Ferrocenyl derivatives of dithizone: photochromic properties and potential as electrochemical sensors

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by

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- Almighty God for making all things possible.

Abstract

New ferrocenyl derivatives of dithizone were successfully prepared and characterised by various analytical techniques. In the first part of this project interactions between photochromic and redox properties were investigated for the new ferrocenylmercury dithizonate complexes (*N*,*S*-dithizonato)(ferrocenyl)mercury(II) **(11)** and (ferrocene-1,1′-diyl)bis[(*N*,*S*-dithizonato)mercury(II)] **(12)**. UV-Vis spectroscopy showed that these complexes exhibited similar photochromic behaviour to related compounds known in the literature, i.e., a change in colour from orange to blue upon irradiation of organic solutions with visible light. The molar extinction coefficient of compound **(12)** was almost double that of compound **(11)**, indicating that there are two chromophores absorbing in compound **(12)** compared to one in compound **(11)**. Cyclic voltammetry on acetonitrile solutions of these photochromic compounds showed no noticeable differences in the voltammograms for the activated blue form compared to the normal orange form when irradiated with sunlight. This suggests that the interactions between the redox-active group and the changes in the conformation of the photochromic group were not significant enough to make any noticeable changes to the voltammetric behaviour.

In the second part of this project the electrochemical recognition of various metal ions by the new ligands *S*-ferrocenyldithizone **(13)** and *S*-ferrocenylmethyldithizone **(14)** was investigated. In both compounds the transducer is the ferrocenyl substituent and the binding site is the formazan group. These receptors showed a reversible redox wave in acetonitrile assigned to the ferrocene/ferrocenium couple: for receptor **(13)**, $E_{1/2}$ = 203 mV and for receptor **(14)**, $E_{1/2}$ = 136 mV relative to ferrocene as a standard reference. Addition of Cu^{2+} ions to ligand solutions in acetonitrile showed contrasting behaviour: ligand **(13)** produced a new wave with shift in $E_{1/2}$ from 203 to 387 mV ($\Delta E_{1/2}$ = 184 mV). For receptor **(14)**, titration with Cu^{2+} ions resulted in a continuous shift of the $E_{1/2}$ of the original receptor from 136 mV up to a maximum of 180 mV ($\Delta E_{1/2}$ = 44 mV). It was discovered that the formazan binding site of the receptor was likely oxidised by Cu^{2+} ions to form a tetrazolium salt, and this was proven from the product obtained during the attempted synthesis of a receptor(**13**)–Cu^{2+} complex: the product obtained was

determined crystallographically to be 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate. On the other hand, upon addition of $PhHg^+$ to a solution of receptor **(13)** a new wave with $\Delta E_{1/2} = 177$ mV was observed resulting from the formation of a receptor–metal complex, while addition of this organomercury ion to a solution of receptor **(14)** resulted in the continuous shift of the original receptor wave up to a maximum of $\Delta E_{1/2} =$ 32 mV. No binding was observed when receptor **(13)** was titrated with Ni^{2+} ions; when receptor **(14)** was titrated with this metal ion a gradual shift of the ferrocenyl wave up to a maximum of $\Delta E_{1/2} = 39$ mV was obtained. Large potential shifts were observed when the receptor **(13)** was titrated with various metal ions compared to small potential shifts which were observed during titration experiments with receptor **(14)**. The methylene link present in receptor **(14)** increased the distance between the binding site and the transducer, decreasing the interaction between the binding events and the transducer. The electronic communication between the transducer and the metal ions during titration of receptor **(13)** with metal ions is most likely a combination of through-space and through-bond interaction, while through-space communication seems likely for receptor **(14)**.

Synthesis of several receptor–metal complexes was attempted in order to elucidate the coordination mode of the ligand with the metal ion; however, no solid compound was successfully isolated. In addition, the data obtained from cyclic voltammetry did not allow confirmation of reliable receptor : metal ratios, thus unambiguous coordination modes for the receptor–metal complexes could not be specified. The possible application in bio-electrochemistry of the new compound **(13)** in its oxidized form as the tetrazolium salt (5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate) has also been recognized and preliminary experiments were conducted.

Presentations

- Oral presentation at the South African National Inorganic Chemistry (INORG007) Conference titled: 'Electrochemical recognition of transition and organotransition metal cations by the new analytical reagents *S*-ferrocenyl- and *S*-methylferrocenyl-dithizone' on 8-11 July 2007 at Club Mykonos, Western Cape, South Africa.

- Presentation at the South African Chemical Institute Young Chemist mini-symposium titled: "Electrochemical Recognition of Transition and Organotransition Metal Cations" on 18 May 2007 at the University of Western Cape, South Africa.

Contents

CHAPTER 1: INTRODUCTION

CHAPTER 2: SYNTHESIS, CHARACTERISATION, AND ISOMERISATION STUDIES

CHAPTER 3: PHOTOCHROMIC AND REDOX PROPERTIES OF FERROCENYLMERCURY(II) DITHIZONATE COMPLEXES

CHAPTER 4: ELECTROCHEMICAL RECOGNITION OF TRANSITION AND ORGANOTRANSITION METAL IONS

List of abbreviations

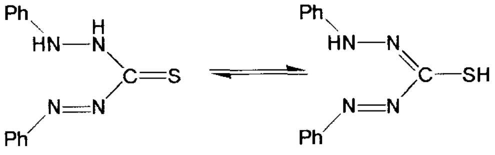
H_2Dz	Dithizone
HDz^-	Dithizonate anion (dithizone with a thio-proton lost)
Me	Methyl
p	Para position
o	Ortho position
hν	Normal light
k_-	Rate constant of reverse reaction
M	Metal
SWV	Square wave voltammetry
Cp	Cyclopentadienyl
Fc	Ferrocenyl
Ph	Phenyl
RC	Redox centre
G	Guest
TLC	Thin layer chromatography
UV-Vis	Ultraviolet visible
ε	Molar extinction coefficient
λ_{max}	Wavelength of maximum absorption
NMR	Nuclear Magnetic Resonance (^1H or ^{13}C)
ppm	Parts per million
δ	Chemical shift
t	triplet
s	singlet
m	multiplet
J	Coupling constant
IR	Infrared
CV	Cyclic voltammetry
$E_{1/2}$	Half-wave potential
TBAP	Tetrabutylammonium perchlorate
ESI-MS	Electro-spray ionisation mass spectrometry

CHAPTER 1

INTRODUCTION

1.1 DITHIZONE

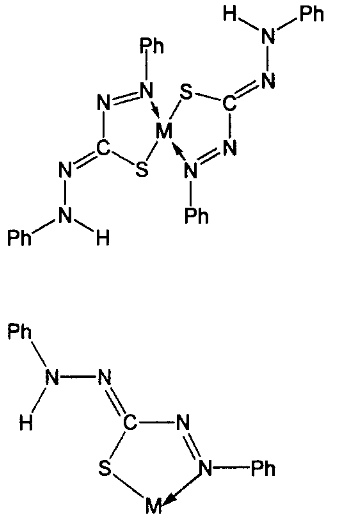
During the early 1920's, when researchers were investigating different reagents for analysis of metals, Hellmuth Fischer discovered the organic reagent, dithizone (1,5-diphenylthiocarbazone, **1a**$\rightleftharpoons$**1b**).[1] The empirical formula of dithizone is $C_{13}H_{12}N_4S$ and it is commonly abbreviated H_2Dz, with HDz^- indicating the anion formed by a loss of a single proton. This reagent has received much attention in the field of analytical chemistry for the quantitative analysis of metals.[1-3] Dithizone and all of its stoicheiometric metal complexes are characteristically and intensely coloured, and some complexes are photochromic. The complexes are almost insoluble in water but soluble in a range of organic solvents such as chloroform and carbon tetrachloride. The photochromism of mercury dithizonates is discussed in Section 1.2 of this dissertation.



(1a) Thione form **(1b)** Thiol form

As an analytical reagent the selectivity of dithizone may be increased by a suitable adjustment of the pH of the aqueous phase, or by the use of appropriate masking agents to produce competitive complex formation in the aqueous phase. In its reactions it mainly forms stable complexes with cations derived from the transition metals of the periodic table (see Table 1.1). Many complexes of organometallic cations such as $PhHg^+$, Et_2Sn^{2+}, Bu_2Ga^+, Ph_3Pb^+ and Me_2Tl^+, are also known,[4] and these may be extracted into organic solvents and determined spectrophotometrically.

Dithizone is, however, not a specific reagent since it forms complexes (bonding through nitrogen and sulfur, Figure 1.1) with all the metals shown in Table 1.1.



M = Ni^{2+}, Cu^{2+}, Pt^{2+}, Pd^{2+} (Square planar)
M = Zn^{2+}, Hg^{2+} (Tetrahedral)

M = Ag^{+}, Cu^{+}, $(CH_3)_3Pb^{+}$, $(CH_3)_2Tl^{+}$, RHg^{+}, (R = alkyl or aryl)

FIGURE 1.1: Some modes of coordination of dithizone to metal cations.

TABLE 1.1: Metals forming complexes with dithizone*

Mn	Fe	Co	Ni	Cu	Zn	-	-	-	Se
-	-	-	Pd	Ag	Cd	In	Sn	-	Te
-	-	-	Pt	Au	Hg	Tl	Pb	Bi	Po

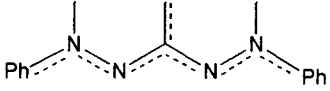
*These metals can be extracted by dithizone from aqueous solution. Some metals (e.g. Fe, Cu, and Hg) form different dithizone complexes according to their oxidation state. In addition, the lanthanons give complexes of low stability in 50% aqueous ethanol, and several other metals may form complexes in the absence of water and at high ligand concentration.[5]

The value of dithizone as a reagent for the determination of lead in organic materials,[6] pharmaceutical preparations,[7] biological materials,[8] and forensic specimens,[9] has been recognized. Its use for the determination of traces of metals in a wide variety of agricultural and animal products, as well as in the analysis of rocks, minerals, and water samples, has rapidly emerged.[9a]

Some analytical applications of dithizone which have been studied include the qualitative identification of heavy metals,[10,11] and the use of drop reactions in micro-test-tubes.[9a,12] Most widely and successfully amongst other applications, such as those in biology,[13] dithizone has been used for detecting the presence of trace metals in steels, brass and base alloys.[14,15] The possible applications of dithizone in liquid-state ion-selective electrodes were first summarized in 1970.[16] Plastic membranes impregnated with dithizone have been proposed for the potentiometric titration of Ag^+ with sodium oxalate, potassium hexacyanoferrate(II), potassium iodide,[17] sodium tungstate,[18] and ascorbic acid. A membrane electrode has been patented for determination of lead. Many analytical applications of dithizone have been reviewed and summarized by Irving.[19]

Although dithizone is a good analytical reagent, like any reagent it suffers from certain disadvantages. It is difficult to obtain absolutely pure in the solid state, and its solutions in organic solvents tend to deteriorate on standing, especially in the presence of alkalis, oxidizing agents, and light. The actual causes of the deterioration of dithizone solutions have never been clearly defined, but it is generally regarded as an oxidation process probably catalysed by light.[20] Dithizone is adsorbed on metal electrodes such as copper and silver in aqueous conditions from pH = 10 and higher.[21] This is a serious drawback in the quantitative analysis of trace metals using electrochemical techniques.

The solid state structure of dithizone (**2**) has been determined by X-ray crystallography.[22] The molecule (**2**) is nearly planar, and of symmetry *mm* (C_{2v}), with the N–N–C–N–N chain extended and the C–S bond lying on the intersection of the mirror planes.



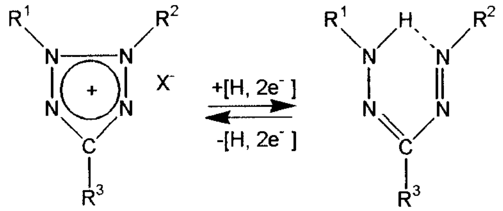
(2)

The phenyl groups are twisted slightly out of the mean plane in opposite senses. It has been established from the measured bond lengths that the π-electrons in the

N–N–C–N–N chain are delocalized throughout and that there are no localized single or double bonds.[22] The two imino hydrogen atoms are located as shown in the structure; both are weakly hydrogen-bonded to the sulfur atom.

Dithizone is formally a 3-thio-1,5-diphenylformazan; the formazans[23] are widely applicable in biological chemistry, mostly as colourimetric reagents for detection of enzymatic oxidation-reduction reactions. This is due to the ability of the colourless tetrazolium salt [as (**3**)] to accept electrons from one or more intermediates in the biological system to form the highly coloured formazan [as (**4**)]. The oxidation process, i.e. (**4**) → (**3**), has been found to be influenced by different factors, such as autoxidation in the air[24] and the nature of the substituent group R^3, which was studied by Wadekind.[25] The substituent group R^3 has an influence on the ease of rotation of the formazan chain (i.e. rotation around the C=N bond). The more readily the substituent R^3 permits rotation, the slower is the oxidation, and also the more electron withdrawing R^3 is, the more the yield of the tetrazolium salt increases (for example, the order of the series R^3 = H, COOH, CH_3, $COCH_3$, N=NPh, COPh, COOPh, Ph and CN corresponds to the order of increasing yield of tetrazolium salt).

The oxidation process of the highly coloured 3-carboxymethylthio-1,5-diphenylformazan [(**4**); $R^1 = R^2$ = Ph, $R^3 = SCH_2CO_2H$] to the tetrazolium salt [(**3**), $R^1 = R^2$ = Ph, R^3 = SCH_2CO_2H], has been adapted to a sensitive and selective spectrophotometric method for



(**3**)

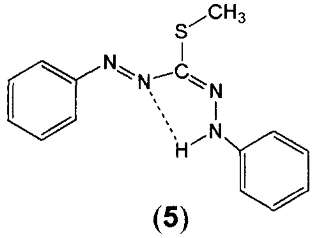
Tetrazolium salt

(**4**)

Formazan

the determination of Tl^{3+} and Au^{3+}.[26] The crystal and molecular structure of the first ferrocenyl-containing tetrazolium salt [(3), $R^1 = R^2 = Ph$, $R^3 = S(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_5)$] will be reported in Chapter 4 of this dissertation.

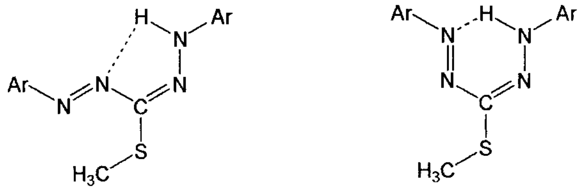
Several derivatives of dithizone have previously been prepared in which the hydrogen bonded to sulfur has been substituted by an alkyl group. For example, methylation of dithizone has been accomplished to form *S*-methyldithizone [3-methylthio-1,5-diphenylformazan; (**5**)],[27] and derivatives of (**5**) with alkyl substituents on the phenyl rings have also been synthsized.[28] A fresh solution of *S*-methyldithizone in, *e.g.* chloroform, is permanganate pink, with well-defined bands at 270 and 550 nm (ε_{550} = 12250 M^{-1} cm^{-1}). On standing in the dark at room temperature the colour changes to yellow, and the spectrum shows bands at 280, 420, and 540 nm (ε_{420} = 17750 M^{-1} cm^{-1}), the original band at 550 nm becoming less intense as the new band appears at 420 nm.[28]



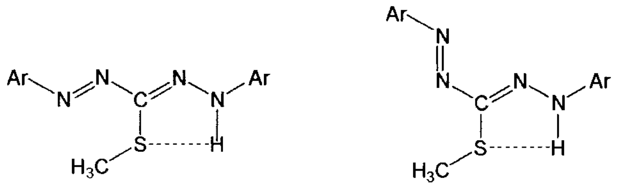
(5)

Similar effects have been found with many red formazans,[29-31] which are converted to yellow isomers on standing or on irradiation of solutions in appropriate solvents. *Cis-trans* isomerisation about the –N=N– bond or *syn-anti* isomerisation about the :C=N– bond was thought to be involved.[32] Concentration of solutions of *S*-methyldithizone (whether in the pink or yellow form) deposited only the magenta-red solid, which was shown crystallographically to have the structure (**5**). A series of alkyl-substituted 3-methylthio-1,5-diarylformazans has also been found to exhibit similar isomerisation (yellow $\rightleftharpoons$ pink).[33] Ignoring all the *cis*-configurations relative to the N=N double bond (which scale models show are unlikely to occur owing to serious steric crowding) leaves four possible isomers which could result from *syn-anti* isomerism about the C=N double bond and isomerisation about the C–N single bond (designated *s-cis* and *s-trans*).

These are shown in Figure 1.2. Studies by IR and ^1H and ^{13}C NMR spectroscopy[33] indicate that the yellow isomer has a single *anti*, *s-trans* structure [Figure 1.2 (c)] whereas the pink isomer comprises *syn*, *s-trans* species [Figure 1.2 (a)] in rapid tautomeric equilibrium. Similar isomerisation behaviour was observed for the ferrocenyl derivatives of dithizone synthesized here, and this is discussed in Chapter 2.



(a) *syn, s-trans* (b) *syn, s-cis*

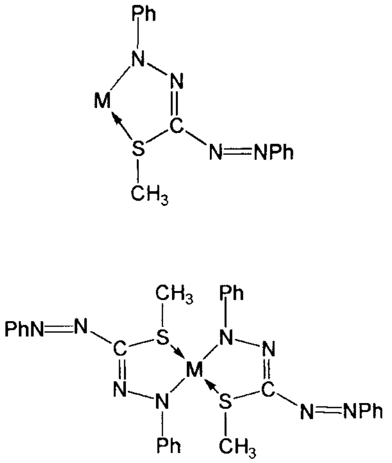


(c) *anti, s-trans* (d) *anti, s-cis*

FIGURE 1.2: Possible isomers of *S*-methyldithizone. Ar = Ph, *p*-tolyl or *o*-tolyl.

Experiments have been performed by various researchers on the reactions of *S*-methyldithizone with different metals. For example, Irving and Bell[27] investigated the reaction of an equivalent number of moles of *S*-methyldithizone and mercury(II) acetate, a red crystalline product being characterised by elemental analysis. A solution of this substance in chloroform rapidly decomposed to give an absorption spectrum characteristic of *S*-MeDz, the ligand-to-metal ratio of 1 : 0.58 indicating that two ligands had coordinated to the mercury centre.

In another study Irving *et al.*[34] treated *S*-methyldithizone with an excess of various metal chlorides in ethanol in the presence of sodium acetate. They found that *S*-methyldithizone reacted with Cu(II), Hg(II) and PhHg(II) chlorides to give 1 : 1 chelates, i.e. MCl(MeDz) and PhHg(MeDz), and with Pd(II) and Ni(II) to give the 1 : 2 chelates, $M(MeDz)_2$. They suggested that the complexes have coordination modes as shown in Figure 1.3, though the proposed structures were not crystallographically proven. This discussion will be taken up again when the mode of interaction with metal ions of the new *S*-ferrocenylated dithizone ligands, synthesized in this work, is discussed (Chapter 4).



M = CuCl, HgCl or PhHg

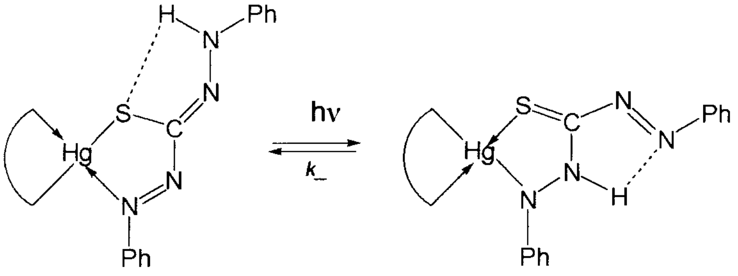
M = Ni or Pd

FIGURE 1.3: Some possible modes of coordination of *S*-methyldithizone to metal cations.

1.2 PHOTOCHROMISM OF MERCURY(II) DITHIZONATE COMPLEXES

While studying the use of dithizone in the determination of traces of mercury in 1946, Irving, Andrew and Risdon[35] were surprised to see an orange-yellow chloroform solution of mercury(II) bis(dithizonate), $Hg(HDz)_2$, (**6a**), change in colour to an intense royal blue upon accidental exposure to sunshine. The yellow colouration returned slowly in diffuse daylight or in the dark, and immediately on shaking in dilute sulfuric acid. When exposed to direct sunlight the blue colouration developed again, and the sequence of colour changes could be repeated at will.[35]

The proposed structure of the photo-excited blue form (**6b**),[36] represents a drastically altered chromophore with a thiocarbonyl group: many organic compounds with this chromophore in a conjugated system are known to be blue, with visible absorption bands in the same region (580-605 nm) as in the activated form of $Hg(HDz)_2$. It was later discovered that Reith and Gerritsma had made the same observation a year earlier,[37] and these workers noted that the photochromic effect was inhibited by the presence of dilute acetic acid.



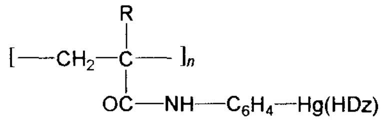
(6a) yellow **(6b)** blue

This photochromic effect was rediscovered five years later,[38] though it was not followed up in depth until 1965 when the American Cyanamid Company recognized its potential use in solar batteries, car windscreens, and sunglasses.[39] Later, some applications were also found in the textile industry,[40] and in hydrodynamics.[41] Applications in optics have also emerged.[42,43] Meriwether's group performed studies to explain the factors that affected the photochromism and investigated the kinetics of the reversion reaction,[44] and the IR spectrum of the blue form was obtained.[45] Meriwether proposed the structure **(6b)** for the blue form, and he proposed a mechanism for the isomerisation involving a shift of the hydrogen atom from the 5-nitrogen to 2-nitrogen of the dithizone moiety, and a redistribution of electrons to yield a thiocarbonyl group in the blue form. The X-ray crystal structure of $Hg(HDz)_2$•2(pyridine) by Harding[36] in 1958 had established a rather distorted tetrahedral coordination with the bonding characteristics shown in structure **(6a)** for the stable yellow isomer.

Paci *et al.*[46] investigated the transient anisotropy of mercury(II) dithizonate in solution with different solvents by picosecond Kerr ellipsometry. In their work they showed that though, mercury(II) dithizonate is photochromic in many organic solvents such as benzene and 1,2-dichlorobenzene, there was no evidence of the isomerization (yellow $\rightleftharpoons$ blue) in 2-methoxyethylether, the reason suggested being the formation of hydrogen bonds with the solvent which inhibits the photo-process.

