) which was left at room temperature with strong agitation. After two hours, no evidence for formation of porphyrin was found. More palladium-on-charcoal (200 mg)

was added but after 24 hours, only traces of porphyrin were observed (Soret band). No attempts were made to isolate the porphyrin formed.

5.8. Attempts to synthesise 5,10,15,20-*tetrakis*arylporphyrins using the "two-pot" method with potassium superoxide (KO_2) as oxidant for the porphyrinogen

Following the procedures described in Section 5.7, the porphyrinogen from 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin was synthesised.

(a) use of aqueous solution of KO_2 and a phase transfer reagent

To perform the oxidation of first stage porphyrinogen to porphyrin, a solution of KO_2 (360 mg; 5 x 10^{-3}mole) together with a phase transfer catalyst, tetrabutyl ammoniumperchlorate (TBAPC; 1.73 g; 5 x 10^{-4}mole) in water (50 ml) was added to the porphyrinogen solution with stirring. After 2 hours, no Soret band was observed and the method was abandoned.

(b) use of a solution of KO_2 in acetic acid

In a second attempt to use KO_2, a sample of the porphyrinogen solution (10ml) was examined, the solvent first being removed 'in vacuo' and the residue being dissolved in acetic acid (5ml) before being warmed to 55°C. The solution gave a pink colour. At this point, a solution of KO_2 (100 mg; 1.4 x 10^{-3}mole) in acetic acid (5 ml) was added dropwise. In 5 minutes, the Soret band had reached a maximum. Using all of the porphyrinogen solution (500 ml) the experiment was repeated. The dichloromethane was removed 'in vacuo', the residue was dissolved in acetic acid (250ml).

Addition of the KO_2 to the remaining acetic acid (250ml) caused a *very* exothermic reaction. This procedure was abandoned for reasons of safety.

5.9. Attempts to synthesise 5,10,15,20-*tetrakis*arylporphyrins using the "two-pot" method with hydrogen peroxide as the oxidant for the porphyrinogen

Following the procedures described in 5.5.17, the porphyrinogen of 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl) porphyrin was synthesised.

(a) use of an hydrogen peroxide adduct: urea. H_2O_2

As before, the porphyrinogen was synthesised and the reaction solution was neutralised with triethylamine (70 μL) before removing the dichloromethane solvent 'in vacuo'. To the residue was added a mixture of urea/hydrogen peroxide adduct (400 mg) in dichloromethane (100 ml) and the new mixture left at 55°C with stirring (solubility of the urea adduct was not very good in the dichloromethane). After 2 hours, no oxidation had taken place. The method was abandoned although, with hindsight, it would have been better to have a properly solubilized adduct and porphyrinogen in the same solution.

(b) first attempts to use H_2O_2 in acetic acid

As in (a) above, a porphyrinogen "residue" was obtained. To this residue was added a solution of aqueous hydrogen peroxide (1.5-2 g; 35% w/w) in acetic acid (100 ml) and the mixture was left to react at room temperature. After 1 hour, the Soret band had reached a maximum and work-up of the solution was carried out following the procedures described for method B. An 18% yield of the porphyrin was isolated as pure purple crystals. Found:

C, 59.27; H, 2.46; N, 6.28; $C_{44}H_{22}N_4Cl_8$ calc. for C, 59.27; H, 2.47; N, 6.28%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.47), 512(4.51), 588(4.08), and 656nm(3.55); m.s. (FAB)[M+H$^+$], m/z 891; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.59(2H, s, NH), 7.60-7.77(12H, m, ArH), 8.62(8H, s, βH).

(c) first attempts to use H_2O_2 in acetic acid to synthesise other 5,10,15,20-*tetrakis*arylporphyrins

Syntheses of 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin were attempted. As in (b) above, the porphyrinogen residue was obtained by removing the solvent at the end of the first condensation step. To these residues was added a solution of aqueous hydrogen peroxide (1.5-2 g; 35% w/w) in acetic acid (100 ml) and the mixture was left to react at room temperature. After 1 hour, the Soret band had reached a maximum and the work-up of the solution was carried out following the procedures described for method B. For 5,10,15,20-*tetrakis*(3',4'-dimethoxyphenyl)porphyrin the yield obtained was 7%. Found: C, 73.10; H, 5.40; N, 6.50; $C_{52}H_{46}N_4O_8$ requires C, 73.00; H, 5.40; N, 6.60%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 424(5.53), 520(4.38), 556(4.29), 594(4.03) and 650nm(4.04); m.s. (FAB)[M+H$^+$], m/z 855; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.75(2H, s, NH), 3.98(12H, s ,CH_3), 4.17(12H, s, CH_3), 7.25-7.26(4H, d, ArH), 7.73-7.74(4H, d, ArH), 7.78(4H, s, ArH), 8.90(8H, s, βH). For 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, the yield was 4%. Found: C, 78.40; H, 5.15; N, 7.61; $C_{48}H_{38}N_4O_4$ requires C, 78.36; H, 5.17; N, 7.61%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 422(5.59), 518(4.34), 556(4.19), 594(4.05) and 652nm(4.06); m.s. (FAB)[M+H$^+$], m/z 735; ^{1}H-nmr (200MHz)($CDCl_3$): δ, -2.76(2H, s, NH), 4.09(12H, s ,CH_3), 7.26-7.30(8H, d, ArH), 8.10-8.14(8H, d, ArH), 8.85(8H, s, βH).

5.10. Simplex Experiments in Three Dimensions

(a) Simplex applied to the synthesis of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin

To begin, four experiments were carried out in which the amount of acetic acid, nitrobenzene and the value of the temperature were chosen at more or less by random (Table P_1, P_2, P_3 and P_4). Pyrrole (0.7 ml; 1.0 x 10^{-2}mole) was added dropwise to a solution of 4-chlorobenzaldehyde (1.41 g; 1.0 x 10^{-2} mole) in a mixture of acetic acid and nitrobenzene, that had been preheated to a certain temperature. The amount of nitrobenzene acetic acid and temperature were variables (see Appendix II). This temperature was maintained for 1 hour and the solution was allowed to cool down to room temperature and left over night. The crystals that precipitated out of solution were filtered, washed with methanol and dried. The filtrate was analysed by visible spectroscopy; when some porphyrin remained in solution, the amount could be calculated from the height of the Soret band above general background absorption due to other products. The calculated amount was added to that found by direct crystallisation. In the case of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin, the yields obtained for the first "random" experiments were P_1(37%), P_2(26%), P_3(42%), and P_4(28%). The worst (P_4) was rejected according to the simplex rules (Appendix I) and the conditions for the new experiment, P_5 could be calculated:

$$\text{(i) } P = (P1 + P2 + P3)/3$$

$$\text{(ii) } P5 = P + (P - P4)$$

The experiment suggested by the new values for P_5 was carried out to get the new simplex, defined by P_1, P_2, P_3 and P_5. Table 18 shows all the

experiments carried out using this method and the experimental values used. Where the Simplex indicated a higher temperature was needed then valeric acid (b. p. 185 °C)was used instead. Valeric acid was used to replace acetic acid in experiments P_5, P_6, P_7, P_{11}, P_{12} and P_{13}. The lowest yield obtained was in P_{10} (14%) and the highest in P_{13} (56%).

Table 18. Yields at each stage of the simplex operations for the synthesis of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin

Experiment Number	RCO_2H[a] (ml)	$PhNO_2$[b] (ml)	Temperature (°C)	Yield (%)
P_1	75	509	120	37
P_2	60	20	100	26
P_3	60	30	130	42
P_4	40	40	110	28
P_5	56	60	140	42
P_6	88	53	150	33
P_7	61	46	160	34
P_8	30	37	136	54
P_9	36	39	111	33
P_{10}	21	61	128	14
P_{11}	36	67	159	15
P_{12}	45	41	140	48
P_{13}	52	43	141	56

a - Volume of carboxylic acid used (P_1, P_2, P_3, P_4, P_8, P_9, P_{10} acetic acid, and P_5, P_6, P_7, P_{11}, P_{12}, P_{13} valeric acid)

P_{12} and P_{13} were obtained by contraction of P_8 (Appendix I):

$$P_{12} = P + 1/2(P\text{-}P_6)$$

$$P_{13} = P + 1/4(P\text{-}P_6)$$

where $P = (P_3 + P_5 + P_7)/3$

(b) Simplex applied to the synthesis of 5,10,15,2-*tetrakis*(4'-biphenyl)porphyrin

Following the same procedures as in (a) the experiments and respective results are shown in the Table 19 below. Here valeric acid was used in experiments P_5, P_6, P_9 and P_{10}. The lowest yield obtained was in P8 with 4.5%, and the highest in P_{11} with 46%.

Table 19. Yields at each stage of the simplex operations for synthesis of 5,10,15,2-*tetrakis*(4'-biphenyl)porphyrin

Experiment Number	RCO_2H^a (ml)	$PhNO_2$ (ml)	Temperature (°C)	Yield (%)
P_1	75	50	130	40
P_2	60	20	100	22
P_3	60	30	120	36
P_4	40	40	110	26
P_5	57	60	140	25
P_6	88	54	150	29
P_7	91	29	126	39
P_8	63	36	100	4.5
P_9	92	46	138	45
P_{10}	109	48	162	43
P_{11}	84	42	129	46

a - Volume of carboxylic acid used (P_1, P_2, P_3, P_4, P_7, P_8, P_{11} acetic acid and P_5, P_6, P_9, P_{10} valeric acid)

In P_{11} contraction of P_9 was done by following the equation below

$$P_{11} = P + 1/2(P-P_3)$$

where $P = (P_1 + P_7 + P_8)/3$

(c) The Simplex approach applied to the synthesis of 5,10,15,20-*tetrakis*(4'-methoxyphenyl) porphyrin

The same procedures as in (a) and (b) above were followed. The experiments carried out and the respective results are shown in Table 20 below. Valeric acid was used in experiments P_1, P_2, P_4, P_5, P_6, P_7, P_8, P_9 and P_{11}. The lowest yield was in P_3 with 33% and highest was in P_{11} with 78%.