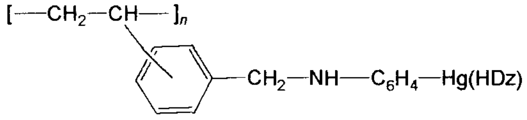
Studies of the photochromism in solution were continued by Sertova *et al.*[47] in order to understand the behaviour of the yellow and the blue forms of mercury(II) dithizonate in polar and non-polar solvents. Different interference filters were used to investigate the photochromic systems for the construction of light sensitive molecular devices. They also did not observe the photochromism in acetonitrile or tetrahydrofuran as solvents. It was proposed that the reason for this was the specific influence of the solvent, for example, the possibility of the acetonitrile molecule forming an exiplex with the excited molecule in the blue form,[48] or the existence of a specific interaction with the compound.[49]

It has been found that incorporation of the fragment –Hg(HDz) within various organic molecules does not affect the photochromism, and the resulting organomercury(II) dithizonates have many practical applications. Several patents exist based upon these organomercury(II) dithizonate compounds. For example, photochromic dyes for fabrics have been reported which change colour (reversibly) in sunlight from yellow to blue,[50,51] the compounds have been incorporated into resins and plastics to form photochromic films, glasses or lenses,[52,53] and they have even been combined as integral parts of photochromic polymers,[54] as (7) and (8). In addition, an interesting study was made for the United States Army on photochromic colourants useful as a chameleon-type camouflage system for military uniforms.[55]



$$[\!-\!CH_2\!-\!\overset{R}{\underset{OC-NH-C_6H_4-Hg(HDz)}{C}}\!-\!]_n$$

(7)



(8)

Due to its insolubility in water, partial solubility in common organic solvents, and rapid reversibility of the yellow $\rightleftharpoons$ blue process, the study of the photochemistry of the mercury(II) bis(dithizonate) system by IR and NMR spectroscopic techniques is difficult. To overcome some of these factors a series of organomercury(II) mono(dithizonates), RHg(HDz) (R = alkyl or aryl), was synthesized.[56] These show only half the value of the molar extinction coefficient of the parent mercury(II) bis(dithizonate) complex since there is only one chromophore absorbing. The 1 : 1 organomercury(II) complexes were also studied using several derivatives of dithizone substituted by methyl groups at various positions on the phenyl rings; these simpler mono-dithizonate complexes allowed conformational changes to be monitored by ^{1}H-NMR spectroscopy.

In a study of organomercury(II) dithizonate compounds directed towards the generation of photochromic liquid crystals, long-chain complexes of the type $[C_nH_{2n+1}OC_6H_4C_6H_4Hg(HDz)]$[57] and $[C_nH_{2n+1}OC_6H_4CH{=}NC_6H_4Hg(HDz)]$ (n = 4, 5, 10, 14 or 18) were synthesized.[58] A new, improved procedure was also developed for the final dithizone complexation step. No mesophases were observed, as revealed by the studies of the thermal behaviour of the complexes by polarized optical microscopy and differential scanning calorimetry. It was interestingly observed that the half-lives of the metastable blue forms increased with the increase in length of the alkoxy substituent.

In spite of many attempts, no crystal structure of the photo-excited blue form of any of these organomercury(II) dithizonates has been obtained, only the stable yellow form crystallizing out. The molar extinction coefficient of the photo-excited blue form is usually estimated or not reported since it is difficult to get 100% conversion; generally only the molar extinction coefficient of the yellow form is reported. Whereas it has been possible to infer the structure of the blue photo-isomer of these compounds from spectroscopic measurements on irradiated solutions, the structure of the yellow form has been established by X-ray crystallographic studies on phenylmercury(II) dithizonate and methylmercury(II) dithizonate.[59] These organomercury(II) compounds exhibit an approximately T-shaped geometry at the Hg atom, with strong, almost linear C–Hg–S bonding and a weaker Hg–N interaction, as depicted in Figure 1.4 (on the next page) for the crystal structure of phenylmercury(II) dithizonate.[59]

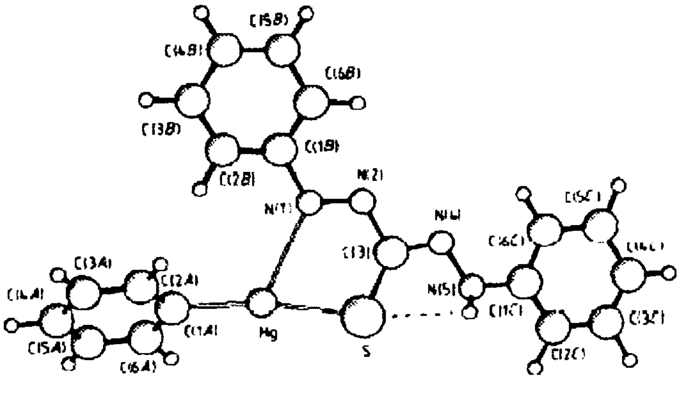


FIGURE 1.4: Crystal structure of phenylmercury(II) dithizonate.[59]

1.3 ELECTROCHEMICAL RECOGNITION: TRANSITION METAL CATION SENSORS

An electrochemical sensor for transition metal cations refers to a molecule which combines a guest binding site in close proximity to a redox active moiety (or transducer, see Figure 1.5, on the next page). The electrochemical recognition of a guest (metal cation) by such a receptor requires that the guest binding site and the redox active group can communicate.[60] Receptors designed to recognise guest molecules electrochemically must couple the complexation process to the redox reaction, i.e. the two reactions must mutually influence each other. The magnitude and the direction of the potential change will depend on the reaction coupling mechanism and the properties of the complexed guest molecule. These variations can be measured, for example, by voltammetric methods.[61]

The two main themes in the study of sensors have always been selectivity and how to sense the guest. The question of selectivity is mainly dealt with by synthetic chemists producing and testing new ionophores, while the other theme concerns the instrumentation used to turn selectivity into an observable and quantifiable phenomenon, i.e., the mode of transduction.

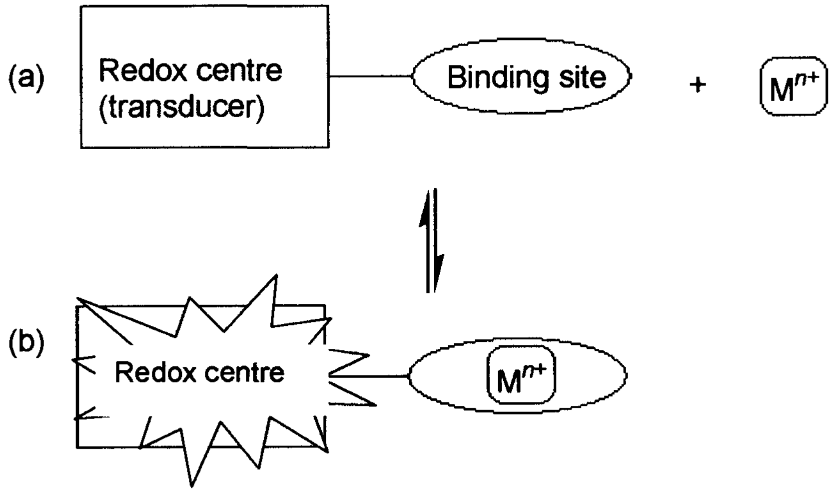
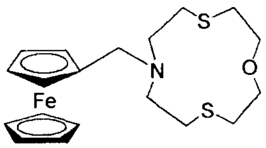


FIGURE 1.5: Components of a sensor: (a) ligand with uncoordinated metal cation, (b) electrochemical response when the metal is coordinated to the ligand.

Sensor molecules which interact with the analyte with an accompanying dramatic visual colour change are especially attractive, since this factor can be used for qualitative analysis. There is a need for increasing research as environmental controls tighten, for the quantitative analysis of waters, to assess river, lake and sea pollution, and to monitor industrial and nuclear effluents. Particular targets include heavy metal ions such as mercury and the very toxic organomercury ions, lead and cadmium. There is also an industrial requirement for analysis at much higher concentrations of certain metals such as lead.[62]

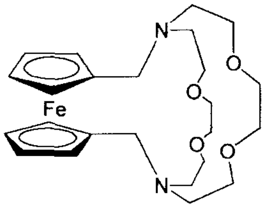
Most of the known sensor molecules contain donor atoms such as oxygen, sulfur or nitrogen on the binding site(s). Some classes of suitable ligands include crown ethers[61-64] and polyaza-macrocycles.[61,62,65,66] Though there are many compounds which have potential as sensors, few have been commercialized.[67] The crystal structures of the metal complexes of some sensor molecules have also been reported; for example, the crystal structures of the metal complexes of the ferrocene-containing sensor molecule (**9**) with metals such as Cu^{2+}, Cd^{2+} and Hg^{2+} have been obtained.[68] This ligand has also shown electrochemical recognition of metal ions such as Zn^{2+} and Pb^{2+}.



(9)

The design of the responsive molecules must focus carefully on the following two points: (i) the selection of subunits (transducer and binding site) and (ii) the degree of communication between them (see Figure 1.5). For instance, in order to prepare a molecule with ion-dependent redox effects, it is necessary to attach covalently a redox centre to an appropriate binding site such as that provided by a good chelating ligand. To attain the desired properties, the binding events must be detected by the redox centre, that is, the redox properties of the transducer must be substantially altered by the presence of bound cations.[61]

The design of a sensor is closely related to the concept of a redox-switchable ligand [for an example, see the ferrocene-containing macrocycle **(10)**].[69] A redox-switchable receptor is a compound capable of forming a complex with a given substrate in such a way that the thermodynamic stability of the complex is determined by the oxidation state of the receptor. These compounds must possess a redox-active subunit and a well-defined binding site. Intimate and efficient communication between these two subunits is a crucial requirement for an effective redox-switchable receptor. Usually, communication between subunits is established by electrostatic interactions. Cyclic voltammetry (CV), square-wave voltammetry (SWV)[70] and rotating disk techniques are widely used to monitor perturbations in the electrochemical behaviour of redox-active receptor species.



(10)

If the interplay between subunits is primarily of an electrostatic nature, some properties of several types of redox-switchable ligands can be predicted, depending on the charge of the bound species and the characteristics of the redox subunit. These properties are summarized in Table 1.2[69] for the cation-bound species.

TABLE 1.2: Properties of redox-switchable ligands

Redox subunit	Bound species	Predicted property
Reducible	Cation	Reduction switches on enhanced binding affinity
Oxidizable	Cation	Oxidation leads to decreased binding affinity

There are different types of redox subunits that are usually utilised. Ferrocene or bis(η^5-cyclopentadienyl)iron(II) (abbreviated Fc) is probably the most popular redox subunit in this context.[71] Ferrocene and its derivatives exhibit fast anodic electrochemistry at very accessible potentials. Therefore, its use is limited to ligands which, upon oxidation, should exhibit a decreased binding affinity for cations. Ferrocene is easily functionalised; many derivatives of ferrocene are commercially available. From a synthetic point of view ferrocene is a very convenient building block for redox-active ligands as it can be easily incorporated in many structures.

The electrochemical molecular recognition process should result in a large shift of the redox potential of the host species.[61] The minimum magnitude of a potential shift is gauged by experimental error, which for most voltammetric techniques is ca. ± 5 mV. So far, the electrochemical communication has been mainly realized through one or a combination of the five pathways described in Figure 1.6 (on the next page).[72]

It is worth noting that the systems in which the ligand donor atom is directly attached to the cyclopentadienyl (Cp) ring of ferrocene, or at least via a conjugated system, are thought to allow through-bond as well as through-space coupling of the electrochemical and complexation processes.[73] These types usually have large shifts of the electrode potential in the presence of metal ions (of the order of 200 – 300 mV), while those having a methylene (or saturated) linker are limited predominantly to through-space interaction. These types of interactions will be further discussed in Chapter 4.

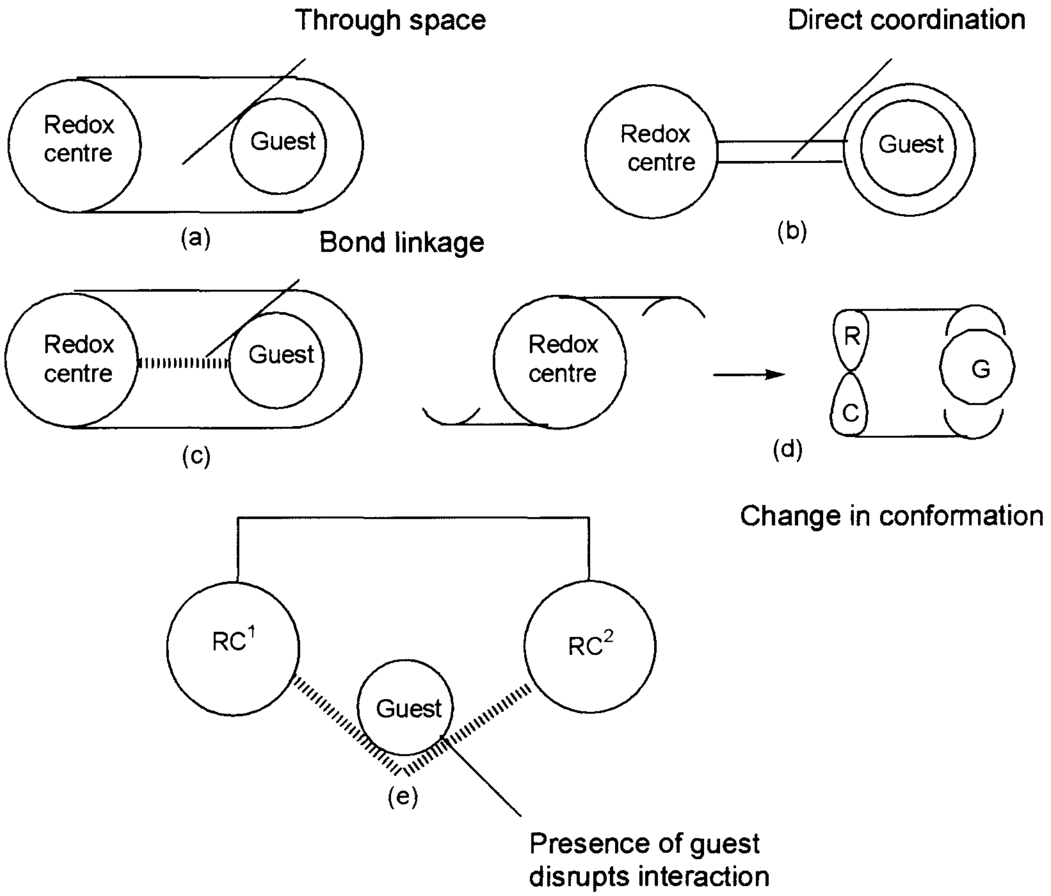


FIGURE 1.6: Mechanisms for coupling electrochemical and complexation reactions:[72]

(a) Through-space electrostatic interaction between the redox center(s) and the complexed guest molecule;[74]

(b) Through-bond communication provided typically by conjugated chemical bond linkage between the redox centre(s) and the binding cavity;[75]

(c) Additional direct co-ordination bond formation between the redox centre and the complexed guest molecule;[76]

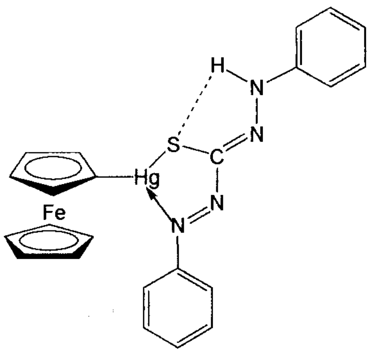
(d) Conformation-induced perturbation of the redox centre(s) caused by the complexation of a guest molecule; [77]

(e) Interference by the guest species in communication between two redox-active centres.[78]

1.4 OBJECTIVES OF RESEARCH

There are two broad areas of investigation that are reported in this dissertation. The first of these describes new photochromic mercury dithizonate compounds containing redox-active substituents. Many different mercury(II) dithizonate compounds with varied applications have been reported and described in Section 1.2; however, there are no reported mercury(II) dithizonate compounds which have redox-active substituents. The aims of this work are therefore to:

1. Synthesize new photochromic mercury(II) dithizonate compounds containing a redox-active ferrocenyl group, namely **(11)** and **(12)**;
2. Investigate the interaction between the photochromic and redox properties; i.e., whether photo-excitation of the new compounds affects the redox properties of the ferrocenyl group.



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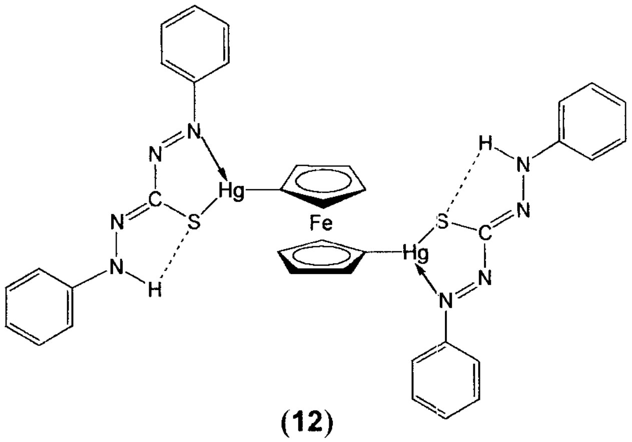

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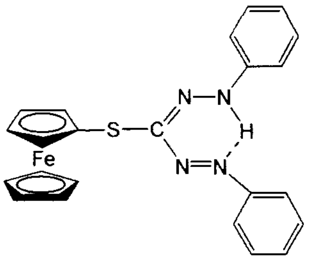
The second area of investigation described in this dissertation is devoted to a study of new cation sensors based on dithizone. As was discussed in Section 1.3, many receptors for transition metal cation guests have binding sites such as are found in crown ethers and polyaza-macrocycles. The coordination properties of the ligand dithizone have been discussed in Section 1.1. We have taken advantage of the complexing ability of this well-known analytical reagent, and have attempted to combine this with the established redox properties of the ferrocenyl moiety. The aims of this part of the work are therefore to:

1. Synthesize new derivatives of dithizone containing ferrocenyl substituents, namely (**13**) and (**14**);
2. Investigate the electrochemical recognition of transition metal ions by these new reagents using cyclic voltammetry (CV).



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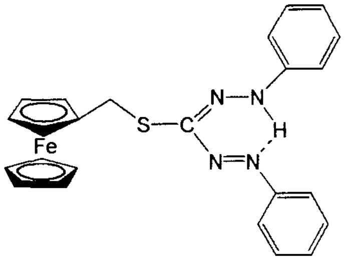

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CHAPTER 2

SYNTHESIS, CHARACTERISATION AND ISOMERISATION STUDIES

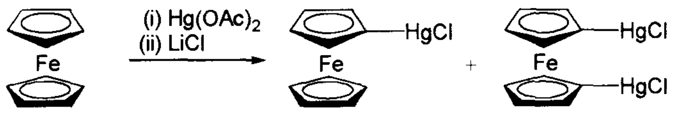
2.1 SYNTHESIS OF PHOTOCHROMIC COMPOUNDS

2.1.1 *Introduction*

Various reaction routes have been previously established for the preparation of mercury dithizonate complexes.[1-3] The route followed in this work involved the reaction between equimolar amounts of the organomercury chloride (R-HgCl) and dithizone (H_2Dz) in the presence of a weak base and in an organic solvent such as dichloromethane [see Equation (1)].[3] The route has fast reaction times and results in good yields. The ferrocenylmercury(II) starting materials **(15)** and **(16)** were synthesized first following the literature methods, and these are discussed below. The analytical reagent dithizone was used without further purification in all reactions. The characterisation of the new compounds is discussed in Section 2.3 and full experimental details will be found in Section 2.6.

$$\text{R-HgCl} + \text{H}_2\text{Dz} \longrightarrow \text{R-HgHDz} + \text{HCl} \qquad (1)$$

2.1.2 *Chlorido(ferrocenyl)mercury(II)* **(15)**



(15) **(16)**

(2)

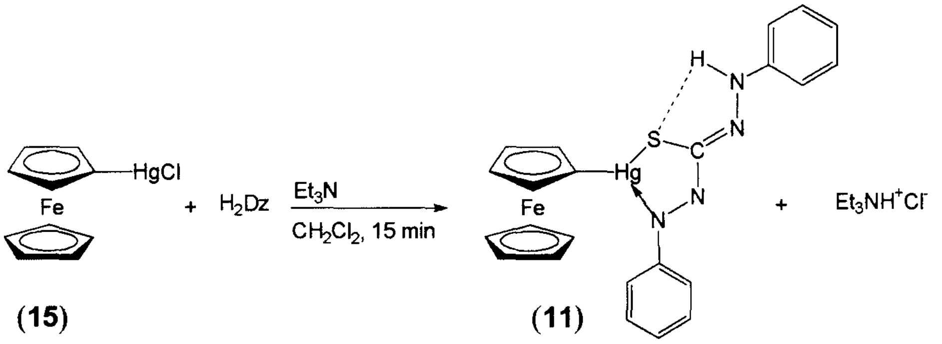
This reaction has been found to give more than one product [see Equation (2)].[4-6] This was advantageous in this work since both products were required. Manipulation of the molar amounts of the starting materials [ferrocene, mercury(II) acetate and lithium chloride] has been found to be lead to a better yield of either one of the products, i.e. the mono-substituted- **(15)** or 1,1′-disubstituted product **(16)**, respectively.[6] Starting with an excess of lithium chloride and equal molar amounts of ferrocene and mercury(II) acetate results in better yields of product **(15)** than **(16)**. The reaction is thought to being taking place as follows: the electron rich site of the cyclopentadienyl (Cp) ring attacks the mercury atom and one acetate anion is displaced. This is followed by the subsequent abstraction of the proton from the Cp ring by the acetate anion produced to form acetic acid and the desired precursor, acetato(ferrocenyl)mercury(II). Addition of lithium chloride leads to the formation of the final products, chlorido(ferrocenyl)mercury(II) and (ferrocene-1,1′-diyl)bis[chloridomercury(II)] by substitution of the acetate with chloride ion.[4-6]

Chlorido(ferrocenyl)mercury(II) **(15)** was prepared using the literature published method.[4] A solution of mercury(II) acetate in methanol and an equimolar amount of ferrocene in benzene was stirred under nitrogen at room temperature for at least 24 hours. A solution of lithium chloride in ethanol-water (1 : 1) was then added and further stirred for two hours. The reaction mixture was set to reflux for one hour, followed by filtration of the crude residue. The residue obtained was purified by Soxhlet extraction with dichloromethane, followed by removal of unreacted ferrocene sublimation. During the soxhlet extraction, the 1,1′-disubstituted product **(16)** is left behind in the Soxhlet thimble due to its insolubility in dichloromethane. After purification by recrystallization from dichloromethane-hexane the yield of the product was 42% and it showed a melting point of 194 – 195 °C, which compared well with the literature m.p. of 194 – 196 °C.[4-6]

2.1.3 *(Ferrocene-1,1′-diyl)bis[chloridomercury(II)]* **(16)**

As mentioned above, during preparation of chlorido(ferrocenyl)mercury(II) **(15)**, (ferrocene-1,1′-diyl)bis[chloridomercury(II)] **(16)** is also formed [see Equation (2)].This compound was found to melt with decomposition at higher temperatures (300 °C), showed poor solubility in many organic solvents and partial solubility in dimethylformamide, as reported in the literature.[4-6] Purification of the product by recrystallisation from hot dimethylformamide solution resulted in no success as the product would not precipitate from the cold solution. The solvent could not be reduced in volume or completely removed by standard techniques due to its high boiling point. The product was then purified by washing the crude material with copious amounts of water to remove any inorganic impurities, and the filtered product was then dried under vacuum to give a 30% yield.