Table 20. Yields at each stage of the simplex operations applied to the synthesis of 5,10,15,20-*tetrakis*(4'-methoxyphenyl) porphyrin

Experiment Number	RCO_2H^a (ml)	$PhNO_2$ (ml)	Temperature (°C)	Yield (%)
P_1	45	5	141	59
P_2	35	15	150	54
P_3	45	15	120	33
P_4	25	20	145	57
P_5	35	30	150	52
P_6	50	12	148	55
P_7	31	18	148	57
P_8	41	12	143	54
P_9	11	25	174	77
P_{10}	12	30	160	57
P_{11}	41	11	120	78

a - Volume of carboxylic acid used (P_3, P_{10} acetic acid and P_1, P_2, P_4, P_5, P_6, P_7, P_8, P_9, P_{11} valeric acid)

In P_{10} and P_{11} a new direction and a contraction of P_8 were done. To follow this new direction, the next to worst point of the simplex that was used to get P_8 was rejected instead of the worst response:

$$P_{10} = P + (P - P_1)$$

where $$P = (P_5 = P_6 + P_4)/3$$

and for the contraction in P_8 to get P_{11}:

$$P_{11} = P + 1/2(P - P_4)$$

where $$P = (P_1 + P_5 + P_6)$$

5.11. Preparations of the cobalt complexes of 5,10,15,20-*tetrakis*arylporphyrins

In a typical experiment, the required porphyrin (0.4 mmol) was dissolved in dimethylformamide (200 ml) and heated under reflux. At this point, five equivalents of a cobalt salt, either $CoCl_2 \cdot H_2O$ or $Co(CH_3CO_2) \cdot H_2O$ (2 mmol) were added to the solution. The course of metallation was monitored by visible spectroscopy. When metallation was complete, the Soret band had shifted and the Q bands had collapsed to only one or two bands. At this point, usually after 5 to 8 hours the DMF was removed 'in vacuo' and the residual solid was dissolved in dichloromethane or chloroform, washed with water several times (3 x 200 ml) and dried (Na_2SO_4). Filtration and evaporation of the solvent gave the cobalt complex which was purified by column chromatography, usually on alumina (grade I or II) or silica gel with dichloromethane, chloroform or ethyl acetate as the eluent. Recrystallisation was effected from a mixture of petroleum ether (b.p. 40/60°C)/dichloromethane.

5.11.1. Metallation of 5,10,15,20-tetrakisphenylporphyrin

Using the procedures just described above, the resulting cobalt complex was chromatographed on alumina (grade II or I) with dichloromethane as eluent. After recrystallisation from a mixture of

petroleum ether (b.p. 40/60°C)/dichloromethane, crystals of the required cobalt complex were dried under vacuum to give a final 97% yield. Found: C, 78.40; H, 4.15; N, 8.30; $C_{44}H_{28}N_4Co$ calc. for C, 78.67; H, 4.17; N, 8.34%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 410(5.35) and 528nm(4.16); m.s. (FAB)[M^+], m/z 671.

5.11.2. Metallation of 5,10,15,20-tetrakis(4'-chlorophenyl)porphyrin

Using the procedures described above, the cobalt complex of this porphyrin was chromatographed on alumina (grade II) or silica gel with chloroform as eluent. After recrystallisation, from a mixture of chloroform/methanol, an 82% yield of crystals were obtained after drying in vacuo. Found: C, 63.92; H, 3.00; N, 6.64; $C_{44}H_{24}N_4Cl_4Co{\cdot}H_2O$ calc. for C, 63.85; H, 3.16; N, 6.77%; $\lambda_{max}(CHCl_3)$(relative %), 412(100) and 530nm(10); m.s. (FAB)[M^+], m/z 809.

5.11.3. Metallation of 5,10,15,20-tetrakis(3'-chlorophenyl)porphyrin

As described above. the cobalt complex was prepared and chromatographed on silica gel with chloroform as eluent. After recrystallisation from a mixture of chloroform/methanol, the product was dried under vacuum, giving a 82% yield. Found: C, 65.02; H, 2.96; N, 6.71; $C_{44}H_{24}N_4Cl_4Co$ requires C, 65.42; H, 2.97; N, 6.94%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 410(5.39) and 528nm(4.20); m.s. (FAB)[M^+], m/z 809.

5.11.4. Metallation of 5,10,15,20-tetrakis(2',6'-dichlorophenyl)porphyrin

As described above, the cobalt complex was prepared and chromatographed on alumina (grade II) or silica gel with chloroform as eluent. After recrystallisation, from a mixture of

dichloromethane/petroleum ether (b.p. 40/60°C), required cobalt complex was dried under vacuum, giving a 73% yield. Found: C, 55.89; H, 2.64; N, 5.50; $C_{44}H_{20}N_4Cl_8Co$ calc. for C, 55.76; H, 2.11; N, 5.90; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 412(5.15) and 530(4.04). m.s. (FAB)[M^+], m/z 947.

5.11.5. Metallation of 5,10,15,20-tetrakis(4'-methoxyphenyl)porphyrin

As described above, the cobalt complex was prepared and was chromatographed on silica gel with chloroform as eluent. After recrystallisation, from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum, giving an 89% yield. Found: C, 72.60; H, 4.64; N, 6.98; $C_{48}H_{36}N_4O_4Co$ calc. for C, 72.75; H, 4.55; N, 7.07%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 410(5.35) and 534nm(4.25): m.s. (FAB)[M^+], m/z 792.

5.11.6. Metallation of 5,10,15,20-tetrakis(3'-methoxyphenyl)porphyrin

As described above the cobalt complex was prepared and was chromatographed on silica with dichloromethane as eluent. After recrystallisation from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum, giving an 50% yield. Found: C, 72.67; H, 4.57; N, 6.98; $C_{48}H_{36}N_4O_4Co$ requires C, 72.75; H, 4.55; N, 7.07%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 410(5.36) and 528nm(4.25); m.s. (FAB)[M^+], m/z 792.

5.11.7. Metallation of 5,10,15,20-tetrakis(3',4'-dimethoxyphenyl)porphyrin

As described above the cobalt complex was prepared and was chromatographed on silica with dichloromethane as eluent. After

recrystallisation, from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum, giving an 62% yield. Found: C, 68.60; H, 4.82; N, 6.11; $C_{52}H_{44}N_4O_8Co$ requires C, 68.45; H, 4.82; N, 6.14%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 416(5.32) and 530nm(4.15); m.s. (FAB)[M^+], m/z 911.

5.11.8. Metallation of 5,10,15,20-tetrakis(3',4'-methylenodioxyphenyl) porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina (grade II) with ethyl acetate as eluent. After recrystallisation, from a mixture of chloroform/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum giving an 5.4% yield. Found: C, 67.70; H, 3.35; N, 6.58; $C_{48}H_{28}N_4O_8Co$ requires C, 68.01; H, 3.29; N, 6.61%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 416(5.04) and 530nm(3.93); m.s. (FAB)[M^+], m/z 847.

5.11.9. Metallation of 5,10,15,20-tetrakis(4'-hydroxy-3',5'-di-tert-butylphenyl) porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina grade I or silica gel with dichloromethane as eluent. After recrystallisation, from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum giving an 43% yield. Found: C, 76.90; H, 7.78; N, 4.59; $C_{76}H_{92}N_4O_4Co$ calc. for C, 77.15; H, 7.77; N, 4.72%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.21) and 530nm(4.01); m.s. (FAB)[M^+], m/z 1183.

5.11.10. Metallation of 5,10,15,20-tetrakis(3',4',5'-trimethoxyphenyl) porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina (grade II) with ethyl acetate/dichloromethane as eluent. After recrystallisation, from a mixture of dichloromethane/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum, giving an 80% yield. Found: C, 65.03; H, 5.24; N, 5.19; $C_{56}H_{52}N_4O_{12}Co$ requires C, 65.18; H, 5.04; N, 5.43%; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 414(4.97) and 528nm(3.92); m.s. (FAB)[M^+], m/z 1031.

5.11.11. Metallation of 5,10,15,20-tetrakis(2',4',5'-trimethoxyphenyl) porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina (grade II) with ethyl acetate as eluent. The cobalt complex was dried under vacuum, giving an 41% yield (no suitable solvent or system of solvents was found from recrystallisation). Found: C, 66.69; H, 4.97; N, 4.90; $C_{56}H_{52}N_4O_{12}Co.2H_2O$ requires C, 62.98; H, 4.87; N, 5.24; $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 418(5.01) and 532nm(4.03); m.s. (FAB)[M^+], m/z 1031.

5.11.12. Metallation of 5,10,15,20-tetrakis(4'-biphenyl)porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina (grade II) with ethyl acetate as eluent. The cobalt complex was dried under vacuum, giving an 87% yield(no suitable solvent or system of solvents was found from recrystallisation). Found: C, 80.84; H, 4.58; N, 5.62; $C_{56}H_{52}N_4O_{12}Co{\cdot}2H_2O$ requires C, 80.69; H, 4.78; N,

5.54; $\lambda_{max}(CHCl_3)$(% relative), 416(100) and 528nm(11.54); m.s. (FAB)[M^+], m/z 975.

5.11.13. Metallation of 5,10,15,20-tetrakis(2',3',4',5',6'-pentafluorophenyl) porphyrin

As described above, the cobalt complex was prepared and was chromatographed on alumina (grade II) with chloroform as eluent. After recrystallisation, from a mixture of diethyl ether/petroleum ether (b.p. 40/60°C), the cobalt complex was dried under vacuum, giving an 88% yield. $\lambda_{max}(CHCl_3)(\log\varepsilon)$, 406(5.16) and 528nm(4.05); m.s. (FAB)[M^+], m/z 1031.

5.11.14. Metallation of 5,10,15,20-tetrakis(4'-methylthiophenyl)porphyrin

As described above, the cobalt complex was prepared. When cooling the dimethylformamide to room temperature, the cobalt complex precipitated out of solution and was washed with water and methanol, isolated and dried under vacuum, giving an 80% yield(no suitable solvent or system of solvents was found from recrystallisation). Found: C, 58.33; H, 3.85; N, 5.65; $C_{56}H_{52}N_4O_{12}Co{\cdot}7H_2O$ calc. for C, 58.71; H, 3.67; N, 5.70%; $\lambda_{max}(CHCl_3)$(% relative), 426(100) and 550nm(12.22); m.s. (FAB)[M^+], m/z 855.

5.12. Cyclic Voltammetry Measurements

The solvent, butyronitrile, was passed through a column of alumina which (30 cm x 2 cm diameter). Using this solvent, a 0.1M (0.1 mole/1 dm^3) solution of tetrabutylammonium perchlorate was prepared

to give the current carrying electrolyte. In use, 25 ml solutions of the cobalt complexes at 1 mM (1 mmol/1 dm^3) concentration were prepared in the tetrabutylammonium perchlorate solution. Once inside the cell, the cobalt porphyrin solutions were purged with nitrogen for 10-15 minutes to remove oxygen and a nitrogen atmosphere was maintained during voltammetry. The electrodes were immersed inside the electrolyte solution and were connected to the potentiometer from which the experiment was controlled. For all measurements, the same scan speed was registered, viz., 200 mvolts/second, however other scan speeds of 100 mvolts/second and 40 mvolts/second were also measured; at all scan speeds the results was the same. The half wave potential ($E_{1/2}$) was obtained by taking the mid-point between the two maxima obtained in the voltagram which represented cathodic and anodic reduction and oxidation of the cobalt metal ion. Table 21. below shows the results obtained for these measurements. The voltage was varied from 0 to 2.000 volts.