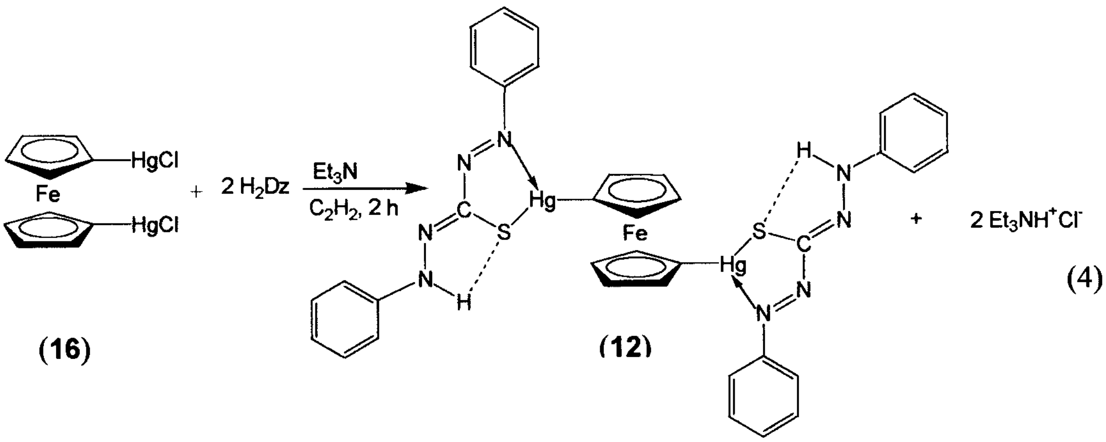
2.1.4 *(N,S-Dithizonato)(ferrocenyl)mercury(II)* (**11**)



(3)

The reaction route shown in Equation (3) was followed. Dithizone was added in a single solid portion to a solution of an equivalent molar amount of chlorido(ferrocenyl)mercury(II) (**15**) in dichloromethane, followed by addition of a few drops of triethylamine to react with the acid that is produced during the reaction, forming the triethylammonium chloride salt. The reaction mixture was stirred for 15 minutes. It was noticed that the product decomposed during recrystallization from either dichloromethane-hexane or benzene-hexane, as seen from the disappearance of the ferrocenyl signals between 4 and 5 ppm in the ^1H NMR spectrum. The decomposition product was not monitored in detail, though it was suspected to be the mercury bis(dithizonate) as seen from close correlation of the elemental analysis data and melting point, and this product was also photochromic in organic solvents such as benzene and dichloromethane. Product (**11**) was consequently purified by column chromatography eluting with benzene or toluene, and the melting point was found to be 168 – 170 °C, with an overall yield of 70%. The new compound was found to be photochromic in different organic solvents this will be fully discussed in Chapter 3.

2.1.5 *(Ferrocene-1,1′-diyl)bis[N,S-(dithizonato)mercury(II)]* (12)



A similar reaction route [Equation (4)] as used in the preparation of (**11**) was followed. In this case dithizone was added as a single portion to a half-equivalent molar amount of (ferrocene-1,1′-diyl)bis[chloridomercury(II)] (**16**) suspended in dichloromethane, followed by the addition of few drops of triethylamine. The reaction mixture was stirred for 30 minutes and after removal of the solvent, the product was purified by column chromatography. The melting point was found to be 175 – 180 °C and a 75% yield was obtained. The product was also found to be photochromic in different organic solvents and this will be discussed in Chapter 3.

2.2 SYNTHESIS OF CATION SENSORS

2.2.1 *Introduction*

It was mentioned in Chapter 1 that it is possible to synthesize dithizone derivatives with substituents at the sulfur atom. The first example was *S*-methyldithizone, which was prepared via two different routes. In the first reaction route, silver dithizonate [Ag(HDz)] was reacted with methyl iodide (MeI), and in the second route, dithizone itself was reacted with dimethyl sulfate (Me_2SO_4) in chloroform as a solvent.[7]

It was first necessary to prepare iodoferrocene (**17**) as the starting reagent for the synthesis of *S*-ferrocenyldithizone (**13**). The synthesis of (**17**) was done via three different routes, as detailed below. The preparation of *S*-ferrocenyldithizone was first attempted by heating under reflux a chloroform solution of iodoferrocene and silver dithizonate. Thin layer chromatography (TLC) showed the unchanged spots of the starting materials, indicating that the reaction did not take place. Similar TLC behaviour was observed when the reaction was performed in higher boiling point solvents like benzene and polar solvents such as tertiary butanol for long reaction times.

Unlike the sp^3 hybridized carbon atom of CH_3I used as a starting reagent in the synthesis of *S*-methyldithizone, the electrophilic carbon on the cyclopentadienyl ring of iodoferrocene is sp^2 hybridized. This meant that a catalyst was needed for the C–S coupling reaction of the sp^2 hybridized carbon. Various catalysts for C–S coupling reactions have been reported,[8-10] including coupling reactions in which the air-sensitive tetrakis(triphenylphosphane)palladium(0), $[Pd(PPh_3)_4]$, is used as a catalyst.[8] In this procedure a solution of sodium ethoxide as a base, equal molar amounts of phenyl iodide (or phenyl iodide derivatives) and the respective thio substituent (PhSH or EtSH) was heated under reflux in the presence of 0.05 mol% $[Pd(PPh_3)_4]$ catalyst in a polar solvent like dimethylsulfoxide (DMSO) or ethanol.[8]

In several ways the cyclopentadienyl rings of ferrocene are analogous to the planar benzene molecule. Both ferrocene and benzene are electron-rich aromatic systems that undergo reactions like electrophilic substitution.[11] Ferrocene derivatives undergo similar reactions to benzene derivatives. For this reason, a similar route for the C–S coupling reaction using $[Pd(PPh_3)_4]$ as a catalyst was followed for the synthesis of *S*-ferrocenyldithizone. The reaction mixture was heated under reflux in ethanol, butanol or dimethylsufoxide. The thio proton in dithizone is likely to be removed in basic solution resulting in the nucleophilic thiolate anion. Unfortunately, there was no positive indication of the formation of the desired product in our reaction. The ^1H NMR spectrum showed only traces of the ferrocenyl signal compared to the more intense signal in the phenyl region. It is suggested that during the reaction the stable Pd(II) complex formed in the nucleophilic substitution step (see Figure 2.1 for the possible catalytic mechanism of the reaction)[8] was so stable that it could not react further to the reductive elimination step which would ultimately result in the coupled product. It is well known that dithizone forms complexes with different metals ions including palladium(II), as was discussed in Section 1.1 of the previous Chapter. This was not expected under the reaction conditions followed.

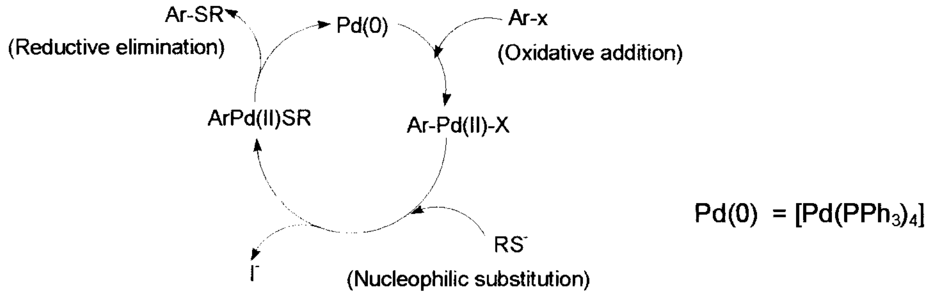


FIGURE 2.1: Proposed catalytic mechanism using $[Pd(PPh_3)_4]$ catalyst for C–S coupling reaction.[8] For our reaction consider Ar = Fc, RS = HDz and X = I.

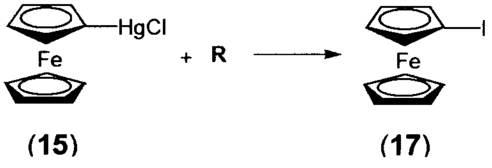
Owing to the lack of product formation when using $[Pd(PPh_3)_4]$ as a catalyst the use of a different catalyst was considered. The C–S coupling reaction established by Kyong and Buchwald was followed.[12] This reaction involves the use of the air-stable copper(I) iodide as a catalyst in the presence of ethylene glycol and a weak base such as potassium carbonate in an alcohol as a solvent. Presumably, ethylene glycol serves as a co-solvent and ligand in the reaction. Its major function may be to sequester and keep the Cu(I) species in solution. It has been reported that this protocol showed a good tolerance in the reactions involving aromatic substrates containing nitrogen atoms, such as in common functional groups like nitrile, nitro and aniline moieties.[12] Nitrogen atoms can coordinate to the metal catalyst through a lone pair of electrons, thus affecting the reaction process. The lone pair of electrons on the imino nitrogen of dithizone could also coordinate to metal ions; however, due to the tolerance of the functional groups in this protocol this reaction route was regarded as good to pursue. The mechanism of this reaction has not been reported; however, it is possible that a Cu(III) complex is formed in the first oxidative addition step (compare to mechanism in Figure 2.1). Various reactions were attempted for the synthesis of (iodomethyl)ferrocene as the starting reagent for the preparation of *S*-ferrocenylmethyldithizone. We attempted the preparation of (iodomethyl)ferrocene by firstly reducing ferrocenecarboxyaldehyde to ferrocenylmethanol. Substitution reactions following different literature methods for nucleophilic substitution of alcohols with halogens in aromatic compounds were not successful.[13-15]

(Ferrocenylmethyl)trimethylammonium iodide (**18**) is a reagent which is widely used in many preparations of ferrocenylmethyl derivatives.[16-18] This includes the substitution reactions of tertiary amines by poor leaving groups such as the cyanide ion (CN^-).[19] It was necessary first to prepare this reagent using the literature procedure.[18] Reagent (**18**) has been reported to react with potassium cyanide to form (ferrocenylmethyl)nitrile.[19] It was considered that AgHDz would be similarly reactive and the synthesis of *S*-ferrocenylmethyldithizone (**14**) was accomplished by the reaction of a small excess of salt (**18**) and silver dithizonate complex (AgHDz) in chloroform. Characterisation of the new analytical reagents is discussed in Section 2.3 and full experimental details are given in Section 2.6.

2.2.2 *Iodoferrocene* (17)

There are many different methods for the preparation of iodoferrocene in the literature. Most of these reactions involve the use of chlorido(ferrocenyl)mercury(II) (**15**) as a precursor.[4,20,21] The following three different methods were followed in attempts to obtain better yields of this reagent.

Method 1 [20]



(5)

R = Iodine or iodosuccinimide

In this preparation, reagent **R** was iodine [Equation (5)]. A solution of iodine in dichloromethane was added to a solution of chlorido(ferrocenyl)mercury(II) in dichloromethane at room temperature under nitrogen. As compared to Grignard reagents the carbon atom that is bonded to mercury is nucleophilic, making it reactive in the presence of electrophiles. The reaction mixture was stirred for several days, then washed with aqueous sodium thiosulfate solution to destroy excess iodine. After concentration and purification by flash chromatography the product separated as an oil which solidified after some hours at *ca.* -15 °C. The yield was found to be 41% and the product had a melting point of 44 °C (lit.[20] m.p. 44 – 45 °C).

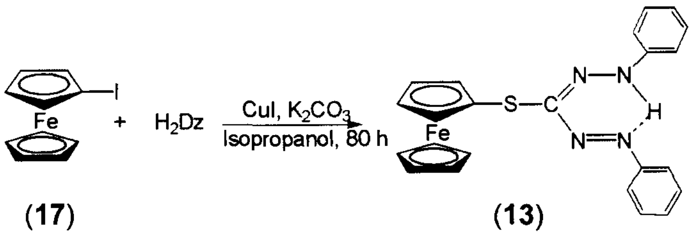
Method 2 [21]

Using the same route with **R** = iodine [Equation (5)], chlorido(ferrocenyl)mercury(II) was stirred with iodine in dry dichloromethane for 1 h. A spatula tip of ascorbic acid as a reducing agent was then added and the mixture was allowed to stir for a further hour. Ascorbic acid is thought to reduce any ferrocenium ions that may have resulted from oxidation of iron in iodoferrocene or chlorido(ferrocenyl)mercury(II) by iodine which might lead to undesired products. The reaction proceeds in a similar way to that of Method 1. Removal of solvent resulted in the product initially as a yellow oil which later solidified on standing when chilled for some hours at *ca.* -15 °C. The yield of the product was found to be 60% and a melting point of 44 °C was obtained.

Method 3 [4]

In this procedure, reagent **R** [Equation (5)] was *N*-iodosuccinimide employed as a halogenating agent. There is a definite advantage to using the electrophilic iodide (which is bonded to the more electronegative nitrogen atom) which is reactive in the presence of nucleophiles. A solution of *N*-iodosuccinimide in dry dichloromethane, previously flushed with nitrogen gas, was added dropwise to a stirred suspension of chlorido(ferrocenyl)mercury(II) **(15)** in dichloromethane cooled in an ice bath. After the reaction had proceeded for several hours aqueous sodium metabisulfite solution was added to remove excess iodine by forming iodide, which was removed by washing with water. The product was purified by flash chromatography, eluting with petroleum ether. Iodoferrocene (**17**) was obtained as an oil, which crystallised after some hours when cooled at *ca.* -15 °C. The yield was 77% and the product melted at 44 °C. This route was found to be the optimum procedure for the preparation of iodoferrocene in this work.

2.2.3 *S-Ferrocenyldithizone* (**13**)

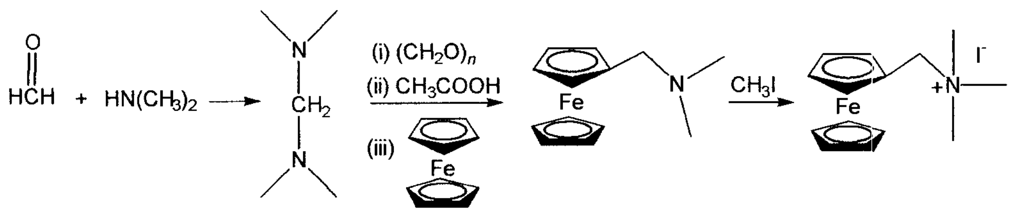


(7)

For this preparation [Equation (7)] the C–S coupling reaction established by Kwong and Buchwald[12] was used. In this reaction, equivalent molar amounts of iodoferrocene and dithizone in isopropanol were heated under an argon atmosphere at 80 °C with ethylene glycol and potassium carbonate as a base in the presence of the air-stable and inexpensive copper(I) iodide (CuI) as a catalyst. It is likely that ethylene glycol serves as a co-solvent and ligand in the reaction. Its major function may be to sequester and keep the Cu(I) species in solution. After purification by flash chromatography, the product was obtained as a red-brown solid (49%) with a melting point of 163 – 166 °C.

To our advantage this reaction route resulted in the formation of the desired product, but unfortunately in lower yields, in contrast to those reported by Kyong and Buchwald in their coupling reactions.[12] Many factors could have contributed to the poor yields of the product in our reaction, such as the production of side products, e.g. the oxidised form of *S*-ferrocenyldithizone (the tetrazolium salt). This was evident from one of the bands eluted from column chromatography during purification of the product. The band had a similar colour and R_f value on a TLC plate as the purple solid product obtained in reaction of copper perchlorate and *S*-ferrocenyldithizone (discussed in more detail in Chapter 4). This purple solid was proven crystallographically to be the tetrazolium salt. Formazans can be oxidised to the corresponding tetrazolium salts in the presence of copper(II) ions.[22] Possible complexation of copper with dithizone cannot be ignored though complexes of copper(I) with dithizone have been reported to be unstable and even more so in a basic environment.[23]

2.2.4 (*Ferrocenylmethyl)trimethylammonium iodide*[18] (**18**)



(18)

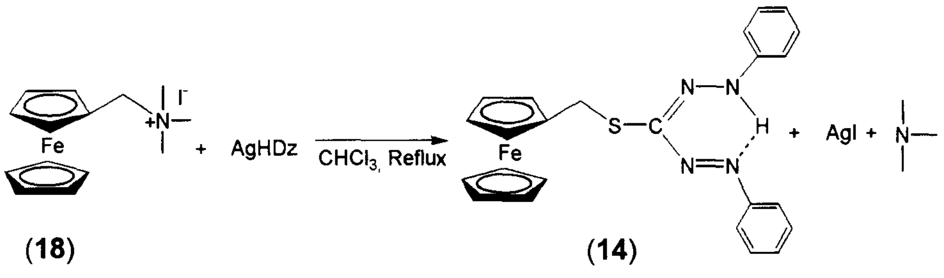
(6)

In the first step *N*,*N*,*N'*,*N'*-tetramethyldiaminomethane was prepared following the literature procedure [see Equation (6)].[18] Aqueous formaldehyde was reacted with an aqueous solution of dimethylamine. Solid potassium hydroxide was added to separate the layers. The organic layer was dried with potassium hydroxide and purified by distillation to give the product. The yield of the product was 21% and a boiling point of 81 – 83 °C was obtained (lit.[24] b.p. 82 – 84 °C).

The second step was the aminomethylation of ferrocene to form *N*,*N*-dimethylaminomethylferrocene [see Equation (6)]. A mixture of *N*,*N*,*N'*,*N'*-tetramethyldiaminomethane, paraformaldehyde and glacial acetic acid was heated for few minutes. During this time the *N*,*N*,*N'*,*N'*-tetramethyldiaminomethane reacted with formaldehyde to give two equivalents of $[H_2C{=}NMe_2]^+$, which is an electrophile. The two molar equivalents of ferrocene were then added to react with this electrophilic species. The reaction mixture was filtered and the filtrate was made alkaline with sodium hydroxide, and then extracted with ether. The dried organic layer was distilled under reduced pressure to give 20% of *N*,*N*-dimethylaminomethylferrocene. A boiling point of 91 °C was obtained (lit.[18] b.p. 91 – 92 °C at 0.4 mmHg at 25 °C).

The final step was the methylation of the resultant tertiary amine to form the desired salt (**18**). This was carried out by adding, dropwise, a solution of iodomethane in absolute methanol to a cold methanol solution of dimethylaminomethylferrocene. The clear solution was boiled under reflux for 5 minutes. This is a simple substitution reaction (S_N2) of iodine in iodomethane by the nucleophilic tertiary amine. The product was precipitated by addition of diethyl ether to give the quaternary salt (**18**). The yield of the product was 78% and a melting point of 220 °C was obtained (lit.[18] m.p. 220 °C).

2.2.5 S-*Ferrocenylmethyldithizone* (**14**)



(8)

S-Ferrocenylmethyldithizone (**14**) was synthesized from the reaction of the silver dithizonate complex and a 10% excess of the salt (**18**) in chloroform (see Equation 8). The reaction is thought to proceed via nucleophilic substitution of the dithizonate (HDz^-) anion by iodide ion to form an insoluble silver iodide salt and (ferrocenylmethyl)trimethylamine. The thiolate anion formed then attacks the electrophilic methylene carbon which is at the α-position to the tertiary amine group in the (ferrocenylmethyl)trimethylamine produced in the first step and trimethylamine is eliminated. Chloroform was added and the solution worked up with an aqueous sodium thiosulfate solution to remove traces of silver iodide. After purification by flash chromatography (eluting with benzene) and removal of solvent the product separated as a red-brown oil which solidified on standing under reduced pressure for some days. The yield was found to be 75% and the product was found to melt at 60 – 64 °C.

2.3 CHARACTERISATION OF COMPOUNDS

2.3.1 *Introduction*

Characterization was performed by several techniques. Products were completely dried under reduced pressure before characterisation, and ^1H and ^{13}C NMR spectroscopy was performed on all compounds synthesised. UV-Vis spectroscopy was used to investigate the absorbance of the chromophores of the new mercury dithizonates **(11)** and **(12)**, and the isomerisation studies on the new analytical reagents **(13)** and **(14)**. Characterisation by mass spectrometry, melting point determination and elemental analysis were also performed. Some techniques were not done for starting materials, as the data obtained was sufficient for the characterisation of known compounds. Complete data are presented at the end of the preparative method for each compound in Section 2.6.2.

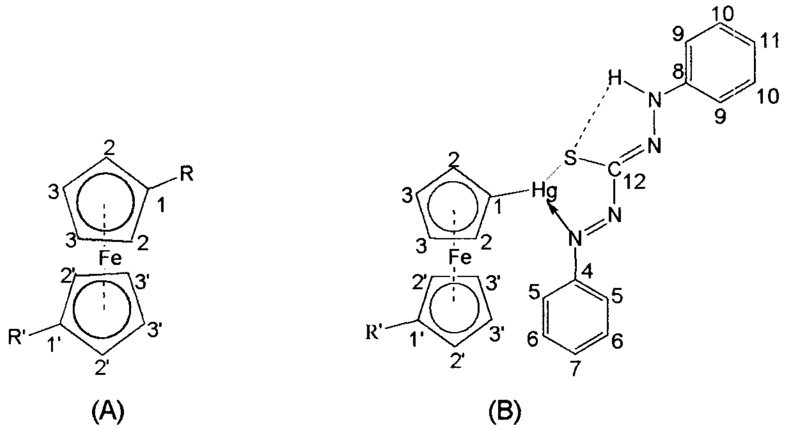
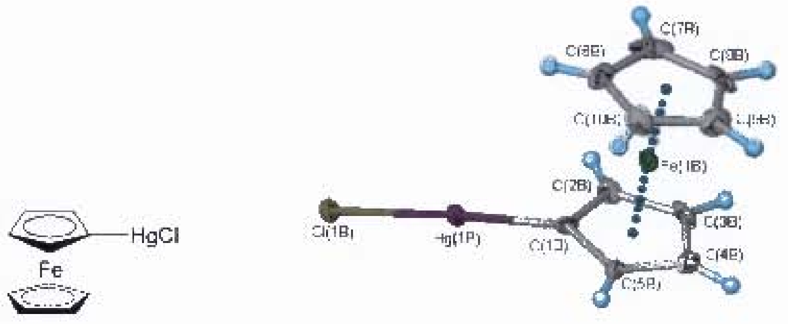


FIGURE 2.2: Assignments of carbon and hydrogen atoms used in the following compounds: (A) ^1H NMR, (**15**, R' = H, R = HgCl), (**16**, R' = R = HgCl); H^2, $H^{2'}$ or H^3, $H^{3'}$ = protons at α or β position to the substituent group R or R', respectively; ^{13}C NMR, C^2, $C^{2'}$ or C^3, $C^{3'}$ = carbons at α or β position, while C^1 or $C^{1'}$ = carbon which is bonded directly to the substituent group R or R', respectively; (B) Numbering system used for ^1H and ^{13}C NMR proton and carbon assignments for compounds (**11**, R' = H) and [**12**, R' = Hg(HDz)]. Note that when R' is a hydrogen atom then all proton or carbon atoms in this cyclopentadienyl ring have the same chemical environment and are reported as either 5H or 5C for ^1H or ^{13}C NMR, respectively.

2.3.2 *Characterisation of photochromic compounds and their precursors*

Compounds **(15)** and **(16)** were purified and characterized by ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, elemental analysis and melting point determination. Where applicable the chemical shifts were assigned using the numbering system outlined in Figure 2.2, on the previous page.

In the ^{1}H NMR spectrum of compound **(15)** the chemical shifts of the protons were observed at 4.47 ($2H^{2}$, t, J = 1.7 Hz), 4.23 (5H, singlet) and 4.11 ($2H^{3}$, t, J = 1.7 Hz). The substituent group on the cyclopentadienyl ring pulls electrons to itself, thus making the protons at the 2-position resonate at low field [i.e. in the ^{1}H NMR spectrum of compound **(15)**, 4.47 ppm ($2H^{2}$)]. In most cases the chemical shifts of the protons in the unsubstituted cyclopentadienyl ring are only slightly affected compared to chemical shift of the protons in ferrocene itself. The molecular structure of a polymorph of compound **(15)** was also discovered (see Figure 2.3). The compound crystallized from dichloromethane-hexane as orange cubes in the monoclinic system and space group of $P2_1/c$ with two independent molecules in the unit cell (both with eclipsed conformation). Previously reported crystal structure of commercial (Aldrich) compound crystallized (from dichloromethane-hexane mixture) in the triclinic with space group of P-1, with two independent molecules in the unit cell (one with staggered and one with an eclipsed conformation).[25] Some molecular parameters of the new polymorph are shown in Table 2.1 (a), while the crystallographic data and refinement details are given in Table 2.1 (b)



(a) (b)

FIGURE 2.3: (a) Chemical structure and, (b) molecular structure of the new polymorph of chloride(ferrocenyl)mercury(II).

TABLE 2.1(a): Selected bond angles (°) and bond lengths (Å) for the molecular structure of the new polymorph of chlorido(ferrocenyl)mercury(II)

Atoms	Bond length (Å)	Atoms	Bond angles (°)
Hg(1B)-Cl(1B)	2.338(2)	Cl(1B)-Hg(1B)-C(1B)	176.7(7)
Hg(1B)-C(1B)	2.036(9)	C(1B)-Fe(1B)-C(6B)	109.1(3)
Fe(1B)-C(1B)	2.053(7)	C(5B)-Fe(1B)-C(10B)	108.7(4)
Fe(1B)-C(6B)	2.033(8)	C(4B)-Fe(1B)-C(9B)	106.7(4)
C(1B)-C(5B)	1.433(10)	C(3B)-Fe(1B)-C(8B)	106.9(4)
C(1B)-C(2B)	1.422(11)	C(2B)-Fe(1B)-C(7B)	108.5(3)
C(6B)-C(7B)	1.425(14)	Hg(1B)-C(1B)-C(2B)	123.7(6)
C(6B)-C(10B)	1.369(12)	Hg(1B)-C(1B)-C(5B)	123.7(7)
Fe(1B)-C(4B)	2.040(8)		
Fe(1B)-C(9B)	2.045(8)		

TABLE 2.1 (b): Crystal data and structure refinement for chlorido(ferrocenyl)mercury(II)

Empirical formula	$C_{10}H_9ClFeHg$
Formula weight	421.06
Temperature	131(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/c$
Unit cell dimensions	a = 24.5611(3) Å, α = 90°
	b = 5.9905(2) Å, β = 106.2790(10)°
	c = 14.1214(6) Å, γ = 90°
Volume	1994.43(11) Å^3
Z, Calculated density	8, 2.805 Mg m^{-3}
Reflections collected/unique	32123/4066 [R(int) = 0.0931]
Goodness of fit on F^2	1.032
Final R indices [I>2sigma (I)]	R_1 = 0.0386, wR_2 = 0.0745
R indices (all data)	R_1 = 0.0636, wR_2 = 0.0820

Due to the insolubility of compound **(16)** in many less polar organic solvents the ^1H NMR spectra were obtained in deuterated dimethylsulfoxide (DMSO-d^6). Four signals of equal integration were observed at chemical shifts of 4.16, 4.26, 4.36 and 4.40 ppm. This might be due to the hydrogen atoms from two isomers in the solution

(HgCl-substituents can either be *cis* or *trans* to each other on the Cp rings resulting in different chemical shifts of the protons); however, this is speculation and impurities might be involved. There is no information on the NMR spectroscopy of this compound in the literature.

In the ^{1}H NMR spectrum of (*N,S*-dithizonato)(ferrocenyl)mercury(II) **(11)** (see Figure 2.4, on the next page) the ferrocenyl proton signals were observed at 4.11 ($2H^3$, triplet), 4.46 ($2H^2$, triplet) and 4.20 ppm (5H, singlet). For the dithizone group the phenyl protons resonate between 7 and 8 ppm (10H, multiplet) and the NH proton at 9.33 ppm. In the ^{1}H NMR spectrum of (ferrocene-1,1'-diyl)bis[(*N,S*-dithizonato)mercury(II)] **(12)** the ferrocenyl proton signals were observed between 4.18 ($2H^3$, triplet), 4.20 ($2H^2$, triplet) and peaks at 4.14 (singlet) and 4.47 ppm (multiplet) which could not be assigned, the phenyl protons between 7 and 8 ppm (20H, multiplet) and the NH protons at 9.30 ppm (2H) for the dithizone groups. For both compounds **(11)** and **(12)** the ^{13}C NMR spectra showed that the ferrocenyl carbon atoms resonated between 60 and 70 ppm, while the phenyl carbons were observed between 120 and 145 ppm. The imino carbon was observed at 150 ppm. A typical ^{13}C NMR spectrum of compound **(11)** is shown in Figure 2.5, on the next page.

The chemical shifts of the protons and carbons in these compounds corresponded to other mercury(II) dithizonate compounds.[1-3] Compounds **(11)** and **(12)** each had a sharp melting point at 168 – 170 and 175 – 180 °C, respectively. The higher melting point of compound **(12)** compared to that of compound **(11)** is indicative of stronger intermolecular interactions in compound **(12)** compared to compound **(11)**. In spite of the satisfactory NMR spectra, elemental analysis of the mercury dithizonates did not correspond well to the expected products, even after performing purification by column chromatography using different eluting solvents of lower polarity (benzene, toluene, and carbon tetrachloride). The amount of the catalyst employed in the analysis was increased to facilitate complete oxidation in an attempt to obtain better elemental analysis. However, this did not improve the analytical results.

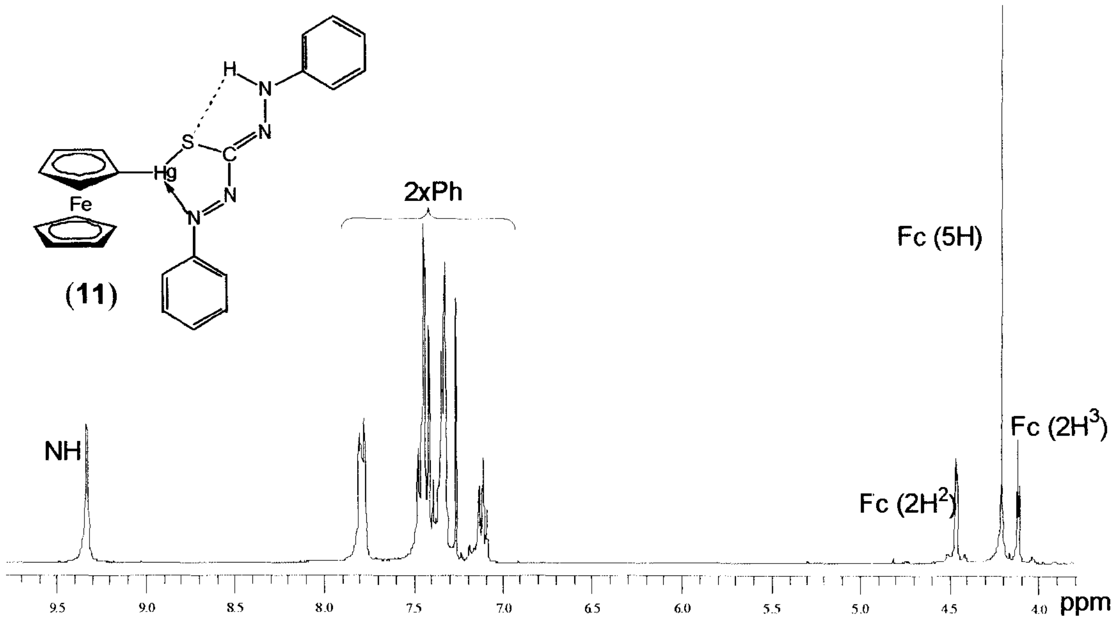


FIGURE 2.4: ^{1}H NMR spectrum of (dithizonato)(ferrocenyl)mercury(II) (**11**).

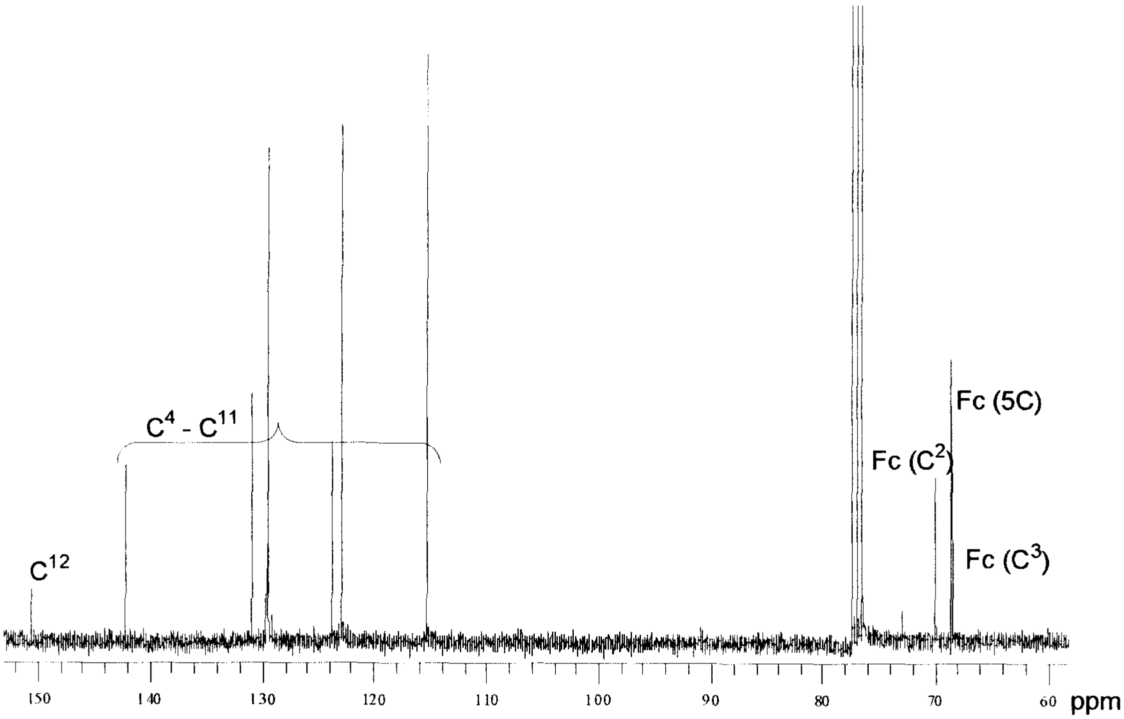


FIGURE 2.5: ^{13}C NMR spectrum of (dithizonato)(ferrocenyl)mercury(II) (**11**).

It is assumed that there might have been traces of a solvent or crystallizing solvent present which were not completely removed despite, drying the compounds under vacuum for long times. In addition, discussions with the microanalyst performing the determinations revealed that unsatisfactory microanalysis results were frequently observed for mercury-containing compounds using the available instrument.[26]

Molecular ion peaks were not observed in the mass spectrometry, though some possible fragmentation values appeared at *m/z* 577, 500 and 120. Possible structures for these fragments are shown in Figure 2.6.

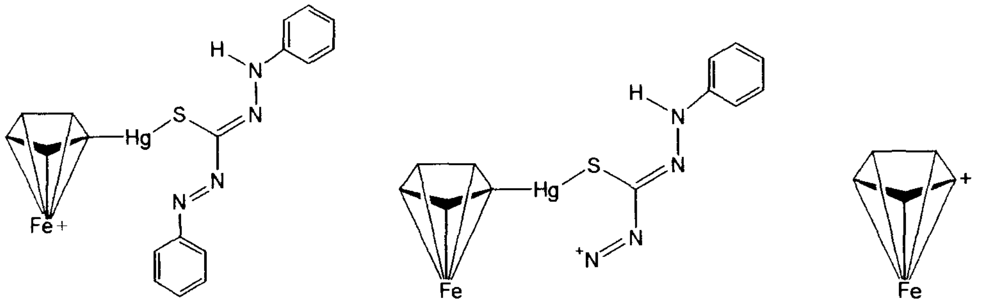


FIGURE 2.6: The possible fragments that are formed in the mass spectrometry of the new mercury dithizonates (**11**) and (**12**).

UV-Vis spectroscopy on chloroform solutions, however, showed the absorption maximum at 485 or 490 nm and molar extinction coefficient of ε_{max} = 29400 or 63400 M^{-1} cm^{-1} for compound (**11**) or (**12**), respectively. It should be noted that molar extinction coefficient of (**12**) was approximately twice that of (**11**), confirming the presence of the two chromophores (dithizone) in compound (**12**) compared to the single chromophore in compound (**11**). In addition, cyclic voltammetry on dichloromethane solutions shows a quasi-reversible wave with half-wave potential $E_{1/2}$ = 212 or 204 mV for (**11**) or (**12**), respectively, relative to the Ag/Ag$^+$ reference electrode. These waves had ΔE_p of *ca.* 60 mV, showing that the wave is due to transfer of one electron, which is confirmation of the presence of ferrocene in the compounds. The electrochemical properties of these compounds will be treated fully in Chapter 3.

The half-wave potential shift was $\Delta E_{1/2} = 21$ and 13 mV for **(11)** or **(12)**, respectively, with reference to the half-wave potential of ferrocene itself ($E_{1/2} = 0$ mV). The half-wave potentials show that it was marginally more difficult to remove an electron from the ferrocene with one mercury dithizonate substituent [as in compound **(11)**] than with two substituents [as in compound **(12)**], and both are marginally more difficult to oxidize than ferrocene itself. Thus the effect of the mercury substituents on the redox properties of the ferrocenyl moiety is minor, and must result from an overall small decrease in electron density on the ferrocenyl group in the mercury-substituted compounds.

2.3.3 *Characterisation of cation sensors and their precursors*

Characterisation data are listed in the experimental section (Section 2.6.2) at the end of preparation method of each compound. Some techniques were not done for starting materials as the data obtained were sufficient for the characterisation of known compounds. Where applicable the assignment convention shown in Figure 2.7, below, was used for all proton and carbon assignments in the ^{1}H and ^{13}C NMR spectra.

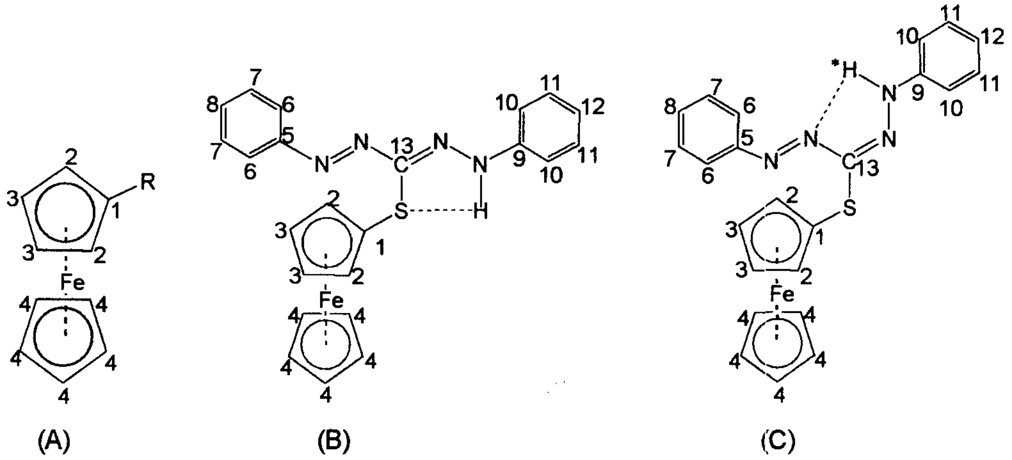


FIGURE 2.7: Assignment of carbon and hydrogen atoms used for the following compounds: (A) ^{1}H NMR, (**17**, R = I) and [**18**, R = $CH_2N^+(CH_3)_3I^-$], H^2 or H^3 = protons at α or β position to the substituent group R, respectively; ^{13}C NMR, C^2 or C^3 = carbons at α or β position- while C^1 = carbon which is bonded directly to the substituent group R. [Isomers, (B), (*anti)* and (C), *(syn)*], Numbering system for ^{1}H and ^{13}C NMR assignments for compounds **(13)** and [**(14)**, additional methylene link between C^1 and sulfur]. H* = NH signal of the *syn* isomer.

For these compounds the important regions in the ^{1}H NMR spectra are between 4 and 5 ppm for the ferrocenyl protons, the phenyl protons between 7 and 8 ppm and the NH proton between 9 and 10 ppm for the dithizone group. The two precursors iodoferrocene (**17**) and (ferrocenylmethyl)trimethylmmonium iodide (**18**) were characterised by ^{1}H and ^{13}C NMR and melting point determination. This data was sufficient for characterisation of these known compounds. Both compounds showed the characteristic ferrocenyl chemical shifts between 4 and 5 ppm and exhibited sharp melting points of 44 – 45 (lit.[20] m.p. 44 – 45 °C) or 219 – 221 °C (lit.[18] m.p. 220 °C) for compound (**17**) and (**18**), respectively.

In the ^{1}H NMR spectrum of compound (**17**) the ferrocenyl protons were observed at 4.35 (triplet, 2H^2), 4.09 (triplet, 2H^3) and 4.12 ppm (singlet, 5H) (for assignment of protons see Figure 2.7). Additional signals for the bridging methylene and aminomethyl protons of compound (**18**) were observed at 4.90 (singlet, CH_2) and 3.24 ppm (singlet, 3CH_3), respectively. Signals for the ferrocenyl protons were observed at 4.32 (triplet, 2H^3), 4.57 (triplet, 2H^2) and 4.29 ppm (singlet, 5H). It was noted that the chemical shifts of H^2 and H^3 were affected by the substituent group R (see Figure 2.7). Electron-withdrawing groups such as in compound (**18**) make the protons at the α position resonate very much downfield. All expected carbon signals were observed in the ^{13}C NMR and the data are summarised in Section 2.6.2.

For *S*-ferrocenyldithizone (**13**), in the ferrocenyl region the signals appeared at 4.19 (triplet, 2H^3), 4.43 (triplet, 2H^2) for the substituted cyclopentadienyl ring and 4.25 (5H, singlet) for the unsubstituted ferrocenyl Cp. ring. Additional peaks were observed at 4.24 and 4.34 ppm, which possibly arise from the other isomer in solution (see discussion of *syn*-*anti* isomerisation in Section 2.4). The phenyl peaks appeared between 7.0 and 7.9 ppm (multiplet, 10H). The two NH peaks for the *anti* and *syn* isomers were observed at 9.50 and 10.21 ppm (NH*), and the ratio of the integrals was 3 : 1 for the signals at 9.50 and 10.21 ppm. This isomerisation behaviour will be fully discussed in Section 2.4. The ferrocenyl ^{13}C NMR signals appeared between 60 and 70 ppm (4C), while the phenyl carbons resonated between 120 and 145 ppm (12C) and the imino carbon appeared at

147.78 ppm. For illustration the ^{1}H and ^{13}C NMR spectra of compound **(13)** are shown in Figures 2.8 and 2.9 (on the next page), respectively. The chemical shifts of the dithizone group corresponded to other *S*-substituted dithizone compounds known in literature.[27]

In the UV-Vis absorption spectrum of S-ferrocenyldithizone **(13)** the λ_{max} was observed at 410 nm with the molar extinction coefficient of $\varepsilon_{410} = 20700\ M^{-1}\ cm^{-1}$. By comparison with other dithizone compounds it is proposed that this band is due to the ($\pi \rightarrow \pi^*$) transition of electrons in the conjugated NNC(S)NN chain of these compounds. Several fragments were observed in the mass spectrum, and important fragments which were assigned are the molecular ion peak (M^+) and FcS^+ which had *m/z* values of 440 and 217, respectively.