Table 21. Halfwave potential for cobalt 5,10,15,20-*tetrakis*arylporphyrin corresponding to the process, Co(III) + e^- ⟶ Co(II)

Aryl group[a]	$E_{1/2}$ (volts)
3-Methoxyphenyl	0.807
2,3,4,5,6-Pentafluorophenyl	0.777
3-Chlorophenyl	0.772
2,6-Dichlorophenyl	0.767
3,4,5-Trimethoxyphenyl	0.760
3,4-Dimethoxyphenyl	0.732
2,4,5-Trimethoxyphenyl	0.662
4-Chlorophenyl	0.645
Phenyl	0.637
3,4-Methylenedioxyphenyl	0.617
4-Methoxyphenyl	0.612
3,5–Di-*tert*-butyl 4-hydroxyphenyl	0.497

a - aryl group in the 5,10,15,20-tetrakisarylporphyrin cobalt complexes.

Visible spectra were obtained for all metalloporphyrins both before cyclic voltammetry and after. The before and after spectra were identical for all complexes.

5.13. Reactions of Cobalt Porphyrin Complexes with Sodium Borohydride and Dioxygen

Solutions of the metalloporhyrins (2.96 x 10^{-6}mole) were prepared in dichloromethane (4 ml) and methanol (1 ml). From each a sample was removed (25 µl) and diluted with dichloromethane (3 ml), before being placed in a uv/visible spectrometer cell. An excess of solid sodium borohydride was added to the cell solution which, the solution was shaken and, after settling, a spectrum was obtained over the range 350 nm to 800 nm. By using a small Pasteur pipette, dioxygen was bubbled into the solution in the cell for 1-2minutes and the spectrum of the resulting solution was again measured. This process was repeated 10 more times occupying a total time of about 25 minutes. The results were the same for all metalloporphyrins tested; when sodium borohydride was added to the solution the wavelength of the Soret band corresponding to a cobalt(II) porphyrin complex was seen and, when dioxygen was bubbled into the solutions, the wavelength changed to that corresponding to a cobalt(III) porphyrin complex. For example, for the cobalt(II) complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin, the band at 416 nm changed to that of the cobalt(III) complex at 428 nm after bubbling dioxygen into the solution and then reverted to that of cobalt(II) on shaking the solution with sodium borohydride. After cycling each experiment 10 times, no degradation of the metalloporphyrins was observed. The

metalloporphyrins tested were as listed here (cobalt[II] and cobalt[III] Soret band wavelenths [nm] are shown in parentheses):

5,10,15,20-*tetrakis*phenylporphyrin (412, 430),

5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin (416, 428),

5,10,15,20-*tetrakis*(3'-methoxyphenyl)porphyrin (416, 432),

5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin (412, 430),

5,10,15,20-*tetrakis*(3-chlorophenyl) porphyrin (412, 428),

5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin (412, 428),

5,10,15,20-*tetrakis*(3,4'-methylenedioxyphenyl)porphyrin (416, 432),

5,10,15,20-*tetrakis*(3',4'-di methoxyphenyl)porphyrin (416, 430),

5,10,15,20-*tetrakis*(4'-biphenyl)porphyrin (416, 432),

5,10,15,20-*tetrakis*(2',3',4',5',6'-pentafluorophenyl)porphyrin (406, 422),

5,10,15,20-*tetrakis*(2',4',5'-trimethoxyphenyl)porphyrin (420, 432),

5,10,15,20-*tetrakis*(3',4',5'-trimethoxyphenyl)porphyrin (416, 428), and

5,10,15,20-*tetrakis*(3',5'-di-*tert*-butyl-4'-hydroxyphenyl)porphyrin (418, 432).

5.14. Synthesis of Dihydroquinones

The requisite quinone (41 mmol) was dissolved in chloroform (60 ml). To this solution was added a solution of sodium sulphite (57 mmol) in water (75 ml) and the mixture was stirred for 10 minutes; the dihydroquinones precipitated from solution and were collected on a Buckner funnel and dried in 'vacuo'.

5.14.1. Synthesis of 2,3,4,5,6-tetrachloro-1,4-dihydrobenzoquinone (H_2TCQ)

Following the above procedure but replacing chloroform by toluene because of the solubility of this quinone, a 91% yield of the desired

dihydroquinone was obtained as a whitish pink powder; m.p. 235-245°C (decomp.); $\lambda_{max}(CHCl_3)$(relative %), 218(100) and 310(66)nm.

5.14.2. Synthesis of 2,3-dichloro-5,6-dicyano-1,4-dihydrobenzoquinone (H_2DDQ)

Following the above procedure, a 61% yield of the desired dihydroquinone was obtained as a yellowish white powder; m.p. 289-290°C (decomp.); $\lambda_{max}(CHCl_3)$(relative %), 220(100), 354(31)nm.

5.15. Oxidation Reactions of Dioxygen Using Dihydroquinones as Substrate and Cobalt Porphyrin Complexes as Catalyst

General Method

A cobalt porphyrin complex (2.96 x 10^{-6}mole) was dissolved in dichloromethane (4 ml), and separately, the chosen dihydroquinone (1.1 x 10^{-5}mole) was dissolved in methanol (1 ml). The methanol solution was added to the dichloromethane solution and left to stand at room temperature. Each minute, a sample (25 µl) was removed, diluted in dichloromethane (3 ml) and a uv/visible spectrum obtained over the range 200 to 700nm. At the same time as the spectrum was being run, a tlc was also obtained. From these experiments, the median velocity [v_m=(moles of substrate)/(moles of catalyst x time)] was calculated.

(a) Oxidation of 2,3,4,5,6-tetrachloro-1,4-dihydroquinone (H_2TCQ)

Following the above procedures, median velocities were calculated and are shown in Table 22.

Table 22. Median velocity for reactions between the cobalt porphyrin complexes with H_2TCQ and dioxygen

Aryl group[a]	v_m (moles/ min/moles catalyst)
Phenyl	0.95
4-Methoxyphenyl	0.95
3,4-Dimethoxyphenyl	0.95
3-Methoxyphenyl	0.63
3,4,5-Trimethoxyphenyl	0.38
2,4,5-Trimethoxyphenyl	0.63
3,4-Methylenedioxyphenyl	0.57
4-Chlorophenyl	0.133
3-Chlorophenyl	0.126
3,4-Di-*tert*-butyl-4-hydroxyphenyl	9.0×10^{-3}
4-Biphenyl	0.06
4-Methylthiophenyl	not soluble[b]
2,6-Dichlorophenyl	0.0
2,3,4,5,6-Pentafluorophenyl	0.0

a - Aryl group in 5,10,15,20-tetrakisarylporphyrin cobalt complexes.
b - The cobalt complex was not soluble in the solvent medium.

(b) Oxidation of 1,4-dihydrobenzoquinone (H_2BQ)

Following the above procedures, medium velocities were calculated and are shown in Table 23.

Table 23. Median velocity for reactions of cobalt porphyin complexes with H_2BQ and dioxygen

Aryl group[a]	v_m (moles/ min/moles catalyst)
4-Methoxyphenyl	0.032
Phenyl	0.012
3,4-Dimethoxyphenyl	4.5×10^{-3}
2,4,5-Trimethoxyphenyl	4.5×10^{-3}
3,5-Di-*tert*-butyl-4-hydroxyphenyl	2.9×10^{-3}
3-Methoxyphenyl	over 24 hours[b]
3,4-Methylenedioxyphenyl	over 24 hours[b]
4-Chlorophenyl	over 24 hours[b]
3-Chlorophenyl	over 24 hours[b]
4-Biphenyl	over 24 hours[b]
4-Methylthiophenyl	over 24 hours[b]
2,6-Dichlorophenyl	over 24 hours[b]
2,3,4,5,6-Pentafluorophenyl	over 24 hours[b]

a - Aryl group in 5,10,15,20-tetrakisarylporphyrin cobalt complexes.
b - The reactions were controlled over 24 hours and were not complete during this period

(c) Oxidation of 2,3-dichloro-5,6-dicyano-1,4-dihydrobenzoquinone (H_2DDQ)

Following the above procedures, reactions of the cobalt complexes with H_2DDQ were carried out. After 24 hours, all the metalloporphyrins tested revealed evidence for production of the quinone but the rate of conversion of dihydroquinone into quinone was not calculated. Table 24 shows all the porphyrins tested and the respective results.

Table 24. Median velocity for reactions of cobalt porphyin complexes with H_2DDQ and dioxygen

Aryl group[a]	Results[b]
4-Chlorophenyl	evidence
3-chlorophenyl	evidence
2,6-Dichlorophenyl	no evidence
2,3,4,5,6-Pentafluorophenyl	no evidence
3,4-Methylenedioxyphenyl	evidence
3,5-Di-*tert*-butyl-4-hydroxyphenyl	evidence
4-Methylthiophenyl	not soluble
Phenyl	evidence
4-Methoxyphenyl	evidence
3-Methoxyphenyl	evidence
3,4-Dimethoxyphenyl	evidence
2,4,5-Trimethoxyphenyl	evidence
3,4,5-Trimethoxyphenyl	evidence
4-Biphenyl	evidence

a - Aryl group in 5,10,15,20-tetrakisarylporphyrin cobalt complexes.
b - "Evidence " means that quinone formation was detected by tlc, but not spectroscopically
c - The cobalt complex was not soluble in the solvent medium

5.16. Oxidation Reaction Using Dihydroquinones, Cobalt Complexes, Dioxygen, and Acetonitrile as Solvent

Cobalt porphyrin complexes (2.96×10^{-6}mole) were dissolved in acetonitrile (5 ml), the dihydroquinone (1.1×10^{-5}mole) was added to this solution and the combined solutions were left to react at room temperature. At regular intervals, a sample (25 µl) was removed, diluted in dichloromethane (3 ml) and a uv/visible spectrum obtained from 200 to 700nm. In this procedure, the solubility of most metalloporphyrins at room temperature was not very good and reaction times for all complexes

were over 1 hour. For these reasons, no further studies were done with this solvent.