From cyclic voltammetry, a reversible wave was observed with half-wave potential of $E_{1/2}$ = 203 mV; this wave corresponded to a one electron transfer as in ferrocene. The shift of half-wave potential relative to ferrocene itself was $\Delta E_{1/2}$ = 118 mV, showing that it was significantly more difficult to remove an electron from the ferrocene when the bulky, electronegative sulfur atom was directly bonded to the cyclopentadienyl ring of ferrocene than for ferrocene itself. Electrons are pulled away from the ferrocenyl group by sulfur which makes the ferrocenyl moiety more difficult to oxidise.[28]

For *S*-ferrocenylmethyldithizone **(14)** in the ferrocenyl region the signals appeared at 4.01 ($2H^3$, triplet), 4.09 ($2H^2$, triplet) for the substituted cyclopentadienyl ring and 4.07 ppm (5H, singlet) for the unsubstituted cyclopentadienyl ring. Methylene protons were observed at 3.84 ppm (CH_2). The phenyl peaks appeared between 7.0 and 8.0 ppm (10H, multiplet). Two NH peaks for the *anti* and *syn* isomers were observed at 9.36 and 10.30 ppm (NH*); the ratio of the integrals was 3 : 1 for the signals at 9.36 and 10.30 ppm, respectively. This isomerisation behaviour will be discussed in Section 2.4. In the ^{13}C NMR spectra, the chemical shifts of the ferrocenyl carbon atoms appeared between 60 and 70 ppm (4C), while the phenyl carbons were observed between 120 and 140 (12C) and the imino carbon at 152.49 ppm. The methylene carbon resonated at 33.80 ppm.

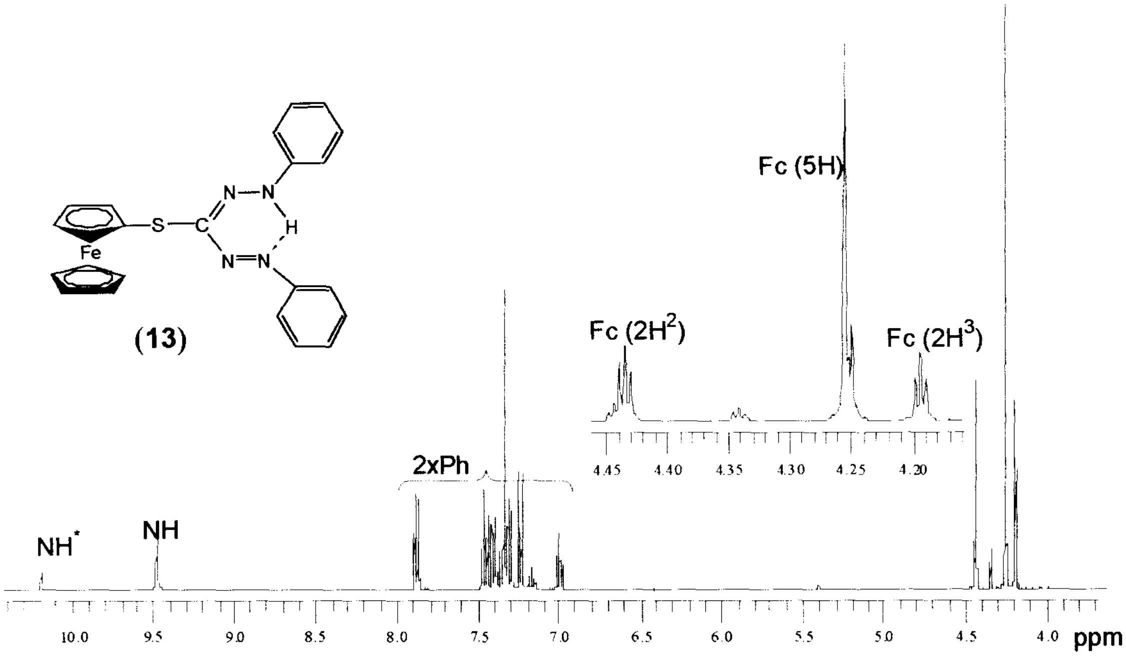


FIGURE 2.8: ^{1}H NMR spectrum of *S*-ferrocenyldithizone (**13**), H* = NH of the *syn* isomer. The more intense signals in the ferrocenyl region are probably due to the protons of the *anti* isomer while the less intense protons are due to the *syn* isomer.

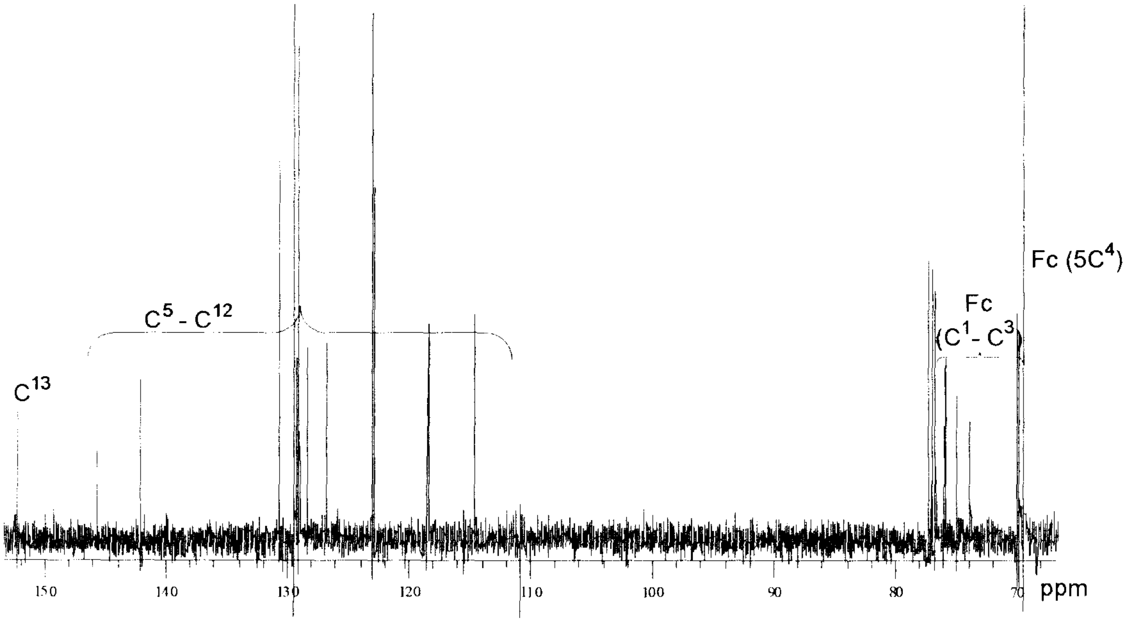


FIGURE 2.9: ^{13}C NMR spectrum of *S*-ferrocenyldithizone (**13**). The signals observed at 70 – 76 and 114 – 146 ppm (i.e. C^1 – C^3 and C^5 – C^{12}) are, respectively, due the carbon atoms in the ferrocenyl and the phenyl regions of the *syn* and *anti* isomers.

In the UV-Vis spectroscopy of S-ferrocenylmethyldithizone (**14**) the λ_{max} was observed at 415 nm and had a molar extinction coefficient of ε_{415} = 18300 M^{-1} cm^{-1}. Several fragments were observed from mass spectrometry, the important ones which were assigned being the molecular ion peak (M^+), $Fc\text{-}CH_2^+$ and HDz^+, which had *m/z* values of 454, 199 and 255, respectively. In cyclic voltammetry, the redox potential of the ferrocene/ferrocenium couple of compound (**14**) had a half-wave potential of $E_{1/2}$ = 136 mV relative to Ag/Ag^+. The shift in half-wave potential relative to ferrocene in compound (**14**) was $\Delta E_{1/2}$ = 51 mV. This showed that it was substantially easier to remove an electron from the ferrocenyl group when methylene carbon is interspersed between the cyclopentadienyl ring and the sulfur of the dithizonate moiety compared to the higher oxidation potential required by compound (**13**).

2.4 ISOMERISATION STUDIES OF CATION SENSORS

It was pointed out in Chapter 1 that the derivatives of dithizone with a substituent on the sulfur atom, such as *S*-methyldithizone, isomerise in solution to form *syn* and *anti* isomers. This was observed in the ^1H NMR spectrum where two NH signals are observed, typically at *ca.* 9.50 and 10.20 ppm.[27] Similar behaviour was observed for the new ferrocenylated dithizone derivatives.

In the case of *S*-ferrocenyldithizone (**13**), two NH signals were observed at 9.50 and 10.21 ppm immediately after preparation of the sample solution in deuterated chloroform. The ratio of the integrals of the signals was 3 : 1 for the protons at 9.50 and 10.21 ppm, respectively. Upon irradiation in sunlight the signal at 10.21 ppm became slightly more intense, making the peak intensities of the two signals nearly equal. Several additional peaks were observed in the ferrocenyl region of the NMR spectrum due to the presence of two isomers in the solution. The UV-Vis spectrum (Figure 2.10, on the next page) of a dilute yellow (*anti* isomer) solution of *S*-ferrocenyldithizone in chloroform immediately after preparation showed only one strong band at 410 nm. Upon irradiation in sunlight for 1 min, the solution turned pink (*syn* isomer), the original band at 410 nm decreased in intensity, and a new band at 530 nm appeared.

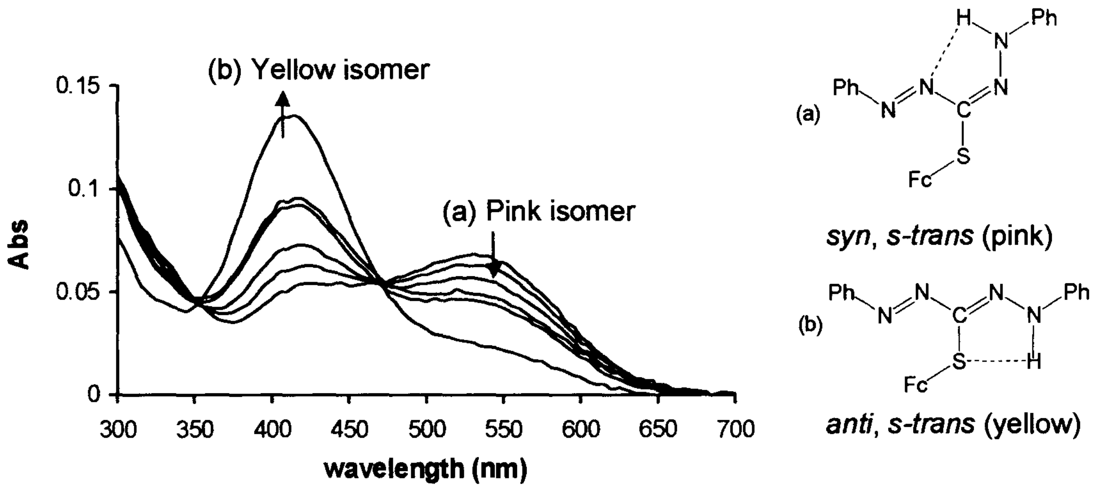


FIGURE 2.10: The UV-Vis spectrum of a solution of *S*-ferrocenyldithizone (**13**) (1.00 x 10^{-5} M), (a) immediately after exposing yellow conformer to the sun for 1 min (to form pink isomer; *syn*, *s-trans*), (b) then 20 min interval cycles in the dark (to revert to yellow isomer; *anti*, *s-trans*).

The 20 min interval runs show the intensity of the band at 530 nm decreasing as the absorbance of the original band at shorter wavelength increased again. Prolonged irradiation (four hours) of the dilute solutions led to decomposition as observed from the UV-Vis spectrum, which showed the disappearance of the original bands and the emergence of new bands at shorter wavelengths which did not correspond to either of the two isomers. Investigation of this decomposition product was not followed up since very dilute solutions were used.

Similar isomerisation was observed in the ^{1}H NMR spectrum of *S*-ferrocenylmethyldithizone (**14**). Two NH signals were observed at 9.36 and 10.30 ppm, with the signal at high field slightly more intense than the one at low field, in the ratio of 3 : 1. The UV-Vis spectrum of a dilute solution of yellow (*anti* isomer) *S*-ferrocenylmethyldithizone in chloroform immediately after preparation showed only one strong band at 415 nm. Upon irradiation in sunlight for 1 minute the solution remained yellow and the spectrum showed the disappearance of the original band at 415 nm along with the appearance of additional new peaks at shorter wavelengths, which did not relate to either of the two isomers. It is assumed that irradiation of dilute solutions of *S*-ferrocenylmethyldithizone in sunlight led to decomposition, as was also observed for compound **(13)** after prolonged irradiation. Traces of acid did not facilitate the isomerisation of either compound, in contrast to what has been observed for *S*-MeHDz.[27]

We assigned the isomers of the new *S*-ferrocenylated dithizones by comparison with the isomerisation studies of *S*-methyldithizone and its derivatives and *S*-isopropyldithizone, all of which have been well studied.[27,29] A fresh solution of *S*-methyldithizone in chloroform gave a permanganate pink colour, with well-defined bands at 270 and 550 nm (ε_{550} 12250 M^{-1} cm^{-1}). On standing in the dark at room temperature the colour changed to yellow and the spectrum showed bands at 280, 420, and 540 nm (ε_{420} 17750 M^{-1} cm^{-1}). The band originally at 550 nm became less intense as the new band appeared at 420 nm. This process was greatly accelerated by traces of acids and alkalis. The isomerisation was found to be reversed on illumination. Analogous effects are found with a number of *S*-alkylated dithizones[30,31] and with many formazans in general,[32-34] where the red forms are converted into yellow isomers on standing or on irradiation of solutions in appropriate solvents.

On the other hand, fresh solutions of the *o*-tolyl homologue of *S*-methyldithizone and *S*-isopropyldithizone (another type of *S*-alkylated dithizone)[29] each gave a yellow colour. The absorption spectrum of a fresh yellow solution of the *o*-tolyl homologue showed a well-defined peak at 423 nm (ε_{423} 29360 M^{-1} cm^{-1}).[27] During several days in the dark the initially yellow solution in chloroform slowly formed a brown equilibrium mixture with a pink isomer having a peak at 560 nm. Exposure of a fresh yellow solution to sunlight for 30 minutes gave the pure pink isomer, while addition of a trace of acetic acid caused an immediate reversion to a red-brown equilibrium mixture. *S*-methyldithizone in the solid form crystallized as *syn, s-trans,* while the *o*-tolyl homologue crystallized in the *anti, s-trans* configuration.[27] The wavelengths of maximum absorption and chemical shifts of the NH protons of some *S*-methylated and the new *S*-ferrocenylated dithizones are summarized in Table 2.3, on the next page. The NH signals of the pink isomers (*syn, s-trans*) are generally observed at *ca.* 10.20 ppm, while the yellow isomers (*anti, s-trans*) show this signal at *ca.* 9.40 ppm.

TABLE 2.3: Molar extinction coefficient , λ_{max} and (in parentheses) ^{1}H chemical shift values of NH resonances at ambient temperature for *S*-alkylated dithizones and the new *S*-ferrocenylated dithizones in chloroform solutions

Compound	λ_{max} /nm (δNH /ppm) Fresh solution	λ_{max} /nm (δNH /ppm) New peak in equilibrium mixture	Extinction coeff.^{a} (M^{-1} cm^{-1})
S-Ferrocenyldithizone (**13**)	410 (9.56)^b	530 (10.21)	20700
S-Ferrocenylmethyldithizone (**14**)	415 (9.36)^b	(10.30)^c	18300
S-Methyldithizone[27]	550 (10.20)	420 (9.46)	17750
S-Methyl-1,5-di(*p*-tolyl)formazan[27]	550 (10.22)	425 (9.43)	14060
S-Methyl-1,5-di(*o*-tolyl)formazan[27]	423 (9.53)	560 (10.28)	29360

^{a}Molar extinction coefficient of fresh chloroform solutions. ^{b}The value represents the more intense signal since both isomers were present in the fresh solution. ^{c}The compound decomposed on irradiation to sunlight.

Cis-trans isomerisation about the –N=N– bond or *syn-anti* isomerisation about the :C=N– bond was thought most likely to be involved.[35] Ignoring all the *cis*-configurations relative to the N=N double bond (which scale models show are unlikely to occur owing to serious steric crowding) leaves four possible isomers which could result from *syn-anti* isomerism about the C=N double bond and isomerisation about the C–N single bond (designated *s-cis* and *s-trans*). As discussed in Chapter 1, the conformational assignments were supported by IR and ^{1}H and ^{13}C NMR spectroscopic studies,[27] which indicated that the yellow isomer has a single *anti*, *s-trans* structure [Figure 1.2 (c)] whereas the pink isomer comprises *syn*, *s-trans* species [Figure 1.2 (a)] in rapid tautomeric equilibrium.

2.5 CONCLUSION

The new photochromic mercury dithizonate compounds (**11**) and (**12**), containing ferrocene as a redox-active substituent, were successfully synthesised. The supporting evidence for their characterisation was obtained from UV-Vis spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry and cyclic voltammetric data. Final purification was difficult to achieve, as observed from the unsatisfactory elemental analyses, though it must be acknowledged that there are often difficulties associated with the elemental analysis of mercury containing compounds. Many attempts were made to grow crystals suitable for X-ray diffraction but these were not successful.

The new analytical reagents **(13)** and **(14)**, i.e., the dithizone derivatives containing ferrocene, were successfully synthesised. The derivative with the ferrocene group bonded directly to sulfur **(13)** was found to exhibit similar isomerisation behaviour to the previously prepared *S*-methyldithizone compounds, while dilute solutions of the dithizone derivative with a methylene group linker **(14)** were found to decompose upon exposure to sunlight. Characterisation was performed by UV-Vis spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, mass spectrometry and cyclic voltammetry. Even after many attempts, crystals suitable for X-ray diffraction were not obtained. However, the crystal structure of the oxidised form **(3)** of *S*-ferrocenyldithizone **(13)** was established and this is discussed in more detail in Chapter 4.

2.6 EXPERIMENTAL

2.6.1 *General*

Melting points were determined on a Kofler hotstage microscope (Reichart-Thermovar) coupled to a digital thermometer. Microanalyses were performed by Mr. Piero Benincasa (University of Cape Town) using a Thermo Flash 1112 Series CHNS-O Analyser. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless otherwise stated using Unity Varian 400 MHz or Varian 300 MHz instruments. UV-visible absorption spectra were obtained at ambient temperature on a Varian Cary 50 Conc UV-Vis spectrophotometer using quartz cuvettes. Mass spectrometry [Fast-atom bombardment (FAB)] was conducted at the University of Witwatersrand Mass Spectrometry Service. Crystallographic data for the compounds were collected at 113 K on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, 54 kV, 22 mA). Data were reduced and scaled using DENZO-SMN software.[36] The structure was solved and refined using the program SHELX97.[37]

Cyclic voltammograms were recorded at room temperature on a BAS 100W Electrochemical Analyzer with a one-compartment three-electrode cell system consisting of a platinum disk working electrode, a platinum wire auxiliary electrode and a $Ag/AgNO_3$ reference electrode (0.01 M $AgNO_3$ and 0.1 M $[n\text{-}Bu_4N][ClO_4]$ in anhydrous acetonitrile). An IR compensation circuit was used for all measurements. A scan rate of 100 mV s^{-1} was used throughout, beginning from the most negative potential and initially scanning in the anodic direction. The half-wave potential of the ferrocene/ferrocenium couple in this cell has never varied by more than 30 mV from a mean value of $E_{1/2} = 85$ mV versus the $Ag/AgNO_3$ reference electrode, with a peak separation falling between $\Delta E_p = 59$ and $\Delta E_p = 66$ mV. Solutions were purged with argon and voltammograms were recorded under a blanket of argon. The platinum disk working electrode was polished between runs. For compound **(13)** and **(14)** cyclic voltammograms were recorded in acetonitrile, while for Compound **(11)** and **(12)** the voltammograms were recorded in dichloromethane solutions (the half-wave potential of the ferrocene/ferrocenium couple in this cell has never varied by more than 30 mV from a mean value of $E_{1/2} = 191$ mV versus the $Ag/AgNO_3$ reference electrode).

All chromatographic columns were packed with Merck 0.063 – 0.200 mm silica gel or 0.063 – 0.200 mm alumina (neutral). TLC was performed on Merck silica gel 60 F_{254} Aluminium-backed TLC plates. All reagents were purchased from Sigma-Aldrich Co, with the exception of silver dithizonate which was available in the laboratory from a previous preparation. All reaction solvents were AR grade, purchased from Kimix Chemicals. Standard drying procedures were followed in cases where dry solvent was required.

2.6.2 *Preparative work*

Experimental details for the syntheses of compounds reported in this dissertation are given in order of compound number. Full characterising data are given at the end of the preparation method of each compound.

(N,S-Dithizonato)(ferrocenyl)mercury(II) (**11**)

Chlorido(ferrocenyl)mercury(II) (**15**, 0.30 g, 0.71 mmol) was dissolved in dichloromethane (50 cm^3) and to this solution dithizone (0.18 g, 0.71 mmol) was added as a single portion of the solid. Triethylamine (0.5 cm^3) was added and the solution changed colour from green to clear red. The mixture was stirred for 15 min. The solvent was removed under reduced pressure, then the residue was subjected to column chromatography on silica eluting with carbon tetrachloride to remove a yellow band, followed by benzene to collect the product. The product was obtained as a red solid (0.32 g, 70%) after removing the solvent under reduced pressure and the melting point was found to be 168 – 170 °C.

^{1}H NMR (CDCl$_3$) δ_H: 4.11 (2H^3, t, J = 1.83, 1.47 Hz), 4.46 (2H^2, t, J = 1.83, 1.47 Hz), 4.20 (5H, s), 7.56 (10H, m) and 9.33 ppm (br. NH). ^{13}C NMR (CDCl$_3$) δ_C: 68.52 (C^2), 69.99 (C^3), 72.93 (5C), 115.31, 122.89, 123.71, 129.39, 129.53, 130.89, 142.11 (C^4 – C^{11}) and 150.54 ppm (C^{12}). Mass spectrometry *m/z*: 120, 500, and 577. Elemental analysis for $C_{23}H_{20}FeHgN_4S$ [found (calculated)]: C 43.42 (43.10), H 3.10 (3.15), N 14.59 (8.74) and S 8.74 (5.00). (best of several analyses).