5.17. Calculations of Turnover Numbers

In a typical experiment, a cobalt porphyrin complex (2.9×10^{-6}mole) was dissolved in dichloromethane (5 ml) was mixed with, 2,3,5,6-tetrachloro-1,4-dihydrobenzoquinone (54 mg; 2.2×10^{-4}mole) dissolved in methanol (5 ml) at room temperature. A uv/visible spectrum from 200 to 700nm was obtained at regular intervals by removing a sample (50 µl) and diluting it in dichloromethane (3 ml). The monitoring was stopped when all the metalloporphyrins had been destroyed, as indicated by the total disappearance of the Soret band and checked by tlc. The amount of quinone formed was calculated spectroscopically using the Lambert-Beer equation ($A=\varepsilon lc$) for the band at 204nm, a characteristic band of TCQ with an extinction coefficient of 15000. From the absorption observed the concentration of the solution was calculated using the equation:

$$C_{sol} = (3\ C_{cell}\ /1000)/50 \times 10^{-3}\text{moles/dm}^3$$

C_{sol} - concentration of the original reaction solution

C_{cell} - concentration of the solution in the cell

Once the concentration in the reaction medium, C_{sol}, had been calculated, the turnover number (TOV) was calculated from the number of moles of quinone produced and the original number of moles of catalyst that had been used for the experiment (the factor 2 emerges because two electrons are transfered):

$$TOV = 2(10C_{sol}/1000)/(2.9 \times 10^{-6})$$

Table 25 tabulates the results.

Table 25. Turnover number for reaction between cobalt porphyrin complexes, H_2DDQ and dioxygen

Aryl group[a]	Turnover Number (TOV)
4-Chlorophenyl	92
3-chlorophenyl	102
2,6-Dichlorophenyl	no reaction[b]
2,3,4,5,6-Pentafluorophenyl	no reaction[b]
3,4-Methylenedioxyphenyl	64
3,5-Di-*tert*-butyl-4-hydroxiphenyl	82
4-Methylthiophenyl	not soluble[c]
Phenyl	98
4-Methoxyphenyl	92
3-Methoxyphenyl	92
3,4-Dimethoxyphenyl	90
2,4,5-Trimethoxyphenyl	66
3,4,5-Trimethoxyphenyl	64
4-Biphenyl	70

a - Aryl group in 5,10,15,20-tetrakisarylporphyrin cobalt complexes.
b - The dihydroquinone was not oxidized and the cobalt complex was unchanged
c - The cobalt complex was not soluble in the solvent medium

5.18. Test for the Importance of the Presence of Dioxygen

The cobalt porphyrin complexes used for this experiment were 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',5'-di-tert-butyl-4'-hydroxyphenyl)porphyrin. The experiment was repeated with all three dihydroquinones, H_2TCQ, H_2BQ and H_2DDQ.

Cobalt porphyrin complexes (2.96×10^{-6}mole) were dissolved in dichloromethane (4 ml) which had been purged previously with nitrogen for 5 minutes. Separately, a dihydroquinone (1.2×10^{-5}mole) was dissolved in methanol (1 ml) and this solution was purged also with nitrogen for two minutes; the two solutions were then mixed. The new mixture was

left to stand under a nitrogen atmosphere at room temperature and at regular intervals, samples (25µl) were withdrawn and monitored for quinone by diluting the sample with dichloromethane (3 ml) and running a visible spectrum to observe the Soret band. After 24 hour, no formation of quinone could be observed, indicating that the process needed oxygen.

5.19. Test for the Importance of Cobalt in these Oxidations

The porphyrins used for this experiment were 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-*tetrakis*(3',5'-di-tert-butyl-4'-hydroxyphenyl)porphyrin. The experiment was repeated with all three dihydroquinones, H_2TCQ, H_2BQ and H_2DDQ.

Free base porphyrin (2.96×10^{-6}mole) was dissolved in dichloromethane (4 ml). Separately, a dihydroquinone (1.2×10^{-5}mole) was dissolved in methanol (1 ml) and this solution was added to the dichloromethane solution. The new mixture solution was left to stand at room temperature and at, regular intervals, samples (25 µl) were removed for monitoring of the presence of quinone, by dissolving the sample in dichloromethane (3 ml) and running a uv/visible spectrum over the range 200 to 700nm. After 24 hour, no formation of quinones had been observed for all three dihydroquinones, H_2TCQ, H_2BQ and H_2DDQ.

5.20. Test for the Effect of a Strongly-bonded Axial Ligand (Imidazole) in these Oxidations

The cobalt porphyrin complexes used for this experiment were 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and 5,10,15,20-

tetrakis(2',6'-dichlorophenyl)porphyrin. The experiment was repeated with all three dihydroquinones, H_2TCQ, H_2BQ and H_2DDQ.

A cobalt porphyrin complex (2.96 x 10^{-6}mole) was dissolved in dichloromethane (3 ml). Separately, the dihydroquinone, either H_2TCQ, H_2BQ, or H_2DDQ (1.2 x 10^{-5}mole), was dissolved in methanol (1 ml), as was imidazole (529.1mg) dissolved in methanol (1 ml). These solutions were mixed together and left to stand at room temperature, exposed to oxygen in the atmosphere. The reactions were monitored by uv/visible spectroscopy over the range 200 to 700nm by withdrawing at regular intervals samples (25 µl) and dissolving the sample in dichloromethane (3 ml). No oxidation of either H_2TCQ, H_2BQ, or H_2DDQ was observed indicating that the strongly complexing axial ligand had blocked access to cobalt or had changed the electron density in such a way as to suppress oxidation. For 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin the Soret band wavelenths shifted from 416nm to 432nm and the Q band was split into two bands at 558 and 600nm, for 5,10,15,20-*tetrakis*(2',6'-dichlorophenyl)porphyrin, the Soret band was shifted from 412nm to 436nm and the Q band from 536nm to 554nm.

5.21. Testing for the Formation of Hydrogen Peroxide by Using Analytical Peroxide Test Strips

(a) experiment carried out under nitrogen

The cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin and its reaction with H_2TCQ was chosen for this test. The cobalt porphyrin complex (2.96 x 10^{-6}mole) was dissolved in dichloromethane (4 ml) which had been purged previously with nitrogen for 5 minutes. Separately the dihydroquinone (1.2 x 10^{-5}mole) was dissolved in methanol (1 ml) and

this solution was purged also with nitrogen for two minutes; the two solutions were mixed and left to stand under a nitrogen atmosphere at room temperature. At regular intervals, samples (25 µl) were removed and monitored for production of hydrogen peroxide by extracting the sample with water (1 ml) and using a of hydrogen peroxide detector strip (Merck); the presence of hydrogen peroxide is measured by a colour change from white to blue. No hydrogen peroxide was detected during these reactions.

(b) experiment done in the presence of air

Exactly as in (a) above, the same metalloporphyrin was mixed with H_2TCQ. At regular intervals, samples (25 µl) were removed from the reaction medium and tested for the presence of hydrogen peroxide formation. This time, a blue colour developed immediately in even the first sample removed after 5 minutes of reaction, showing that, in the presence of air, hydrogen peroxide was being produced.

5.22. Destruction of Cobalt Porphyrin Complexes in the Absence of Dihydroquinones

As before, the metalloporphyrin chosen for this test was the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin. The cobalt porphyrin complex (2.96×10^{-6}mole) was dissolved in dichloromethane (4 ml). At regular intervals samples (25 µl) were removed, diluted in dichloromethane (3 ml) and a uv/visible spectrum was obtained as well as a tlc. No degradation of the porphyrin was detected either in the appearance of its uv/visible spectrum or in its performance on tlc. This

indicates that, in the absence of dihydroquinone no destruction of the cobalt complexes occurs.

5.23. Detection of the Formation of Hydrogen Peroxide During Oxidation by Use of the Luminol Test

It was felt that the previous detection of hydrogen peroxide using test strips was perhaps not sufficiently specific. Accordingly, a luminol test for hydrogen peroxide was carried out since, it is well known that, in the presence of hydrogen peroxide luminol reacts with characteristic emission of light (fluorescence).

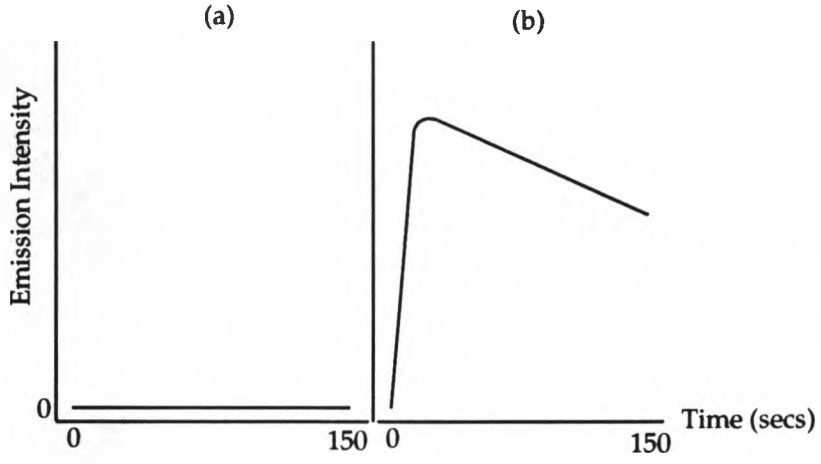
As before, the metalloporphyrin chosen for this test was the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin in reaction with H_2TCQ. A buffer solution (pH 8.6) was prepared from tris(hydroxymethyl) methylamine. A luminol solution (100 μM) was prepared in the buffer and set on one side. Separately, a solution of horseradish peroxidase (10 mg/10 ml) was prepared in the same buffer and set aside.

A test reaction was prepared by dissolving the cobalt porphyrin complex (2.96×10^{-6}mole) in dichloromethane (4 ml) and adding to it a solution of dihydroquinone (1.1×10^{-5}mole) in methanol (1 ml). The mixed solutions were left to stand at room temperature. A second identical test reaction was prepared using the same procedures but was stored under nitrogen.

In a fluorimeter cell, a luminol sample solution (3 ml) was mixed with some of the peroxidase solution (100 μl). Separately, using distilled water (2 ml) the reaction under test was extracted after 5minutes of reaction. From this aqueous extract a sample (100 μl) was removed and

was added to the luminol/peroxidase solution in the fluorimeter cell. This mixture was shaken quickly, introduced into the spectrofluorimeter and emission of light was measured. Graphics (a) and (b) illustrate what happens during measurement. For the reaction exposed to oxygen in the atmosphere (b), light emission was observed but it was not for the reaction set up under nitrogen alone (a).

The fluorometer was set up to detect fluorescence at 425nm with a 20nm slit width. Emission was recorded over a period of 150 seconds.