(Ferrocene-1,1'-diyl)bis[(N,S-dithizonato)mercury(II)] (**12**)

The purified reagent (ferrocene-1,1'-diyl)bis[chloridomercury(II)] (**16**, 0.10 g, 0.09 mmol) was suspended in dichloromethane (50 cm^3) and to this mixture dithizone (0.05 g, 0.18 mmol) was added as a single portion of the solid. Triethylamine (0.5 cm^3) was added and the solution changed colour from green to clear red. The mixture was stirred for 30 min. The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica eluting with benzene. The product was isolated as dark red solid after evaporation of the solvent (0.13 g, 75%) and the melting point was found to be 175 – 180 °C.

^{1}H NMR (CDCl$_3$) δ_H: 4.14 (2H^3, t, J =1.83, 1.47 Hz), 4.18 (5H, s), 4.20 (2H^2, t, J = 1.83, 1.47 Hz), 4.47 (m), 7.42 (20H), 9.30 ppm (br. NH). ^{13}C NMR (CDCl$_3$) δ_C: 68.35 (C^2), 69.98 (C^3), 123.66, 129.04, 129.37, 129.51, 130.85, 142.14 ppm (C^4 – C^{11} and C^{13} – C^{20}).

Mass spectrometry *m/z*: 120, 500 and 577. Elemental analysis for $C_{36}H_{30}FeHg_2N_8S_2$ [found (calculated)]: C 42.78 (37.54), H 3.30 (2.63), N 11.64 (9.73) and S 6.56 (5.57) (best of several analyses).

S-*Ferrocenyldithizone* (**13**)[12]

A Schlenk tube containing iodoferrocene (**17**, 200 mg, 0.6 mmol), CuI (10 mg, 0.53 mmol) and K_2CO_3 (207 mg, 1.50 mmol) was evacuated and flushed with argon (3 cycles), then isopropanol (1 cm^3) and ethylene glycol (0.5 cm^3) were added through a septum using a syringe. The tube was heated at 80 °C for 80 h and monitored by TLC. When the reaction was over (after 80 h), ethyl acetate (5 cm^3) was added. The mixture was then filtered. The solvent was removed and the remaining material was subjected to column chromatography (silica) eluting with chloroform. The main red-brown band was collected and after removal of the solvent an oil was obtained. The crude product was subjected to flash chromatography (alumina) eluting with benzene. Recrystallization of the oily material from various solvent systems (i.e. dichloromethane-hexane) or triturating from methanol to give a solid product was unsuccessful. The product was isolated as a red-brown solid (0.13 g, 49%) after evaporation of the solvent under reduced pressure and the melting point was found to be 163 – 166 °C.

^{1}H NMR ($CDCl_3$) δ_H: 4.22 (2H^3, t, J = 2.20 Hz), 4.28 (5H, s), 4.31, 4.46 (2H^2, t , J = 1.83 Hz), 7.48 (10H, m), 9.50 (NH) and 10.21 (NH*). ^{13}C NMR ($CDCl_3$) δ_C: 69.96 (5C), 73.87 (C^2), 74.97 (C^3), 110.83, 114.61, 122.79, 126.75, 129.02, 129. 28, 129.45, 130.70, 142.08, 145.66 (C^5 – C^{12}) and 147. 78 ppm (C^{13}). Mass spectrometry *m/z*: 440 and 217. Elemental analysis for $C_{23}H_{20}FeN_4S$ [found (calculated)]: C 63.10 (62.74), H 4.60 (4.58), N 12.26 (12.72) and S 6.57 (7.28).

S-*Ferrocenylmethyldithizone* (**14**)

A mixture of 10% mole excess of (ferrocenylmethyl)trimethylammonium iodide (**18**, 200 mg, 0.44 mmol) and silver dithizonate (135 mg, 0.35 mmol) in chloroform (100 cm^3) was boiled under reflux for 5 h. A precipitate of silver iodide was noticed within 5 min of the start of the reaction. After the mixture had been cooled, chloroform (25 cm^3) was added. The reaction mixture was then filtered under vacuum and washed with 10% aqueous $Na_2S_2O_3$ solution to remove silver iodide, followed by water. The organic layer was dried with sodium sulfate. The solvent was removed under reduced pressure and the residue subjected to flash chromatography (silica, benzene), collecting the main red-brown band. Recrystallization of the oily product from different solvent systems was unsuccessful. The product was then purified by flash chromatography (10 cm long, 2 cm diameter, alumina, benzene). After removal of the solvent, *S*-ferrocenylmethyldithizone (**14**), (0.18 g, 75%) was obtained as oil which solidified on standing in vacuum for several days. The melting point of the product was found to be 60 – 64 °C.

^{1}H NMR ($CDCl_3$) δ_H: 4.04 (2H^3, t, J = 1.47 Hz), 4.07 (5H, s), 4.19 (2H^2, t, J = 1.47 Hz), 3.86 (CH_2), 7.54 (10H, m), 9.36 (NH) and 10.30 ppm (NH*).^{13}C NMR ($CDCl_3$) δ_C: 68.73 (5C); 68.55 (C^3), 68.24 (C^2) 33.80 (CH_2), 130.62, 129.36, 129.32, 129.05, 123.05, 122.93, 118.40, 114.92 (C^5 - C^{12}) and 152.49 ppm (C^{13}). Mass spectrometry *m/z*: 454, 198.9 and 255.1. Elemental analysis for $C_{24}H_{22}FeN_4S$ [found (calculated)]: C, 63.72 (63.44), H 4.89 (4.88), N 10.80 (12.33) and S 6.60 (7.06).

Chlorido(ferrocenyl)mercury(II) (**15**)[4-6]

A solution of mercury (II) acetate (10.52 g, 33.0 mmol) in methanol (90 cm^3) was added to a solution of ferrocene (12.50 g, 33.0 mmol) in benzene (60 cm^3). The reaction mixture was stirred under nitrogen at room temperature for 10 h. A solution of lithium chloride (2.96 g, 70 mmol) in ethanol-water (1 : 1, 10 cm^3) was added slowly to the reaction mixture, changing it from dark brown to light orange. The reaction mixture was stirred for 2 h at room temperature and an orange suspension was observed. The reaction mixture was set to reflux for an hour, followed by filtration of the crude product under vacuum. The solid obtained was purified by Soxhlet extraction with dichloromethane, followed by sublimation to remove unreacted ferrocene. The Soxhlet thimble residue was composed of the 1,1'-dimercurated product (**16**) and other impurities. Recrystallization of the unsublimed portion from dichloromethane-hexane yielded the product as fine golden

crystalline cubes (5.80 g, 42%). The melting point of the product was found to be 194 –196 °C dec. (lit.[4-6] m.p. 194 – 198 °C dec.)
^{1}H NMR ($CDCl_3$) δ_H: 4.47 ($2H^2$, t, J = 1.7 Hz), 4.23 (5H) and 4.11 ppm ($2H^3$, t, J = 1.7 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 73.01 (C^3), 70.38 (C^2) and 68.98 ppm (5C).

(Ferrocene-1,1′-diyl)bis[chloridomercury(II)] **(16)**[4-6]

(Ferrocene-1,1′-diyl)bis[chloridomercury(II)] was formed during the preparation of chlorido(ferrocenyl)mercury(II) **(15)**, as above. During the Soxhlet extraction of compound **(15)** with dichloromethane, product **(16)** is left as a residue in the Soxhlet thimble since it is insoluble in this solvent. Recrystallization of the product from dimethylformamide or dimethylsulfoxide was unsuccessful since the product would not precipitate from the solution. The product was purified by washing the crude material with copious amount of water to remove inorganic impurities, then with methanol, followed by diethyl ether. The product was obtained as a yellow powder (6.50 g, 30%) and the melting point was found to be 300 °C dec. (lit.[4-6] m.p. 300 °C dec.)
^{1}H NMR δ_H (DMSO-d^6): 4.16, 4.26, 4.36 and 4.40 ppm. ^{13}C NMR (DMSO-d^6) δ_C: 67.97, 69.44, 73.21 and 73.90 ppm.

Iodoferrocene **(17)**

Method one[20]

A solution of iodine (2.26 g, 17.80 mmol) in dichloromethane (100 cm^3) was added slowly to a solution of chlorido(ferrocenyl)mercury(II) (**15**, 2.50 g, 5.94 mmol) in dichloromethane (200 cm^3) at room temperature under nitrogen. The reaction mixture was stirred for several days, concentrated under reduced pressure and subjected to flash chromatography, eluting with petroleum ether (40 – 60 °C). The eluant was washed with an aqueous solution of sodium thiosulfate (10%) followed by water. The organic fractions were collected and dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The residue obtained was subjected to column chromatography on silica, eluting with petroleum ether (40 – 60 °C). The product was obtained as yellow crystals (0.92 g, 50 %). The melting point of the product was found to be 43 – 45 °C (lit.[20] m.p. 44 – 45 °C).

^{1}H NMR ($CDCl_3$) δ_H: 4.35 (2H^2, t, J = 1.83 Hz), 4.12 (5H, s) and 4.09 ppm (2H^3, t, J = 1.83 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 74.85 (C^3), 71.42 (5C) and 69.20 ppm (C^2). Spectral data were the same for compounds obtained using all three different methods.

Method two[21]

This is a modified version of the above method used by Imrie and co-workers.[21] Chlorido(ferrocenyl)mercury(II) (**15**, 1.50 g, 4 mmol) was stirred with iodine (2.54 g, 10 mmol) in anhydrous dichloromethane (75 cm^3) for 1 h under nitrogen. A spatula tip of ascorbic acid was then added and the mixture was stirred for another hour; after this time the mixture was thoroughly washed with water. The organic layer was washed successively with a 10% sodium thiosulfate solution and water prior to drying over anhydrous sodium sulfate. The solvent was removed and the organic residue subjected to flash chromatography on silica, eluting with petroleum ether. A single yellow fraction was eluted and the solvent was removed under reduced pressure. The remaining orange oil solidified to give an orange crystalline material upon placing in the fridge (0.75 g, 60%). The melting point of the product was found to be 43 – 45 °C (lit.[20] m.p. 44 – 45 °C).

Method three[4]

A solution of *N*-iodosuccinimide (1.20 g, 5.10 mmol) in dry dichloromethane (100 cm^3) previously flushed with nitrogen was added dropwise to a stirred suspension of chlorido(ferrocenyl)mercury(II) (**15**, 2.10 g, 5.00 mmol) in dichloromethane (75 cm^3) cooled in an ice bath and maintained in a nitrogen atmosphere. After allowing the reaction to continue for 12 h, 10% aqueous sodium metabisulfite solution (50 cm^3) was added, followed by an equal volume of a 10% sodium carbonate solution. The organic layer was separated and the aqueous portion was extracted with dichloromethane. The combined organic extract was washed successively with 10% sodium carbonate solution followed by water, and dried over magnesium sulfate. Removal of the solvent left an oil which was taken up in small amount of petroleum ether and purified by flash chromatography on alumina. After removal of the solvent from the first band, iodoferrocene (**17**) was obtained as an oil which crystallised after some hours at *ca.* -15 °C, (1.00 g, 70%). The melting point was found to be 43 – 45 °C (lit.[20] m.p. 44 – 45 °C).

(Ferrocenylmethyl)trimethylammonium iodide (**18**)[18]

A solution of 40% aqueous dimethylamine (27 cm^3) was added to an ice-cold stirred solution of 37% aqueous formaldehyde (10.00 g, 0.12 mol). The solution was maintained at a temperature below 15 °C. After stirring for 30 min solid potassium hydroxide was added until two layers separated. The upper layer was removed and dried over solid potassium hydroxide. The mixture was filtered and the product was purified by distillation to give *N,N,N',N'*-tetramethyldiaminomethane (2.62 g, 21%). The boiling point of the product was found to be 81– 83 °C (lit.[24] b.p. 82 – 84 °C).

A mixture of *N,N,N',N'*-tetramethyldiaminomethane (2.62 g, 0.03 mol), paraformaldehyde (0.95 g, 0.30 mol) and acetic acid (24.00 g, 0.40 mol) was heated for a few minutes until solution occurred, and ferrocene (11.16 g, 0.06 mol) was added with stirring. This mixture was stirred and heated under reflux for 5 h. All of the ferrocene dissolved within about 1 h. The solution was cooled slightly and water (15 cm^3) was added with stirring. The resulting mixture was filtered and the solid was washed with dilute acetic acid followed by water. This solid consisted largely of unreacted ferrocene. The clear filtrate and washings were chilled in an ice bath and made strongly alkaline with 50% NaOH solution (50 cm^3). The resulting mixture was extracted three times with ether and the combined extract was washed with water. The ethereal solution was dried over magnesium sulfate and the solvent was removed after filtering. The residue was distilled under reduced pressure to give *N,N*-dimethylaminoferrocene (1.23 g, 20%) as an orange oil. The boiling point of the product was found to be 91 °C (lit.[18] b.p. 91 – 92 °C, 0.40 mmHg at 25 °C).

A solution of iodomethane (1.06 g, 7.50 mmol) in absolute methanol (1 cm^3) was added dropwise to a cooled solution of *N,N*-dimethylaminoferrocene (1.23 g, 5.00 mmol) in an equal volume of absolute methanol. The clear solution was boiled under reflux for 5 min, and after cooling diethyl ether (15 cm^3) was added. The resulting precipitate of the quaternary salt (**18**) was collected on a funnel and washed with ether until the washings were colourless. The product was obtained as yellow micro-crystals (1.50 g, 78%) and the melting point was found to be 220 °C (lit.[18] m.p. 220 °C).

^1H NMR ($CDCl_3$) δ_H: 4.32 ($2H^3$, t, J = 1.83 Hz), 4.57 ($2H^2$, t, J = 1.83 Hz), 4.29 (5H), 4.90 (CH_2) and 3.24 ppm (9H, s). ^{13}C NMR ($CDCl_3$) δ_C: 52.74 (3 x CH_3), 67.29 (CH_2), 69.65 (5C), 70.72 (C^2) and 72.24 ppm (C^3).

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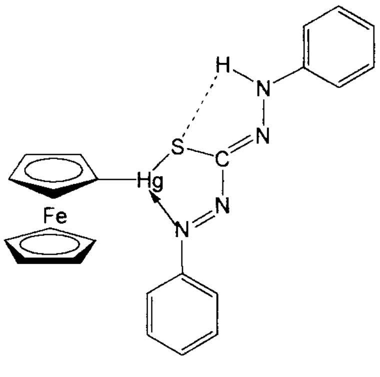
CHAPTER 3

PHOTOCHROMIC AND REDOX PROPERTIES OF FERROCENYLMERCURY(II) DITHIZONATE COMPLEXES

3.1 INTRODUCTION

The photochromic properties and applications of some mercury dithizonate complexes were discussed in Chapter 1. It was mentioned that in a range of photochromic compounds known in the literature, i.e. R-HgHDz, there are no compounds reported in which the substituent group R is a redox-active group. In this work new photochromic compounds **(11)** and **(12)** containing ferrocene as a redox-active substituent group were prepared using the methods established and discussed in Chapter 2. Compounds containing both photochromic and redox-active groups in one molecule have been found to have potential applications as molecular switches and in memory devices.[1-3] Of interest is the possibility of communication between these groups, i.e. whether the electrochemistry of the redox-active group is affected by a change in conformation of the photochromic ligand upon irradiation of a solution of the compound or, conversely, whether the change in conformation of the photochromic group is affected by a variation of the electrochemical properties of the redox-active group.



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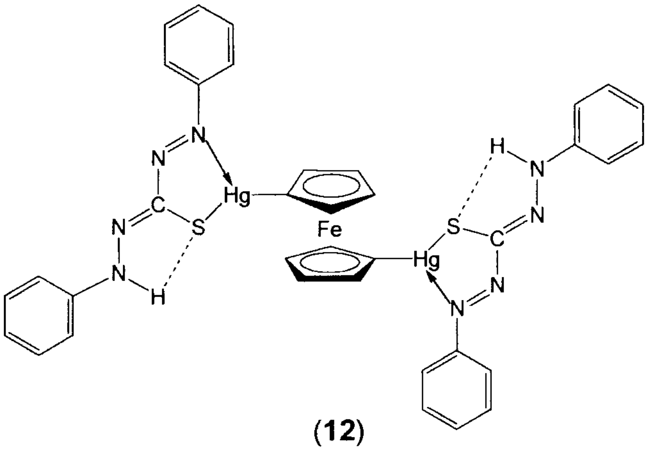


(12)

The new compounds were found to be photochromic in organic solvents such as benzene, dichloromethane and toluene. Previous studies on mercury(II) dithizonate complexes[4] have shown that the photochromism is affected by factors such as traces of moisture and acids, so solvents were carefully dried before use. Chloroform was chosen as a suitable solvent since the photochromism in this solvent was slow enough for studies to be conducted. The photochromism of these new compounds in dry chloroform solutions was investigated using UV-Vis spectroscopy and the molar extinction coefficients were calculated and compared to other mercury(II) dithizonates. The spectrophotometric results are discussed in Section 3.2. The interaction between the photochromic and redox properties was investigated by cyclic voltammetry using dichloromethane solutions. In a specific experiment the voltammogram of an orange solution of the unexcited form was firstly recorded, followed by excitation of this solution to the blue form by irradiation with sunlight, and the voltammogram was again recorded. The solution was put in the dark for the reverse reaction to take place (to the orange form). During this time voltammograms were repeatedly recorded (one per minute). The results of these experiments will be discussed in Section 3.3.

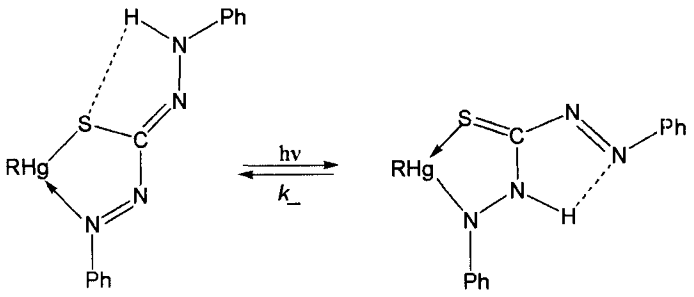
It has been shown that irradiation by visible light of solutions of mercury(II) bis(dithizonate) [$Hg(HDz)_2$; (**6a**, R = HDz)] in organic solvents induces a colour change from yellow to blue.[4] Researchers extended this study and investigated other primary metal dithizonates, e.g. $Pt(HDz)_2$, $Pd(HDz)_2$, etc., but the reverse reaction was generally too rapid to allow visual observation of a colour change.[4] The rate of return to the normal colour depended on the metal, with half-lives varying from about 30 seconds for the mercury complex at room temperature to less than 1 second for other heavy metals, even when solutions were cooled to -80 °C. It was found that at high levels of illumination at 24 °C a steady state could be reached, with 80 – 90% of a solution of $Hg(HDz)_2$ in benzene in the activated form. The strongest photochromic effects were found with dry, non-polar solvents such as benzene, toluene, carbon tetrachloride or chloroform and hydroxylic solvents were notable for their effect in acceleration of the back-reaction.

Studies on various organomercury(II) dithizonates showed that these compounds were photochromic in the same way as mercury(II) bis(dithizonate).[5-9] These compounds show only half the value of the molar extinction coefficient of the parent mercury(II) bis(dithizonate) complex since there is only one chromophore absorbing. When following changes in the IR spectra of solutions in CCl_4 during irradiation by white light, the shift of the N–H stretching mode to higher frequencies in the activated blue form indicated formation of a weaker hydrogen bond.[4] The weakening of the hydrogen bond as was observed from the IR spectra of organomercury(II) dithizonates was illustrated by a shift of the ν(N–H) band produced by irradiation and consequent photoisomerisation from 66 to 71 cm^{-1} in the organomercury(II) dithizonates and to 69 cm^{-1} in $Hg(HDz)_2$, the shift being to higher wave-number in all cases. This was consistent with the formation of an N–H···N hydrogen bond which is weaker because of the lower basicity of the azo nitrogen (see Figure 3.1 on the next page).[7]

^1H NMR spectra of the stable yellow forms of dithizonate or dithizonate derivatives (with various aliphatic substituents on the phenyl ring), all of which contained methylmercury, showed the methyl singlet at δ 1.10.[7] Irradiation by an intense beam of visible light using glass-fibre optics enabled the spectra of the blue photo-isomers to be recorded and a downfield shift of the $HgCH_3$ resonance by 0.16 ppm was observed, indicating a change in the character of the ligand donor atoms. This showed that the change in conformation of the ligand influences the chemical environment of the methyl substituent group on mercury. However, the protons of methyl groups attached to either arylmercury or dithizonate aromatic rings were not affected by irradiation of solutions, and it was assumed that any changes were too small to be resolved. In all the organomercury dithizonate complexes that have been studied the formation of a different hydrogen bond in the activated form was clearly seen in the disappearance of the N*H* resonance of the original orange form at about δ 9.2 (S···H–N) and its appearance at about δ 10.5 ppm (N–H···N) in the activated form.[7]

The return rate was studied spectrophotometrically by observing the replacement of the band due to the activated form (ε_{604} = 39000 M^{-1} cm^{-1}) by that of the normal form (ε_{485} = 70000 M^{-1} cm^{-1}) in the mercury(II) bis(dithizonate) complex, and pseudo-first-order kinetics were observed.[10] From the results obtained Meriwether *et al.*[10] eliminated a number of possible structures for the activated complex, and proposed the reaction scheme as **(6a)** $\rightleftharpoons$ **(6b)** (Figure 3.1). There was a small hypsochromic shift in the visible spectra of the normal yellow organomercury(II) dithizonate complexes (λ_{max} between 470 and 480 nm) when compared to the absorption of $Hg(HDz)_2$ (at 485 nm) in chloroform solutions. ^1H NMR, visible and IR spectral data and structures determined crystallographically for organomercury(II) compounds (one example is shown in Chapter 1, Figure 1.4)[11] provided evidence in support of

Meriwether's proposed scheme for the photochromic reaction (**6a**) $\rightleftharpoons$ (**6b**).[10] However, numerous attempts to isolate the blue solid so that the structure of the excited photo-isomer could be solved crystallographically were unsuccessful.