5.24. Attempts to Prevent Attack by Hydrogen Peroxide on the Cobaltoporphyrins

As before, the metalloporphyrin chosen for this test was the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin in reaction with H_2TCQ.

(a) with palladium-on-charcoal

Because palladium-on-charcoal is known to decompose hydrogen peroxide into water and dioxygen, its action in protecting porphyrins was examined.

The cobalt porphyrin complex (2.96 x 10^{-6}mole) was dissolved in dichloromethane (3 ml). Separately the H_2TCQ was dissolved in methanol (1 ml) and then the two solutions were mixed, together with added palladium-on-charcoal (5 mg; 10%) with stirring. Monitoring by uv/visible spectroscopy over the range 200 to 700nm at regular intervals revealed that the cobalt complex was being steadily destroyed and the palladium-on-chacoal appeared to offer no protection. Possibly because the temperature was too low.

(b) using a radical scavenger

As there may have been a problem with the heterogeneity of the reaction medium, a homogeneous protection was sought through use of a soluble radical scavenger.

The cobalt porphyrin complex (2.96 x 10^{-6}mole) was dissolved in dichloromethane (3 ml). Separately, H_2TCQ (1.1 x 10^{-5}mole) was dissolved in methanol (1 ml) and a radical scavenger [2,6-di-tert-butyl-1-hydroxybenzene; 40mg] was added to the dichloromethane solution. The mixed solutions were left to stand at room temperature exposed to oxygen in the atmosphere. Monitoring by uv/visible spectroscopy over the range 200nm to 700nm at regular intervals revealed that the cobalt complexes were still being destroyed and at faster rate.

Extraction of the reaction mixture with water (2 ml) after 5 minutes from the start of reaction and following the procedures described for the luminol test in Section 5.22, the formation of hydrogen peroxide test was sought. Emission of light confirmed that hydrogen peroxide was still being formed.

5.25. Attempts to Indentify the Position of Attack of Hydrogen Peroxide in the Cobalt Porphyrin Complexes

As before, the metalloporphyrin chosen was the cobalt complex of 5,10,15,20-*tetrakis*(4'-methoxyphenyl)porphyrin. The Cobalt porphyrin complex (2.5×10^{-4}mole) was dissolved in a mixture of dichloromethane (100 ml) and methanol (45 ml). To this solution was added aqueous hydrogen peroxide (10g; 70% w/w) and this mixture was stirred. After 12 hours the solution was black and no precipitated products were formed. The solution was washed with water to remove excess hydrogen peroxide and solvents were removed "in vacuo". During the removal of solvent the colour of the solution turned yellow. The visible spectrum of the yellow solution shows two broad bands at 326 and 402nm. By the ^{1}H-nmr it appears that the cobalt was removed and three hydroxyl groups were incorporated into the *meso*-positions of the porphyrin. $\lambda_{max}(CHCl_3)$(relative %), 336(100), 402nm(50); ^{1}H-nmr (200MHz)($CDCl_3$): δ, 1.22(4H, s, NH), 3.79(3H, s, OCH_3), 3.85(9H, s, OCH_3), 6.85(4H, s, βH), 6.87(4H, s, βH), 6.89-6.94(2H, d, ArH), 6.95-7.00(6H, d, ArH), 7.92-7.96(6H, d, ArH), 8.01-8.06(2H, d, ArH).

Appendix I

Introduction

Many activities of chemists involve observing the *response* of a system, whether it is an instrument, a mathematical model, or a reaction, as a function of a number of experimental variables. The values of the experimental variables are then optimised to improve the response of the system. Improvement can mean increased selectivity, increased sensitivity, decreased interferences, faster operation, greater precision or some other desired response. In organic synthesis, the conditions are frequently varied in order to seek the best yield of the desired product but, sometimes, selectivity is more important as a response. The first problem in optimising a real system lies in its multidimensional nature, that is there are usually many variables to optimise simultaneously. If the variables are independent of one another then it is necessary to vary them one at a time whilst observing the response. Using this method of changing the variables one at a time necessitates carrying out a large number of experiments. In some situations, the problem is even more complicated than just the large number of experiments needed. This occurs when the variables of a system are not completely independent of one another, so a collective study is required. To optimise the response of such a system and avoid a large number of experiments, there are several optimisation methods available. Four of these methods are single-factor variation, grid-searches, random approaches, and the simplex method.[179]

The simplex method; definition

The simplex method is a sequential optimisation of any system that involves repeated observation of the system response, selection of new values for the variables, followed by another observation, and so on.[179] A

simplex is a geometric figure with its number of vertices equal to one more than the number of dimensions in the factor space.[179] A simplex in two dimensions is a triangle, and in three dimensions it is a tetrahedron. In four or more dimensions, simplexes cannot be drawn or readily visualised.

To start a simplex investigation of a given factor space, (n + 1) observations (n = the number of dimensions) are needed to establish the initial simplex. For example, to start a two dimentional Simplex, three initial responses are needed to the three different sets of the two variables. After the initial (n + 1) experiments, each move requires just one additional observation. The simplex moves about in the factor space quite efficiently, sampling the response values in an orderly manner.

If the yield or conversion of a chemical reaction is the response observed then the variables (e.g. pressure, temperature, concentration, time) may be optimised to a best yield, or best conversion. Before using the simplex method a criterion must be chosen by which movement of the simplex can be judged. In the research presented in this thesis, the yield of reaction product is the criterion or response. To force the simplex to move to an optimum of any given criterion (yield, conversion, peak shape, etc.), a number of rules must be followed. The moves made according to these rules are made *after* observation of the responses to a given initial set of values for the variables.

Rules for the movement of a Simplex[206]

1: A move is made after each observation of the responses to a set of experimental conditions (the operating parameters).

2: A move is made into an adjacent simplex which is obtained by discarding the point on the current simplex that corresponds to the least

desirable response (e.g. worst yield) and replacing it with its mirror image across the (hyper)face of the remaining points.

3: If the reflected point has the least desirable response in the new simplex then rule 2 is not re-applied since this would return the Simplex to the original. Instead, the second worst response is rejected in the new Simplex.

4: If any one vertex or optimum has been retained in k+1 simplexes then, before applying rule 2, the response at the persistent vertex must be observed again to check for spurious errors.

5: If a newly formulated vertex lies outside the boundaries of the independent variables, no experimental observations are made but, instead, the response is described as undesirable.

An Example of a Simplex Procedure[206,178,207,179]

To understand how these rules work, one may consider a two-dimensional (n = 2) simplex (a triangle; figure 20). Three experiments (A, B, C; n +1 = 3) must be carried out first, using different sets of parameters for each experiment. These parameter sets can be chosen randomly or may be based on estimates of likely good responses. The results (responses) from these three experiments can be plotted on a graph. In this example, the parameters chosen for investigation are temperature and concentration. Let the results (responses) of the initial three experiments be represented by the simplex (ABC) shown in figure 20. A, B and C are the points representing temperature and concentration for each of three initial experiments. It is found that A represents the least desirable response (i.e., the parameters of temperature and concentration chosen for experiment A gave the worst yield). To carry the simplex forwards, point A must be reflected across the line BC to generate a new point D to give a

new simplex, BCD. The point D represents a new set of conditions for temperature and concentration for a new experiment; this experiment must be carried out and the yield (response) measured again. Now, there are three responses in the new simplex (BCD). Suppose C is now the least desirable response then, it must be rejected and reflected across the line BD to give another new simplex BDE. Again, the experiment corresponding to parameter values determined by E must be carried out to give a new response. Suppose B is now the worst response of BDE. Then, B is reflected across the line DE and another simplex DEF is defined. The points on the simplex are vectors and, for n parameters ($n \geq 3$), the simplexes cannot be represented graphically, but can still be moved in hyperspace using rules of vector analysis.

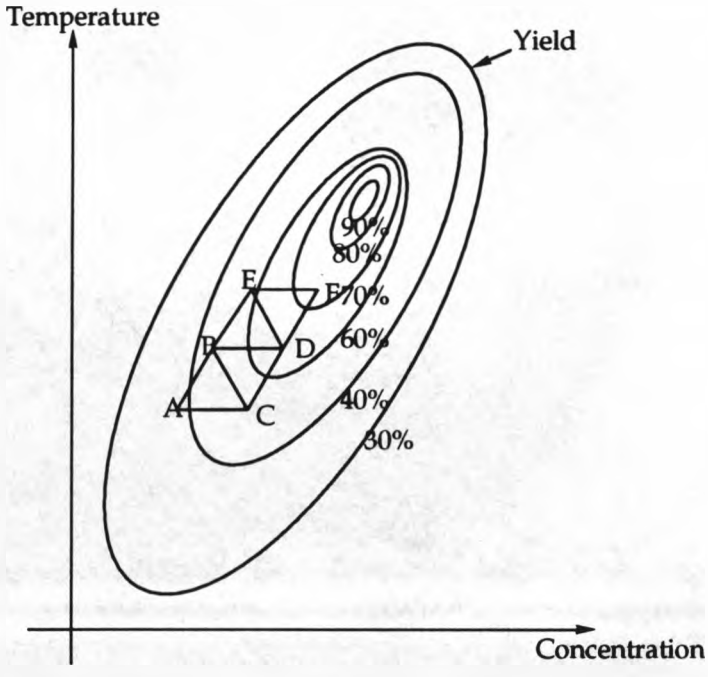


Figure 20. A two dimensional simplex. The contour lines represent all points having the same response (in this example they are yields). The contour lines define the surface that the system can move over by changing the variables (temperature and concentration). Viewed three-dimensionally, this hypothetical example would be a "hill" getting higher (increasing yield) with optimisation of temperature and concentration. The Simplex 'climbs' the hill. In hyperspace, the Simplex 'climbs' to the optimum response.

For a K-dimensional simplex, each point in hyperspace can be represented by a vector P_1, P_2, P_3, ..., P_k, P_{k+1}. The elimination of the undesirable response P_j leaves the hyperface P_1, P_2, P_3, ..., P_{j-1}, P_{j+1}, ..., P_k, P_{k+1} in which the centroid (**P**), can be defined by the equation:

$$\mathbf{P} = (1/k)\,(P_1 + P_2 + P_3 + \ldots\ldots + P_{j-1} + P_{j+1} + \ldots\ldots + P_k + P_{k+1})$$

According to rule 2 the new simplex is defined by reflection across this hyperface through **P** to give a new vertex (P_j^*); this is the reflection of the rejected vertex P_j:

$$P_j^* = \mathbf{P} + (\mathbf{P} - P_j)$$

Some Problems with the Simplex Approach

There are some problems with the Simplex method of optimisation. They are: (i) the size of the initial Simplex may make the number of experiments too large for the Simplex to achieve its best response or may make it very difficult to refine the best response, and (ii) the difficulty of deciding that an optimum response has been achieved.

To solve the first problem, a new modified simplex method was developed in 1965, known as the variable-size simplex.[206,178,179] This was a great improvement for simplex optimisation and was achieved by allowing the simplex to expand and contract as it probes the response surface.

Modified Simplex Method[206]

In addition to reflection, two other operations can be used: expansion and contraction (figure 21).

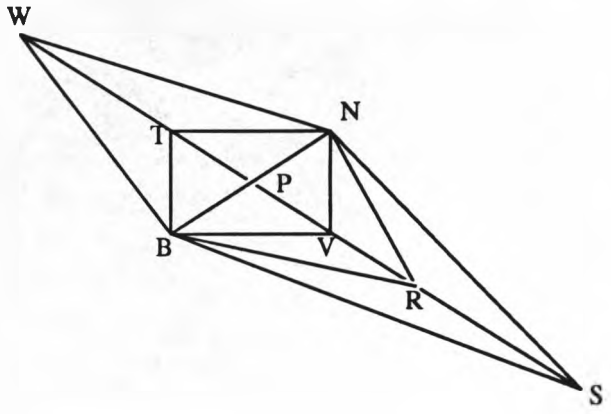


Figure 21. Operations that can be applied to move a simplex across a hyperface under conditions where the simplex oscillates between two sets of parameters, possibly lying in a false minimum.[206]

Consider an initial simplex represented by BNW (figure 21). If B is the best response, W the worst and N the next-to-worst and **P** is the centroid of the hyperface BN then W must be reflected across BN to generate R using the equation:

$$P_R = \mathbf{P} + (\mathbf{P} - P_W)$$

Three responses from R are possible: (i) R can be better than B and in this case further investigation in that direction would be required, the new simplex would be BNS, by expanding in the direction of R, using the following equation (γ is an expansion coefficient that must be greater than 1):

$$P_S = \mathbf{P} + \gamma(\mathbf{P} - P_W) \qquad (\gamma > 1)$$

(ii) the response at R is neither better than the response at B, nor worse than that at N, so the new simplex is BNR

(iii) the response at R is less desirable than the response at N, indicating unsatisfactory movement and suggests contraction may be needed in this particular direction of investigation.[206]

In the last case, if the response at R is less desirable than the response at the worst previous vertex (W), then the new contracted simplex should lie at T, closer to W than to R. To effect such a move, a contraction coefficient (β; $0<\beta<1$) must be used:

$$P_T = \mathbf{P} - \beta(\mathbf{P} - P_W) \quad (0 < \beta < 1)$$

If the response at R is not less desirable than the response at the worst previous vertex, then the new contracted simplex should lie at V, which is closer to R than to W, using a contraction coefficient β in the equation:

$$P_V = \mathbf{P} + \beta(\mathbf{P} - P_W)$$

To illustrate how useful it can be to contract and expand a simplex, figure 22 shows the movement of a simplex in a surface where the best response is far away from the chosen set of experimental conditions and, by doing expansions and contractions of the initial simplex, this is allowed to travel quickly across the surface towards the best response. Finally, by reducing the size of the simplex the best response can be refined.

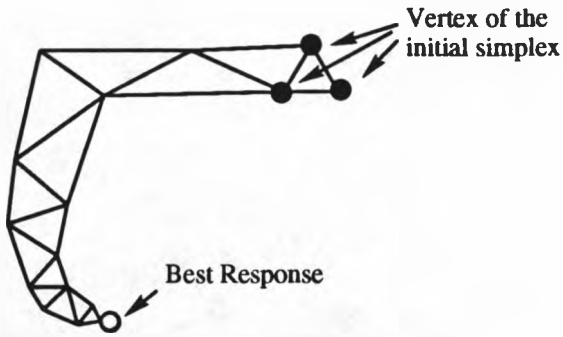


Figure 22. Progress of a simplex towards the best response. The use of operations such as reflection, expansion and contraction, allow for a fast and refined movement of the simplex across the surface.

For the second problem of deciding whether or not an optimum has been located, some criteria can be followed, to help reach a conclusion.

For a three dimensional simplex it is easy to visualise what happens when a maximum has been achieved because, at that point, the rules force the simplex to circulate (figure 23).

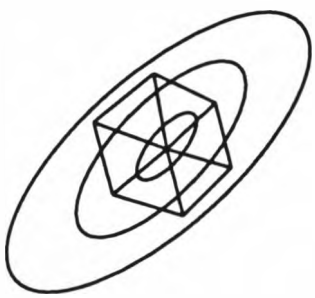


Figure 23. The simplex reaches the best response for a system and circulates around the optimum response. Further application of the simplex rules in such a situation only serves to cause the simplex to circulate around the best response.[206]

More than three dimensions make a graphical representation more difficult but the result is just the same. There are other criteria for convergence: (i) some are based on the values of the response found if the absolute change or relative change in the response must fall below a known threshold, (ii) some are based on the actual values of the factors

and the absolute or relative changes in these values can be used, (iii) some decisions are reached by model fitting to several values of a response to try to get a picture of the response surface.[179] As reported, none of these criteria guarantees that the optimum response has been found. In practice, it is better to use more than just one criterion.[179]

Some care must be taken when using the simplex method. For example, if a vertex appears to be outside the boundaries of the system being examined, it should not be discarded immediately. This point needs to be considered because the actual boundaries might not be real and may need to be changed. Also, whenever working with simplexes which are too small, indeterminate errors may occur more easily and can mask the true effects.[206]

Example of an Application of the Simplex Method

To exemplify the use of the simplex method, its use to improve the yield (response) in the synthesis of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin (presented in chapter 2) is shown next.

Very briefly and before going into the simplex application it is worth repeating how the synthesis is performed. To a solution of carboxylic acid and nitrobenzene at a certain temperature are added an equal number of moles of pyrrole and aldehyde. The new solution is left to react for one hour and then to cool overnight. The precipitated porphyrin is collected on a filter, washed with methanol and dried. The amount of porphyrin that does not precipitate out of solution in this way is calculated from visible spectroscopy on the Soret band in the filtrate and this is added to the total obtained. Since the solubility of the porphyrin in the solvent is finite, this last number is the same for all experiments <u>if</u> the solvent remains unchanged.

The variables chosen as parameters were firstly, the amount of carboxylic acid, secondly, the amount of nitrobenzene, and thirdly, the temperature; this gives n factors and an n + 1 dimensional Simplex where n = 3. The amounts of pyrrole and aldehyde were kept constant. The response was the percentage yield of 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin. As the number of parameters chosen to vary is three, this Simplex could be represented as a tetrahedron that moves across the hyperspace. The fourth vertex, the response that is being observed, is the yield.

To apply the Simplex rules, since n + 1 = 4, then four random experiments must first be performed; these give the initial vertices P_1, P_2, P_3, and P_4. For this experiment, values for P_1-P_4 were chosen at random and Table 26 shows the values chosen together with the respective responses observed after these first four experiments had been carried out.

Table 26. First experimental conditions defining the four vertices used to start the Simplex.

Vertex	Amount of RCO_2H (ml)[a]	Amount of $ArNO_2$ (ml)[b]	Temperature (°C)	Yield % (response)
P_1	75	50	120	37
P_2	60	20	100	26
P_3	60	30	130	42
P_4	40	40	110	28

a - An aliphatic carboxylic acid. Initially, R = CH_3.
b - An aromatic nitro compound. Initially, Ar = phenyl.

The worst response corresponds to P_2 with a yield of 26%. Therefore, P_2 is reflected across the hyperface defined by the other three vertex, P_1, P_3 and P_4. To do this, the centroid defined by the three must be found. The centroid is found for each variable independently, viz., for the

amount of carboxylic acid, the amount of nitrobenzene and the temperature.

For the centroid point corresponding to the amount of carboxylic acid, **CA**

$$\mathbf{CA} = (CA_1 + CA_2 + CA_3)/3$$

$$\mathbf{CA} = (75 + 60 + 40)/3 = 58$$

then, by reflection, $CA_5 = 58 + (58 - 60) = 56$

Similarly, for the amount of nitrobenzene, **NB**

$$\mathbf{NB} = (NB_1 + NB_2 + NB_3)/3$$

$$\mathbf{NB} = (50 + 30 + 40)/3 = 40$$

and, by reflection, $NB_5 = 40 + (40 - 20) = 60$

And, for the temperature, **T**

$$\mathbf{T} = (T_1 + T_2 + T_3)/3$$

$$\mathbf{T} = (120 + 130 + 110)/3 = 120$$

and, by reflection, $T_5 = 120 + (120 - 100) = 140$

Thus, the new set of experimental conditions (CA_5, NB_5, T_5) will be the point (P_5),

$$P_5 = (56; 60; 140)$$

After carrying out a synthesis using these conditions, the response was a yield of 42% for 5,10,15,20-*tetrakis*(4'-chlorophenyl)porphyrin (Table 27).

In this way new vertices from P_5 to P_{11} were obtained by following the same rules and calculations and the Simplex moved in hyperspace. However, on reaching responses of P_{10} and P_{11} there was a sign of the simplex moving in the wrong direction, viz., the yield was going down from vertex P_8 (Table 27). It was decided to go back to P_8, where the best response had been obtained and to contract the simplex into smaller simplexes so as to refine the yield. Thus, P_8 was again obtained using the vertices indicated in Table 27.

Table 27. Values of the vertices used to reach P_8 and the first values for P_9-P_{11}

Vertex	Amount of RCO_2H (ml)	Amount of $ArNO_2$ (ml)	Temperature (°C)	Yield % (Response)
P_3	60	30	130	42
P_5	56	60	140	42
P_6	88	53	150	33
P_7	61	46	160	34
P_8	30	37	136	54
P_9	36	39	111	33
P_{10}	21	61	128	14
P_{11}	36	67	159	15
P_{12}	45	41	140	48
P_{13}	52	43	141	56

To calculate P_8 the worst response obtained of P_6 was rejected and reflected through the hyperface defined by P_3, P_5, and P_7.