(**6a**) yellow

(**6b**) blue

(**11**) (*N*,*S*-Dithizonato)(ferrocenyl)mercury(II) : R = Fc
(**12**) (Ferrocene-1,1'-diyl)bis[(*N*,*S*-dithizonato)mercury(II)] : R = Fc{Hg(HDz)}

FIGURE 3.1: Mercury(II) dithizonate complexes containing the ferrocenyl substituent prepared in this work. In compound (**12**) the mercury(II) dithizonate groups are bonded to the two different cyclopentadienyl rings of ferrocene [see structure (**12**)]

3.2 PHOTOCHROMISM STUDIES BY UV-Vis SPECTROSCOPY

Photochromism studies on dilute (*ca.* 0.01 mM) dry chloroform solutions of the new mercury dithizonate complexes containing the redox-active ferrocenyl substituent were performed using UV-Vis spectroscopy. The visible absorption data are summarized in Table 3.1. The UV-Vis spectra of the new compounds were recorded immediately after preparation of solutions of suitable concentration.

TABLE 3.1: UV-Vis data obtained for mercury dithizonate complexes with ferrocenyl substituents

Compound	λ_{max}/nm **orange form** (ε_{max}/M^{-1} cm^{-1})	λ_{max}/nm **blue form**	Isosbestic point/nm
FcHg(HDz) (**11**)	485 (29400)	595	535
Fc{Hg(HDz)}$_2$ (**12**)	485 (63400)	595	535

The maximum of the absorption band of the orange form of compound (**11**) was found to be at 485 nm with molar extinction coefficient of $\varepsilon_{485} = 29400\ M^{-1}\ cm^{-1}$. The orange form of compound (**12**) with a mercury dithizonate moiety on each of cyclopentadienyl ring was found to have an absorption maximum at 485 nm with molar extinction coefficient of $\varepsilon_{485} = 63400\ M^{-1}\ cm^{-1}$, almost double that of compound (**11**). This was expected since there were two chromophores absorbing. This absorption maximum was at the same wavelength as that of $Hg(HDz)_2$. Most organomercury(II) dithizonate complexes showed a maximum absorbance of the orange form between 460 and 480 nm compared to mercury(II) bis(dithizonate), which has a maximum absorption at 485 nm.[11] The shift to shorter wavelengths in the substituted organomercury dithizonates is most likely a result of electronic effects transmitted from one side of the mercury ion to the other.

Excitation of the orange to the blue form was performed by irradiation with sunlight and quickly placing the cuvette in the spectrophotometer for analysis. This method made it difficult to obtain the spectrum of the completely converted blue form. In most attempts only 50% of conversion to the blue form was obtained, as can be seen in the UV-vis spectra shown in Figures 3.2 and 3.3 for compounds (**11**) and (**12**), respectively.

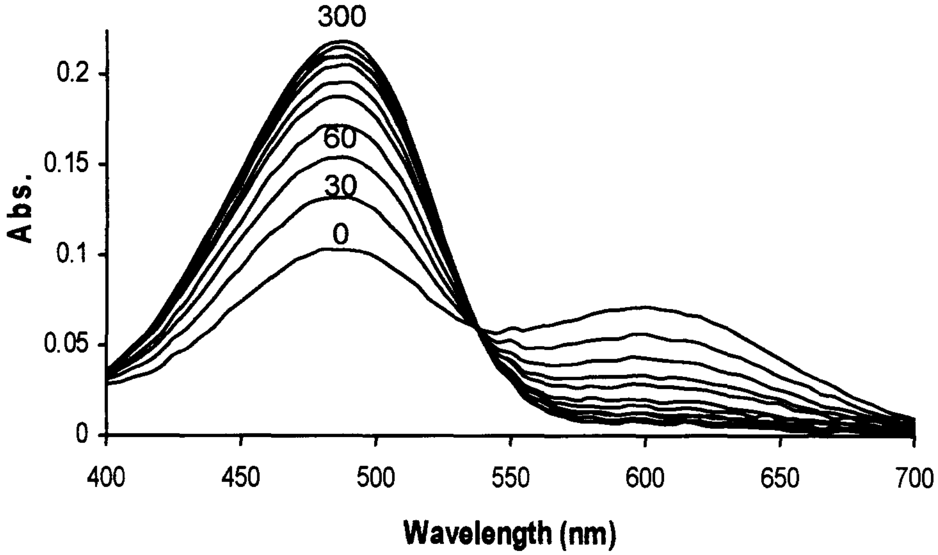


FIGURE 3.2: Visible spectra of return reaction of 7.40 μM FcHg(HDz) (**11**) after irradiation of solutions in dry chloroform. The numbers indicate sequential scans at 30 s intervals.

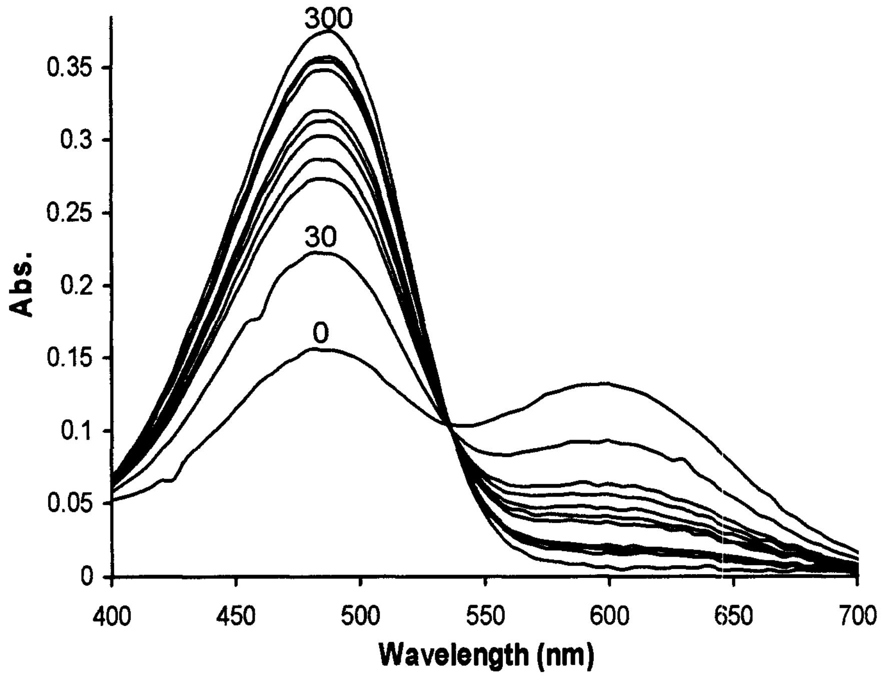


FIGURE 3.3: Visible spectra of return reaction of 5.90 μM Fc{Hg(HDz)}$_2$ (**12**) after irradiation of solutions in dry chloroform. The numbers indicate sequential scans at 30 s intervals.

The λ_{max} for the excited form was found to be at 595 nm for both compounds. This is similar to mercury bis(dithizonate) and compares with other mercury(II) dithizonate complexes, which have been found to have a maximum absorption band in the range 604 – 611 nm. Most organic compounds with this chromophore in a conjugated system have visible absorption bands in this region (580 – 605 nm). The single absorption band of the excited form suggests that the two chromophores in compound (**12**) are acting independently of each other. The visible absorption curves were found to exhibit a very well-defined isosbestic point at 535 nm (comparable to other mercury(II) dithizonate complexes),[5-7] which confirmed that there were only two species involved in the orange $\rightleftharpoons$ blue equilibrium, (unless there were another species with the same ε_{535}, which is very unlikely).

3.3 INTERACTIONS BETWEEN PHOTOCHROMIC AND REDOX PROPERTIES INVESTIGATED BY CYCLIC VOLTAMMETRY

Solutions of compounds (**11**) or (**12**) were prepared in dichloromethane containing tetrabutylammonium perchlorate (TBAP) as a supporting electrolyte. Dichloromethane was chosen as a suitable solvent for voltammetric studies. Test experiments performed on each of the dilute orange solutions showed activation to the blue form proving that the supporting electrolyte salt did not affect the photochromism. Voltammograms of the original yellow forms of the two compounds are shown in Figure 3.4, where only the ferrocenyl wave is considered. Half-wave potential values of $E_{1/2}$ = 212 or 204 mV for ferrocenylmercury dithizonate compounds **(11)** or **(12)**, respectively, showed that the ferrocenyl substituent in each compound was slightly more difficult to oxidise than ferrocene itself, which had a half-wave potential of $E_{1/2}$ = 191 mV. Electrons were withdrawn away from the iron centre in compound **(11)** more than in compound **(12)**, and the effect of mercury substitution is surprisingly small. The ΔE_p values of 73 and 78 mV for the ferrocenyl substituent in compounds **(11)** and **(12)**, respectively, compared to that of ferrocene itself (which had ΔE_p = 68 mV) showed that the redox waves were quasi-reversible and one electron transfer was involved in the oxidation-reduction process.

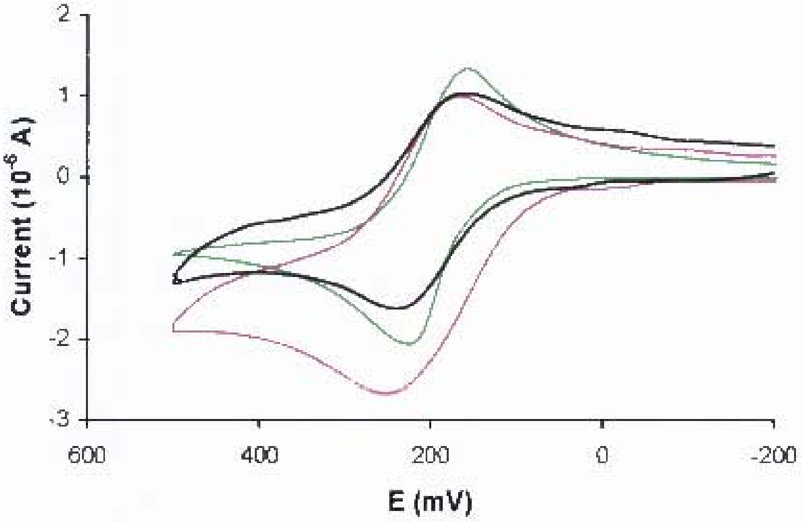


FIGURE 3.4: Voltammograms of 1 mM dichloromethane solutions of (–) FcHg(HDz) **(11)**, (–) Fc{Hg(HDz)}$_2$ **(12)** and (–) ferrocene as a reference.

The solutions of the orange forms were irradiated with sunlight to activate the compounds to the blue form. During this time the colour of the solutions darkened and voltammograms were recorded. No changes in half-wave potential of the ferrocenyl substituent of either compound were observed. Various scan rates and sensitivities were used to detect any changes in the voltammograms, but no changes were observed. A minimum concentration of 1 mM in sample was found to be enough for obtaining a good voltammogram. Unfortunately, this was 100 times more concentrated compared to dilute concentrations of *ca.* 0.01 mM in which conversion of up to 90% of blue form has been obtained.[11h] This was confirmed from the colour change of the solution which turned from orange to grey, suggesting that there was a mixture of blue and orange forms in solution. Different factors may be suggested to explain why the voltammograms were the same after irradiation of solutions with sunlight; activation to the blue form might have not been effective enough, making the concentration of the compound in the activated form too small to be detected. It is also possible that the change in conformation of the dithizone group did not influence the iron centre significantly enough for a change to take place or be resolved (i.e. change in conformation of dithizonate group does not withdraw or donate electrons to the iron centre).

It was mentioned earlier that the protons of the yellow form of methylmercury(II) dithizonate in the ^{1}H NMR spectra showed that a change in conformation of the dithizonate group upon irradiation by an intense beam of visible light changes the chemical environment of the methyl substituent.[7] This was observed from a downfield shift of the HgCH_3 resonance (which was originally at δ 1.10 in the orange form) by 0.16 ppm, which showed that electrons were withdrawn from the methyl substituent through the mercury ion, thereby de-shielding the protons. These shifts were not observed for the methyl protons of the methyl substituents on the phenyl groups of dithizone or phenylmercury(II) dithizonate complexes. There is a correlation between NMR and electrochemical data in most ferrocenyl derivatives.[12-14] Derivatives in which substituents on a Cp ring of ferrocene make the protons at the α-position resonate downfield (compared to the protons in ferrocene which resonate at δ 4.19 ppm) have higher oxidation potentials than ferrocene itself. Lower oxidation potentials has been observed in ferrocene derivatives with donor substituents.[12-14] From these discussions it can be suggested that the change in conformation might influence the electrochemistry of the iron centre. However, these influences may not have been sufficient to significantly affect the half-wave potential of iron in the ferrocenyl substituents of compounds **(11)** and **(12)** investigated in this work.

3.4 CONCLUSIONS

The new mercury(II) dithizonate compounds prepared in this work were found to be photochromic in various non-polar organic solvents. The data obtained from UV-visible spectroscopy for compounds **(11)** and **(12)** were found to be similar to the spectral data that have been obtained for other known mercury(II) dithizonate complexes. There were no interactions observed between the photochromic and redox properties in either compound, as evidenced from the cyclic voltammetric results.

Other possible investigations for this potential interaction that could be pursued would be the preparation of mercury(II) dithizonate complexes with ferrocenyl substituent on mercury and on one of phenyl group of dithizone. The interaction between these two redox-active substituents could be investigated in different photo-isomers of the resulting compound. Mercury(II) dithizonate complexes with ferrocenyl substituents on both phenyl rings of dithizone could also be interesting to investigate; conjugation in the thiocarbazone ring will allow through-bond interaction between redox-active substituents which may be either weaker or stronger in the blue or orange forms. Through-space interactions between substituents will also be different in the orange or blue forms; there should be a shorter distance between the iron centres in the blue compared to the orange form of the resulting mercury(II) dithizonate compounds. These varying distances could result in different electrochemical interactions between the iron centres.

3.5 EXPERIMENTAL

All experimental details for solvents, conditions, and instrumental methods for UV-Vis spectroscopy and cyclic voltammetry were similar to those already described in Chapter 2, Section 2.6.1 and are not repeated here.

3.5.1 *UV-Vis spectroscopy*

The concentration of the compounds was 0.01 mM in dry chloroform. The UV-Vis spectrum of the original orange forms were recorded first, then the compounds were activated by irradiation with sunlight to give the blue forms. The cuvette was immediately placed in the instrument and the spectra were recorded at 30 second intervals until the solution was composed of the orange form only.

3.5.2 *Cyclic voltammetry*

All voltammograms were recorded under blanket of argon. The concentration of compounds was 1 mM in dry dichloromethane (10 cm^3) containing tetrabutylammonium perchlorate (0.10 M) as a supporting electrolyte. A voltammogram of the compound in the stable orange form was recorded first, scanning anodically from most negative potential. The solution was then activated to the blue form by irradiation with sunlight and voltammograms were repeatedly recorded using various scan rates (20 mV s^{-1} – 500 mV s^{-1}) and sensitivities. The solutions were covered with a dark material for the reverse reaction to take place and the voltammograms were again recorded.

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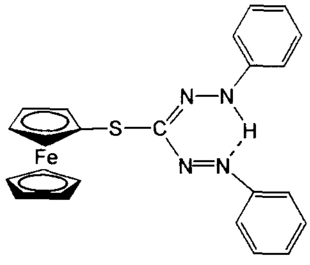
CHAPTER 4

ELECTROCHEMICAL RECOGNITION OF TRANSITION AND ORGANOTRANSITION METAL IONS

4.1 INTRODUCTION

The properties of a sensor molecule required for applications in electrochemical recognition of metal ion guests, and those of dithizone as a good metal chelating ligand, have been pointed out in Chapter 1. New analytical reagents *S*-ferrocenyl- (**13**) and *S*-ferrocenylmethyl-dithizone (**14**), which contain the dithizone moiety as a binding site and ferrocene as a redox-active group, were prepared by the methods discussed in Chapter 2. The suitability of these reagents for electrochemical recognition of metal and organotransition metal ions was investigated in acetonitrile solutions by cyclic voltammetry (see Sections 4.2 and 4.3). The ferrocene/ferrocenium redox couple was monitored during titration with different metal ions. All the redox waves reported in this work apply to this redox couple. The metal ion salts investigated in this work were chosen primarily because of their availability and solubility in acetonitrile, as well as for their importance as possible environmental contaminants. Receptor–metal interactions were also investigated by UV-Vis spectroscopy (see Section 4.4). Attempts to synthesize solid metal complexes were performed in order to elucidate the active binding sites and the modes of coordination of the ligands to metal ions (see Section 4.5).



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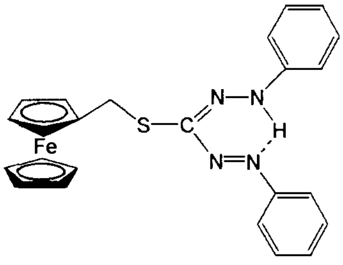

(14)

4.2 ELECTROCHEMICAL RECOGNITION EXPERIMENTS WITH RECEPTOR (13)

The voltammogram of a 1 mM solution of the free analytical reagent (**13**) in acetonitrile solution (see Figure 4.1 on the next page) showed a reversible wave with $E_{1/2}$ = 118 mV relative to ferrocene itself as a standard reference. Upon titration with metal ions a new reversible peak appeared at higher oxidation potential. For example, during titration with Cu^{2+} or $PhHg^{+}$ ions a new reversible wave appeared at higher oxidation potential with maximum potential shifts of $\Delta E_{1/2}$ = 184 or 177 mV, respectively, compared to the original receptor wave. The results for the metal ions investigated in this work are summarised in Table 4.1. The appearance of the new reversible peak during titration was found to be dependent on the metal salt investigated. In general, no signal was observed when the titration was performed with R-MCl or MCl_2 salts. This might have been because of the slow reactivity of these metal salts with receptor (**13**).

TABLE 4.1 Electrochemical shifts (mV, vs. Ag/Ag^{+}) of the ferrocenyl redox couple of compound (**13**) in acetonitrile solution on addition of metal ion salts[a]

Compound	$E_{1/2}$ (mV)	$\Delta E_{1/2}$ (mV)[b]	Addition of HBF_4 ($E_{1/2}$, mV)
(**13**)	203		304
(**13**) + PhHg(OAc)	380	+177	369
(**13**) + MeHg(OAc)	385	+182	-[c]
(**13**) + $Cu(ClO_4)_2$	387	+184	367
(**13**) + $Ni(X)_2$[d]	203	0[e]	-[c]

[a] $E_{1/2}$ for ferrocene itself as a standard reference under the same conditions was 85 mV. Data are accurate to ±5 mV. [b] Maximum potential shift of receptor (**13**)–metal ion interaction. [c] Not investigated. [d] Various nickel ion salts were investigated, X = BF_4^-, ClO_4^- and NO_3^-. [e] No new peak was observed.

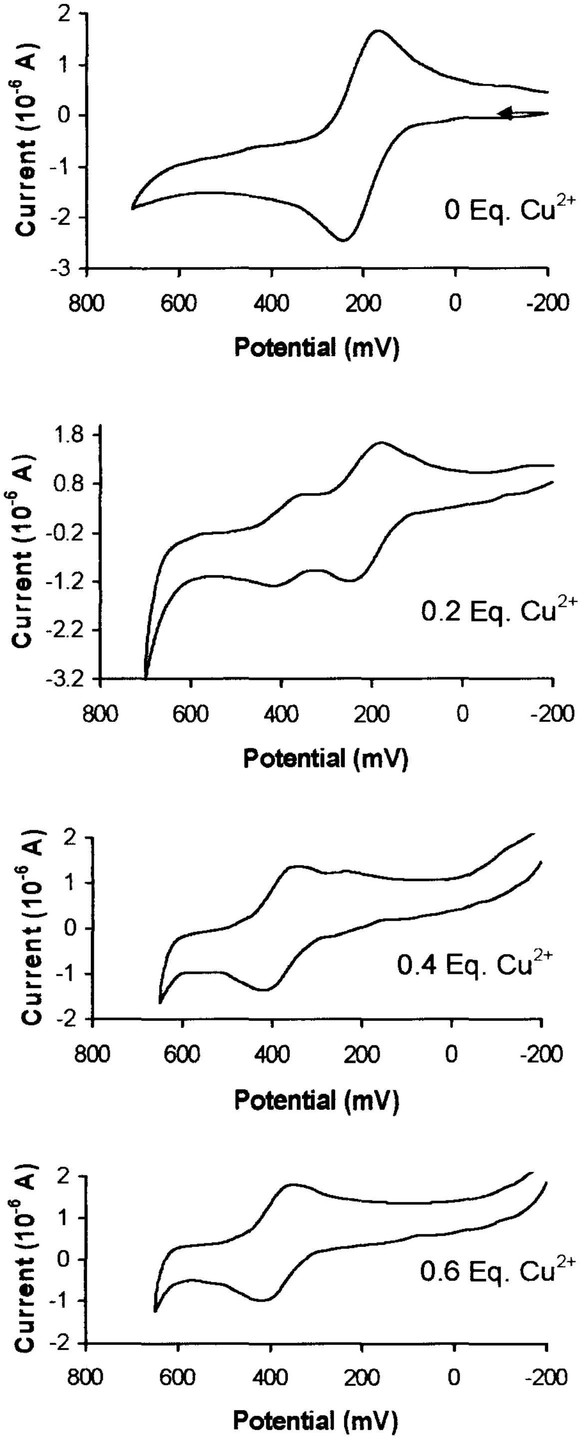

FIGURE 4.1: Electrochemical recognition of Cu^{2+} by (**13**, 1 mM) in acetonitrile. Voltammograms show the appearance of the new reversible wave and the disappearance of the original ligand wave during titration with Cu^{2+} solution. The potential is referenced to Ag/Ag^{+} (see Experimental).

In addition to the new reversible wave that was observed at 380 or 385 mV during titration with phenyl- or methyl-mercury salts, respectively, an irreversible anodic wave not observed in the titration with Cu^{2+} was observed at a potential value similar to the original receptor, i.e. at E_a = 232 mV [see Figure 4.2 on the next page, for voltammograms showing the titration of receptor (**13**) with $PhHg^+$]. The current of this anodic wave increased and the potential shifted slightly to lower potential values. This anodic wave was only observed after addition of 0.4 equivalents of organomercury ions and it was still visible even after three equivalents had been added. This wave is possibly due to the acetate anion from the salt.[1] Further investigation of this wave with mercury acetate was not performed as this salt was insoluble in acetonitrile.