For the amount of carboxylic acid, **CA**

$$\mathbf{CA} = (CA_1 + CA_2 + CA_3)/3$$

$$\mathbf{CA} = (60 + 56 + 61)/3 = 59$$

and, $$CA_8 = 59 + (59 - 88) = 30$$

For the amount of nitrobenzene, **NB**

$$\mathbf{NB} = (NB_1 + NB_2 + NB_3)/3$$

$$\mathbf{NB} = (30 + 60 + 46)/3 = 45$$

and, $$NB_8 = 45 + (45 - 53) = 37$$

For the value of temperature, **T**

$$\mathbf{T} = (T_1 + T_2 + T_3)/3$$

$$\mathbf{T} = (130 + 140 + 160)/3 = 143$$

and, $$T_8 = 143 + (143 - 160) = 136$$

The new set of experimental conditions required are,

$$P_8 = (30; 37; 130)$$

To contract P_8, a factor of 1/2 was chosen and therefore, a new set of reflected and contracted values was calculated as follows:

$$CA_{12} = 59 + (1/2)(59 - 88) = 45$$

$$NB_{12} = 45 + (1/2)(45 - 53) = 41$$

$$T_{12} = 143 + (1/2)(143 - 160) = 140$$

Using the new set of values (P_{12}), another experiment was performed to get the response which was found to be a yield of 48%. To obtain P_{13}, P_8 was contracted by using a factor of 1/4 and following the same kind of calculations:

$$CA_{13} = 59 + 1/4(59 - 88) = 52$$

$$NB_{13} = 45 + 1/4(45 - 53) = 43$$

$$T_{13} = 143 + 1/4(143 - 160) = 141$$

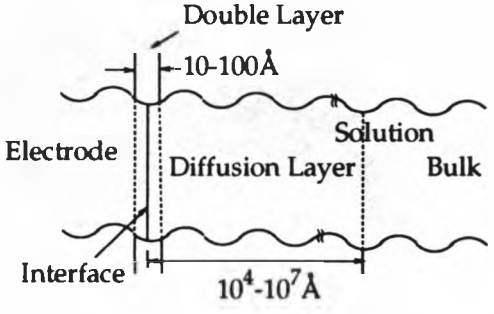
After carrying out the synthesis corresponding to point P_{13} (52, 43, 141), the response for P_{13} was 56% (yield). At this point it was decided to stop the simplex because, after this, it started to give yields always inside the limits of 48 < % yield < 56. With more time, the optimum could have been refined more closely by reducing the simplex size around P_{13}.

Appendix II

Some Aspects of Electrochemistry

In order to measure redox potentials electrochemical processes may be used. These heterogeneous chemical processes involve the transfer of electrons to (or from) an electrode surface, generally a metal or a semiconductor. The electrode reaction may be an anodic process whereby a species is oxidised by the loss of electrons to the electrode. Conversely, the charge transfer may be a cathodic reaction in which a species is reduced by the gain of electrons from the electrode.

In such electrochemical processes there are different zones which need to be defined (Scheme 73). The zones are not well differentiated.[208]



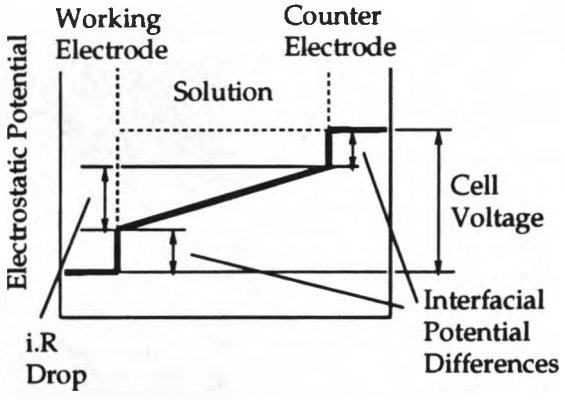
Scheme 73.

The electrode acts as a source, or sink, for species involved in the electrochemical process.[208] The boundary between the electrode and the electrolyte solution forms a double layer where there is an excess of charge on the metal surface and an oppositely charged excess of ionic charge in solution.[208] Here adsorption and desorption processes take place, as well as electron transfer involving the electrode. Heterogeneous reactions, other than charge transfer, also take place here. Usually, this double layer has a thickness typical of molecular coulombic interactions and is reckoned to be about 10-100Å.[208]

The diffusion layer comprises a zone about 10^4-10^7Å thick where there is a concentration gradient of electroreactants or products caused by the reaction taking place at the electrode. The bulk solution is all the region which is far enough from the electrode such that there is homogeneous composition.[208]

Cell Potential and Components

To carry out measurements of redox potentials a cell must be constructed in which there are at least two electrodes which, together with an electrolyte solution, make up the cell (Scheme 74).



Scheme 74.

The electrode where the electrochemical process takes place is called the working electrode. Here, either an anodic or cathodic process can take place. This electrode is connected externally to a counter electrode that serves to meet the requirement of electroneutrality. The amount of reduction taking place at the cathode, must be equal to the oxidation at the anode. The counter electrode works as a cathode or anode, depending on the working electrode reactions.[208]

In addition to electron transfer at the cathode and anode surfaces, ions must pass through the solution between the electrodes, and electrons through the external wires interconnecting the two electrodes. From this flow of electrons, it is possible to measure the voltage between the electrodes. However, the overall cell voltage also includes a difference in potential due to the bulk solution between the two electrodes (Scheme 74). This contribution, caused by the resistance of the bulk solution to the flow of electrical current, is the "iR drop" (i - current, R - resistance); voltage = i x R. When the iR drop is zero or negligible, the overall voltage is just the sum of the electrode interfacial differences, and is called the cell potential.[208]

It is very difficult to control a cell voltage without changing its internal potential difference (iR). Because any change in a cell potential is distributed between the working and counter electrode potentials, the internal iR drop changes in a manner that may not be predictable. To resolve this problem, a special electrode must be introduced. This electrode has a composition which is not very sensitive to current flow, so that any change in cell voltage is distributed between the working electrode potential and the iR drop. But, if the latter is negligible all of the voltage change is applied to the working electrode interface.[208] This new electrode is an electrostatic standard that functions as a reference. Usually the reference electrode is also used as the charge compensator and it serves two functions, being both a counter and a reference electrode.[208] A good example of such an electrode is the saturated calomel electrode (SCE):[208]

$$Hg/Hg_2Cl_2/KCl\ (saturated, aqueous)$$

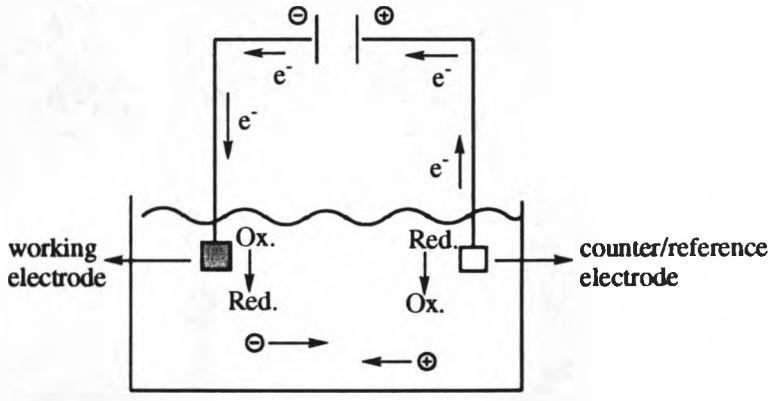
The SCE has a mercury pool in contact with solid mercurous chloride and potassium chloride. The internationally accepted standard

for the potential scale is the standard hydrogen electrode (SHE) or normal hydrogen electrode (NHE):[208]

$$Pt/H_2\ (a=1)\ /\ H^+\ (a=1)$$

The potential of this electrode is, by convention, taken to be zero. The SHE or NHE are not convenient for general use and other reference electrodes are more convenient in specific experimental situations; many different ones have been devised.

Scheme 75 shows an example of a cell used for voltammetric measurements.



Ox. - oxidised species
Red. - reduced species
⊕ - positive ions
⊖ - negative ions

Scheme 75.

The cell shows the charge movement where species are being reduced at the working electrode. For each mole of electrons being used up in the reduction process at the working electrode, a mole of electrons is replaced by charge drawn from the external circuit. In order to preserve electroneutrality, the external circuit obtains the electrons from the electrolyte itself via a second electrode, the counter electrode. Of course, an electrode reaction must take place at this second electrode in order to

deliver that charge, and it must be an oxidation.[208] The ion and electron movements transfer charge from place to place, so there is no appreciable charge build up.

Cyclic Voltammetry

In cyclic voltammetry the potential applied to the working electrode is set to some value (often zero volts) and then this potential is varied in a cyclical fashion. There is a linear increase in electrode potential (positively or negatively) with time, up to a pre-set maximum voltage, followed by a reversal of the scan and a linear decrease of potential (negatively or positively) with time at the same scan rate back to the starting potential. The current flowing in the cell is recorded as a function of the applied potential; as the potential is scanned uniformly, it is also a time axis.[185]

One usefulness of cyclic voltammetry (CV) lies in the possibility of estimating the stability of intermediates formed in an electrode process. If, for example, an intermediate is formed on a first anodic scan and is stable towards the reagents present on the time scale used, it will be reduced back to starting material on scanning in the cathodic direction. The reverse scan shows a matching cathodic peak in the cyclic voltagram to that produced by the forward scan.[185]

For a reversible process the half wave potential $E_{1/2}$ is virtually interchangeable with the classical polarographic redox value $E_{p1/2}$. In these cases where the half way potential ($E_{1/2}$) and the polarographic halfway potential ($E_{p1/2}$) are virtually interchangeable, the halfway potential $E_{1/2}$ is also interchangeable with the thermodynamically significant standard redox potential (°E). It must be emphasised that a reversible cyclic voltagram can only be observed if both species, reduced and oxidised, are stable and the kinetics of the electron transfer process are

fast, so that, for all potential scan rates, electron transfer at the surface of the electrode is an equilibrium process. The surface concentrations follow the Nernst equation. Figure 24 illustrates one example of a typical cyclic voltagram of a reversible process. The halfway potential $E_{1/2}$ is measured by taking the mid point between the two maxima in the voltagram.

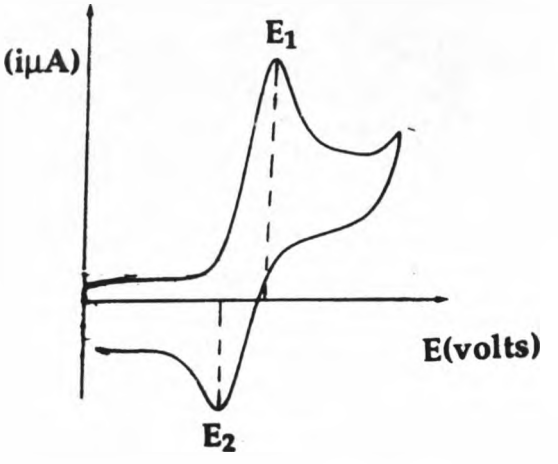


Figure 24. Voltagram of a typical reversible reaction; i(μA) is the current flowing to or from the electrode of potential E which may be positive or negative. The E_1 value is the maximum for the first (forward scanning) wave and E_2 is obtained from the reverse scan. The difference between E_1 and E_2 is due to the mass transport velocity. The half wave potential $E_{1/2} = (E_1 + E_2)/2$ is the mid-point between these two maxima.

For irreversible systems there are no observable reverse scan peaks. It is quite common for a reversible system, at low scan rates, to become irreversible at high scan rates, having passed through a *quasi*-reversible system. This occurs when the relative rate of electron transfer, with respect to that of mass transport to the electrode, is insufficient to maintain the Nernstian equilibrium, at the electrode surface.[185] Figure 25 illustrates an example of an irreversible process where there is no mirroring of the forward scan in the reverse scan.

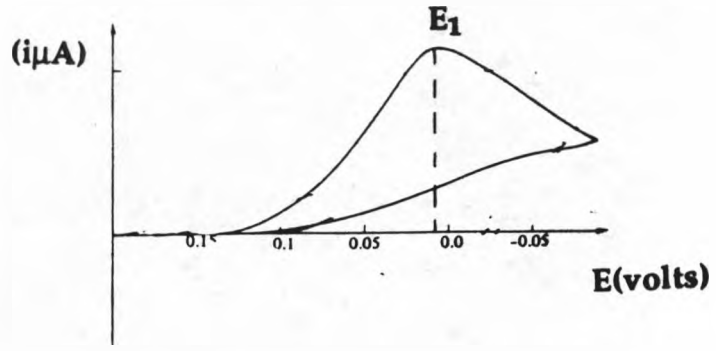


Figure 25. Cyclic variation in current flow of the forward scan from 0 to -0.25volts. There is no mirroring of the potential (E_1) and the reduced (oxidised) substrate must be unstable on the time frame of the voltagram (i.e., it has disappeared from the electrode surface).

Current and Potential

The potential is an expression of the electron energy. At more positive potentials, established with a less negative or positive excess charge at the electrode, the electron has low energy.[208] At more negative potentials, reached by increasing the negative excess charge on the electrode, the electron is at relatively high energy.[208]

The flow of electrons (current) is an expression of the reaction rate. As the scan rate increases, the concentration gradient increases in order to satisfy the Nernst equation. As a result, a current proportional to the value of this gradient at the electrode surface flows in the external circuit and is measured, generally in microamperes, μA (see figures 24,25).[208]

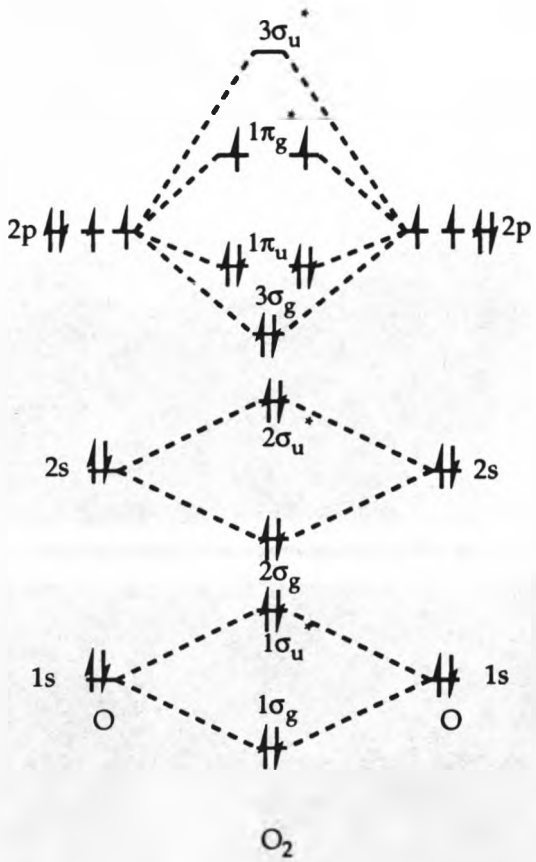
The potential on the working electrode controls the energetics of reaction and therefore the rate of reaction. The current flow measures the amount of reaction. Controlling the potential sets the current.

Controlling the current forces the system to the corresponding potential.[208]

Appendix III

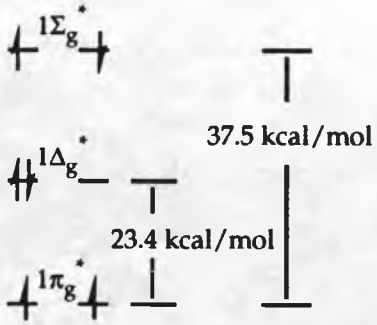
The Dioxygen Molecule (O_2): Electronic Structure

Dioxygen is a paramagnetic molecule, with two unpaired electrons in its ground state.[48,36] Scheme 76 shows the electronic configuration of the oxygen atom, and the molecule. The half arrows represent electrons. Each has a spin quantum number that has the value of $m_s = \pm 1/2$. There are five bonding and five antibonding orbitals for the quantum levels n=1,2 in dioxygen. The neutral molecule has sixteen electrons so that fourteen go into the first seven orbitals. They are distributed among the orbitals according to Pauli exclusion principle (which states that no two electrons may have all four quantum numbers n, l, m and m_s identical). The last two are found in two degenerate antibonding molecular orbitals $1\pi_g^*$.[36]



Scheme 76.

According to Hund's rule of maximum multiplicity (which states that the ground state of a species will be the one having the greatest multiplicity) the two electrons in the two antibonding orbitals have parallel spins and occupy different orbitals.[209] The summation of all electronic spins of a molecule is characterised by a quantum number, S.[209] By using the quantum number in the expression (2S + 1) the *multiplicity* of a molecule is calculated.[209] For dioxygen, S equals one and 2S + 1 =3. Thus, the ground state is a triplet. According to Hund's rule, in most cases, a triplet state has a lower energy than a singlet state.[209] Therefore, energy is required to promote an electron from a triplet ground state to an excited singlet state, more so than to the corresponding triplet state. Thus it would seem that, promotion of any given electron in a molecule could result in either singlet or triplet state depending on the energy used. However, that is not the case. Transition between energy levels are governed by rules which "allow" or "disallow" the transitions; some are highly improbable.[210] In most cases, direct promotion from a singlet ground state to triplet excited state or from a triplet ground state to a singlet excited state with spin inversion are so improbable that they are not observed.[210] Dioxygen is a very good example of a case were the rules for "spin-forbidden" transitions does not apply. Scheme 77 illustrates the ground state for the highest occupied molecular orbital and the two first electronically excited states for dioxygen.[211]



Scheme 77.

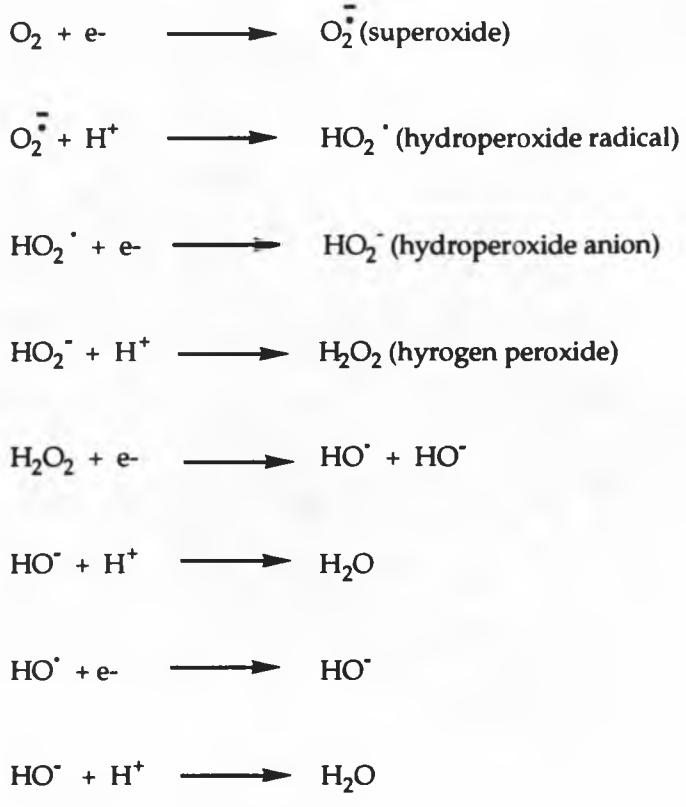
The two electronically excited states are characterised by relocation and/or pairing of the unpaired electrons in the $1\pi_g^*$ antibonding orbitals. Both excited states are singlets.[211]

Dioxygen Molecule as an Oxidant

Most molecules in their ground states have a multiplicity of one because all their electrons are paired and S = 0.[210] They have singlet ground states (2S + 1 = 1). In its triplet ground state, molecular oxygen is very unlikely to react with singlet molecules because this would lead to the formation of unpaired diradicals from stable paired species.[48,36] Triplet oxygen is relatively unreactive, which is just as well for all living matter!

The primary fate of molecular oxygen, in higher biological organisms, is its reduction, eventually to form water. This process, which needs an overall transfer of four electrons, is highly exothermic under both standard conditions ($[H^+]$=1.0M), and at biological concentrations of H^+ (pH 7.4). This makes molecular oxygen a powerful oxidising agent even in the triplet ground state.[48,36] Therefore, oxygen is considered to be a powerful oxidant, but it has to be activated before it can be of use.

Triplet oxygen can react by successive single electron transfers. Scheme 78 illustrates this process and the respective species formed during the electron and proton transfer.



Scheme 78.

The first electron added to form superoxide is an endoergic process and therefore unfavourable.[48,36] This is due primarily to the large reduction in the O-O bond strength on going from dioxygen, O_2 to superoxide $O_2^{-\bullet}$.[48,36] The next three electrons are added exoergically. The highly favourable reduction of the hydroperoxide radical, $HO_2^{\bullet}$ to hydrogen peroxide, H_2O_2 can be attributed to the rather small difference in bond energies between the two species, hydroperoxide radical, $HO_2^{\bullet}$ and hydroperoxide anion, HO_2^{-}.[48,36]

To activate dioxygen, either the first endoergic step must be made easier, or the dioxygen must be used in a spin-paired singlet state. The singlet state of dioxygen, and the peroxide species formed during reduction of dioxygen (Scheme 78) are extremely reactive and it may be difficult to achieve selectivity in their use. Because oxygen is such a cheap and readily available reagent that is utilised in natural metabolic processes in a

delicate, controlled manner considerable research has been carried out into activating dioxygen and controlling its reactivity and selectivity.[48,36]

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