Typical Cu^{2+} or RHg^+ titration curves, which show the plot of current versus the number of equivalents of copper or organomercury ions added, are shown in Figures 4.3, 4.4 and 4.5, respectively. The results from three different independent experiments showed that the original wave due to the free receptor disappeared after addition of 0.8 equivalents of Cu^{2+} ions and the current of the new wave due to the receptor–metal complex increased until reaching a plateau after addition of one equivalent of copper ions. This suggests a receptor : metal ratio of 1 : 1 (see Figure 4.3). The $PhHg^+$ ion titration curve also showed that the free receptor wave disappeared after addition of *ca.* 0.5 equivalent of this organometallic ion. Similar results were also observed in the titration curve of $MeHg^+$. In both cases the data suggested a receptor–metal ratio of 2 : 1. The titration curves of $PhHg^+$ and $MeHg^+$ are shown in Figures 4.4 and 4.5, respectively. The additional anodic wave observed (at approximately similar oxidation potential as the original receptor), as mentioned before, made it difficult to confirm the accurate redox potential and the number of equivalents at which the original receptor disappeared (thus affecting the accurate determination of receptor : RHg^+ ratio), i.e. there was possibly more than one species that was oxidised at the same potential value.

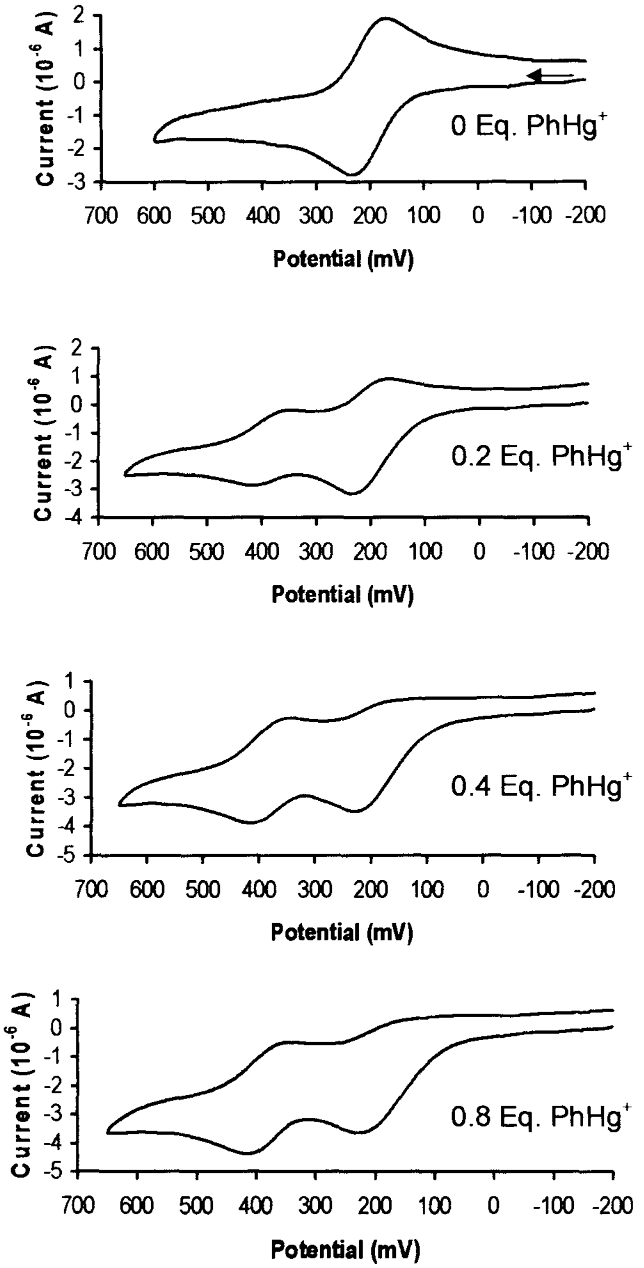

FIGURE 4.2: Electrochemical recognition of PhHg$^+$ by (**13**, 1 mM) in acetonitrile. Voltammograms show the appearance of the new reversible wave and the disappearance of the original receptor wave during titration with PhHg$^+$ solution (anodic wave at ca. 200 mV was observed even after addition of 3 equivalents of PhHg$^+$). The potential is referenced to Ag/Ag$^+$ (see Experimental).

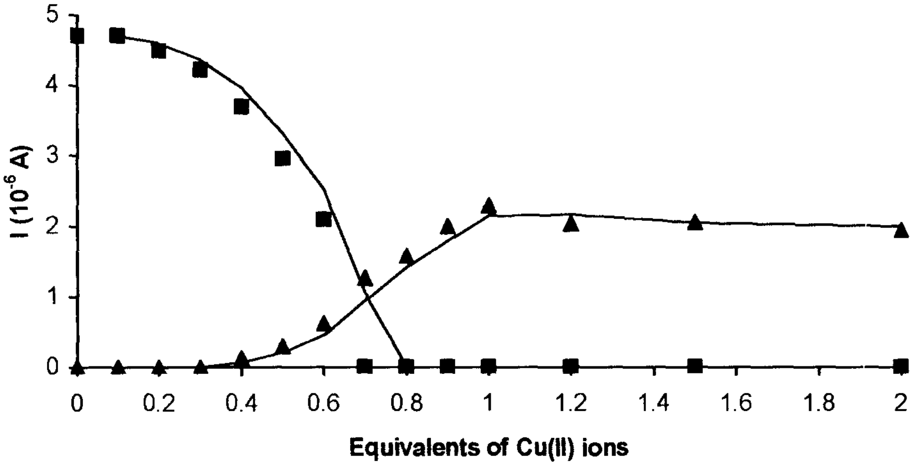

FIGURE 4.3: Titration curve of the equivalents of Cu^{2+} to a 1 mM receptor (**13**) solution. (■) receptor, (▲) receptor–metal complex.

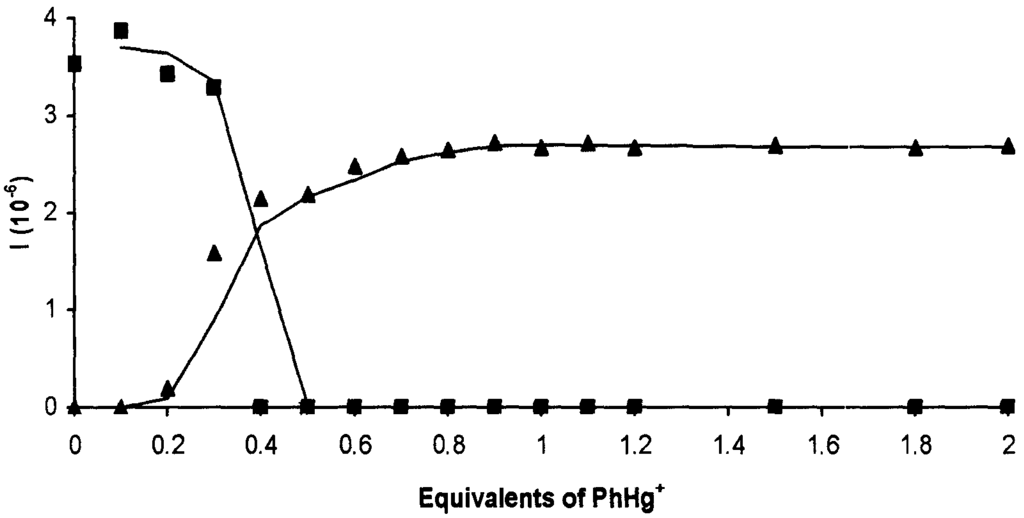

FIGURE 4.4: Titration curve of the equivalents of $PhHg^{+}$ to a 1 mM receptor (**13**) solution. (■) receptor, (▲) receptor–metal complex.

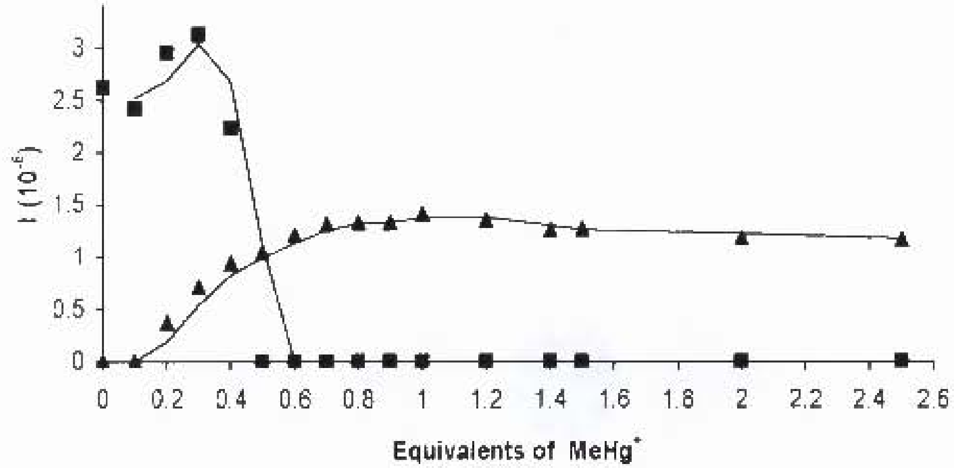

FIGURE 4.5: Titration curve of the equivalents of $MeHg^+$ to a 1 mM receptor (**13**) solution. (■) receptor, (▲) receptor–metal complex.

An additional method to confirm the exact receptor : metal ratio would be the determination of the crystal structures of the metal complexes (see Section 4.5). Mass spectra (ESI-MS) might also assist in order to identify the species that are present in the solution.[2] Maximum potential shifts of between 200 – 400 mV have been reported in the literature for recognition of metal ions such as Cu^{2+} and Hg^{2+} by different receptors.[3-7,8,9]

There was no change in the free receptor wave when Ni^{2+} ions were added to the solution of the receptor. To confirm this, various nickel(II) salts were used, i.e. with BF_4^-, ClO_4^- and NO_3^- anions. Interestingly, the new reversible wave that was observed in the Cu^{2+} titration was still observed in the presence of four equivalents of Ni^{2+} ions, making the determination of copper in the presence of nickel ions a feasible proposition. Metals that gave a response resulted in different colour changes of the original ligand solution after addition of 0.3 equivalent of the metal ion (*ca.* 10 mg L^{-1}) to the reagent solution. For example, the red colour of the receptor solution changed drastically to green or yellow when the receptor was titrated with phenylmercury or copper ions, respectively (pictures of flasks containing solutions of the free receptor (**13**) and with added Cu^{2+} or $PhHg^+$ ions are shown in Figure 4.6 on the next page).

FIGURE 4.6: Solution of receptor (**13**) during titration with various metal ions in acetonitrile: (1) Solution of *S*-ferrocenyldithizone (**13**), (2) Solution of (**13**) + 2.5 molar equivalent of Hg^{2+}, (3) Solution of (**13**) + 2.5 molar equivalent of Cu^{2+}.

This was expected since metal complexes of dithizone or dithizone derivatives give different colour solutions;[10] however, a yellow solution colour has never been observed and is unusual for copper complexes of dithizone. This was the first indication that during titration with copper ion the copper complex was not forming but the receptor binding site was being oxidised to the yellow tetrazolium salt (see Section 4.5). There are several possible coordination modes that can take place during titration of the receptor with metal ions in solution. For example, in the case of Cu^{2+} or Ni^{2+}, if the receptor–metal complex is formed by a receptor : metal ratio of 2 : 1, and the imino proton in the binding site of the receptor is displaced, then two of the receptor molecules can each coordinate to the metal through nitrogen and sulfur (*N,S*-coordination) [see Figure 4.7 (a), on the next page], or alternately through only the nitrogen atoms (*N,N'*- coordination) [Figure 4.7 (b)]. If the imino proton is not displaced the coordination modes through sulfur only (*S*-coordination) are most likely [see Figure 4.7 (c) and (d)]. The possible coordination modes for the case in which receptor–metal complex is formed by a receptor : metal ratio of 1 : 1 are shown in Figure 4.8. The coordination modes shown in Figures 4.7 (c, d) and 4.8 (c, d) are most probable where the base is absent in the solution (as used to assist deprotonation of the imino proton that has proved difficult to displace).

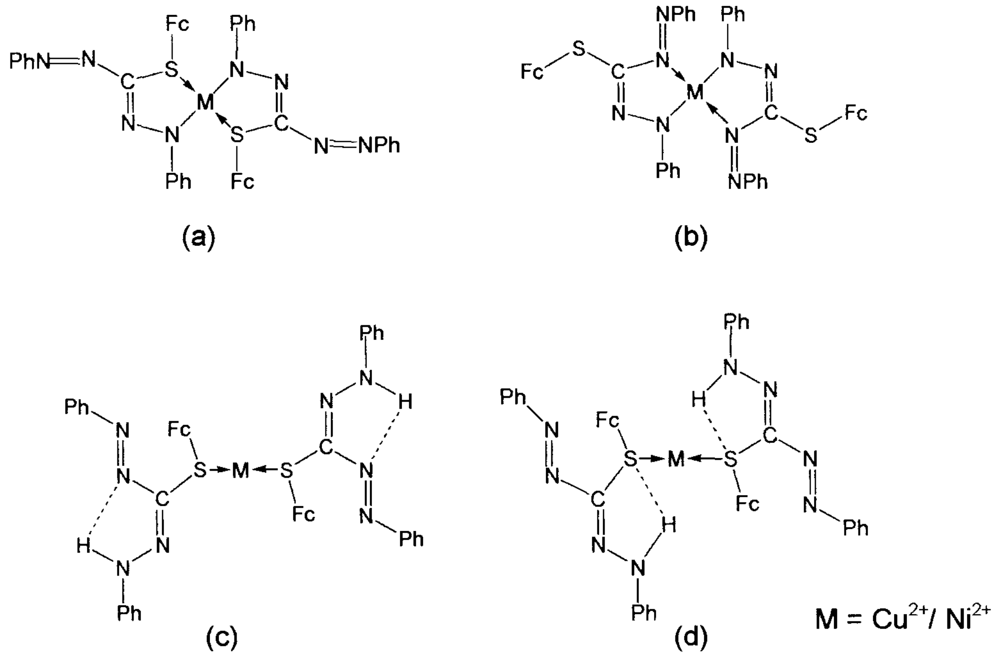

FIGURE 4.7: Possible coordination modes of compound (**13**)–metal complex. The complexes show the receptor : metal ratio of 2 : 1. (a) shows a coordination of the receptor through nitrogen and sulfur (*N,S*-coordination), while (b) shows coordination through nitrogen atoms (*N,N*-coordination). (c) and (d) show two different possible conformations of the ligand when coordinating to the metal through sulfur when the receptor binding site is not deprotonated.

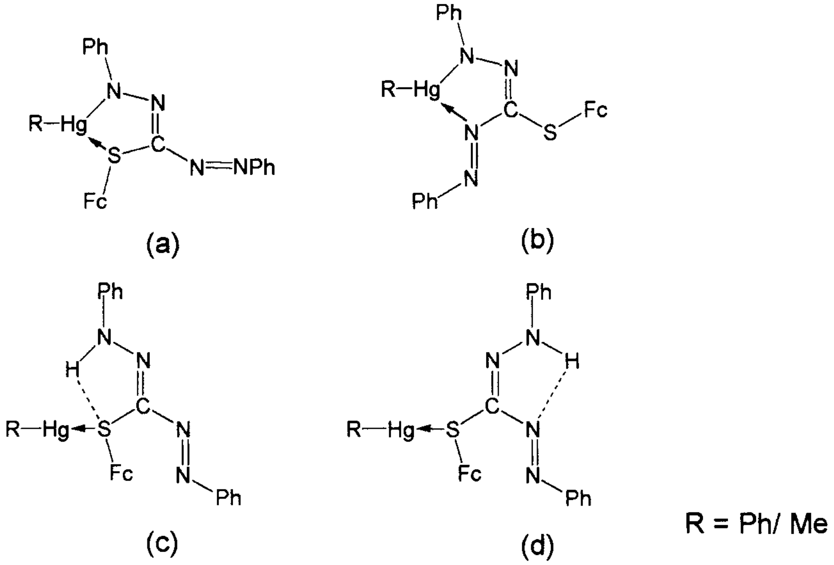

FIGURE 4.8: Possible coordination modes of compound (**13**)–organomercury complex. The complexes show the receptor : metal ratio of 1 : 1. (a) shows a coordination of the receptor through nitrogen and sulfur, while (b) shows coordination through nitrogen atoms. (c) and (d) show two different possible conformations of the receptor when coordinating to mercury through sulfur when the receptor binding site is not deprotonated.

Theoretically we would expect the receptor : metal ratio of 1 : 1 for receptor–RHg$^+$ complex (R = Me/Ph), since organomercury compounds are very stable compounds as the organic substituent group bonds strongly to mercury. In this case coordination modes listed in Figure 4.8 are possible. The receptor : metal ratio [compound (**13**) : RHg$^+$] of 2 : 1 obtained from our data might be because of inaccuracy associated with the determination of the potential and the number of equivalents for the disappearance of the redox wave of the original receptor.

During formation of the *S*-ferrocenyldithizone–phenylmercury complex in the solution the bulky phenyl group on mercury might be the influential factor that drives the coordination to the mercury ion by the receptor through nitrogen atoms only [see Figure 4.8 (b)]. It would be unusual for this kind of coordination to take place as the coordination of mercury through sulfur would be expected. However, a single crystal structure of the *S*-methyldithizone–phenylmercury complex has been found to have this type of coordination.[11] There is a small distance between the coordination sites and the transducer in receptor (**13**) for the possible coordination modes shown in Figure 4.8 (a), (c) and (d), since sulfur is bonded directly to the cyclopentadienyl ring. Large potential shifts of the ferrocenyl couple of this compound in the presence of metal ions are observed. Thus, a combination of through-space and through-bond type communication is suggested to be taking place when receptor (**13**) is titrated with organomercury salts. However, only through-space communication is suggested for the coordination mode shown in Figures 4.7 (b) and 4.8 (b). From the potential shifts observed during titration with a small methyl- or bulky phenyl-substituted mercury ion it is not possible to distinguish between these coordination modes, i.e. which proposed coordination mode is taking place when the receptor is titrated with methyl- or phenyl-mercury ion. It has been previously noted that nickel(II) reacts very slowly with dithizone.[12] It has been suggested that the reason for these slow reactions is the difficulty of displacement of water of solvation (which coordinates strongly to nickel ion) by other coordinating atoms. It is known that Ni^{2+} substitution reactions are typically several orders of magnitude slower than Cu^{2+}, viz. d^8 vs. d^9. This factor has been overcome by replacing the water of solvation with less powerfully co-ordinating but bulkier ligands such as nitrogen bases:

2,2′-bipyridyl, 2,6-lutidine and 1,10-phenanthroline. The crystal structure of the adduct of Ni(HDz)$_2$ with bipyridyl has been obtained.[13] These slow reactions of dithizone with nickel can also be confirmed by the experiments performed by Irving and Sahota[14] for the preparation of the metal complexes of *S*-methyldithizone. Bis(*S*-methyldithizonato)nickel(II) was obtained when an ethanol solution of a nickel salt and *S*-methyldithizone was boiled under reflux for 2 hours, compared to reactions of copper or mercury salts, where the product was obtained within 30 min with stirring at room temperature. This could be the reason why no response was observed during titration of receptor (**13**) with nickel ions.

Protonation-type behaviour was investigated to confirm if any protonation of the binding atoms by water of crystallisation from metal salts was taking place. Partially acidic protons of water of crystallization in hydrated metal salts have a tendency of protonating the binding atoms of sensor molecules. Researchers have investigated this type of behaviour for many receptors by addition of a Lewis acid (e.g. HBF$_4$) to the reagent–metal solution.[3,15] If a new redox wave is not observed after addition of a Lewis acid to the ligand–metal solution, then it is concluded that protonation rather than coordination is taking place on the binding atom(s). On the other hand, if a new redox wave appears after addition of acid, then coordination type recognition is suggested to be taking place. Addition of HBF$_4$ (1 mol equivalent to receptor) to receptor (**13**)–metal solutions resulted in a potential shift of the receptor–Cu^{2+} complex to slightly lower potential values ($E_{1/2}$ = 367 mV) compared to the initial receptor–Cu^{2+} wave ($E_{1/2}$ = 387 mV) (see Table 4.1).

The potential of the redox couple of the free receptor shifted to higher potentials when the acid was added to the solution. The new redox waves observed after addition of acid to the receptor–metal or to the free ligand solutions had different $E_{1/2}$ values of 367 or 304 mV, respectively. The potential shift was also observed in comparison experiments performed by addition of acid to the solution of receptor and non-hydrated metal ion salts such as PhHgOAc. Due to these differing $E_{1/2}$ values observed when acid was added to receptor or to various receptor–metal solutions, it cannot be safely concluded that the protonation type recognition was taking place. If protonation of the receptor was taking place then one type of protonated product would be expected to form in all cases resulting in similar $E_{1/2}$ values for the ferrocenyl substituent. This was not the case in our observations. In all cases, solutions of the receptor or receptor–metal complex turned maroon immediately after adding acid. Attempted ^1H NMR experiments conducted by adding acid (HBF_4, one equivalent) to the receptor–metal solution in deuterated methanol did not add any useful information as the spectra had many peaks making them difficult to interpret. The tendency of formazans to rearrange to form undesired cyclised products in the presence of concentrated acids cannot be ruled out.[16]

4.3 ELECTROCHEMICAL RECOGNITION EXPERIMENTS WITH RECEPTOR (14)

The voltammogram of the new compound **(14)** in acetonitrile solution shows a reversible wave at $E_{1/2} = 51$ mV compared to ferrocene itself as a standard reference (see Figure 4.9, on the next page). The original half-wave potential of the receptor shifted continuously to higher oxidation potentials when titrated with different metal solutions. For example, during titration with Cu^{2+} or $PhHg^+$ ions the redox wave corresponding to the receptor–metal complex shifted to a maximum of $\Delta E_{1/2} = +44$ or $+32$ mV, respectively. The results for redox shifts of the metal ions investigated are summarised in tabulated form (see Table 4.2). A potential shift of +39 mV was observed when receptor **(14)** was titrated with Ni^{2+} solution.

TABLE 4.2: Electrochemical shifts (mV, vs. Ag/Ag^+) of the ferrocenyl redox couple of compound **(14)** in acetonitrile solution on addition of metal ion salts[a]

Compound	$E_{1/2}$ (mV)	$\Delta E_{1/2}$ (mV)[b]	Addition of HBF_4 ($E_{1/2}$, mV)
(14)	136		218
(14) + PhHg(OAc)	168	+32	358
(14) + $Cu(ClO_4)_2$	180	+44	355
(14) + $Ni(ClO_4)_2$	175	+39	203

[a] $E_{1/2}$ for ferrocene itself as a standard reference under the same conditions was 85 mV. Data are accurate to ±5 mV. [b] Maximum potential shifts of compound **(14)**–metal complex.

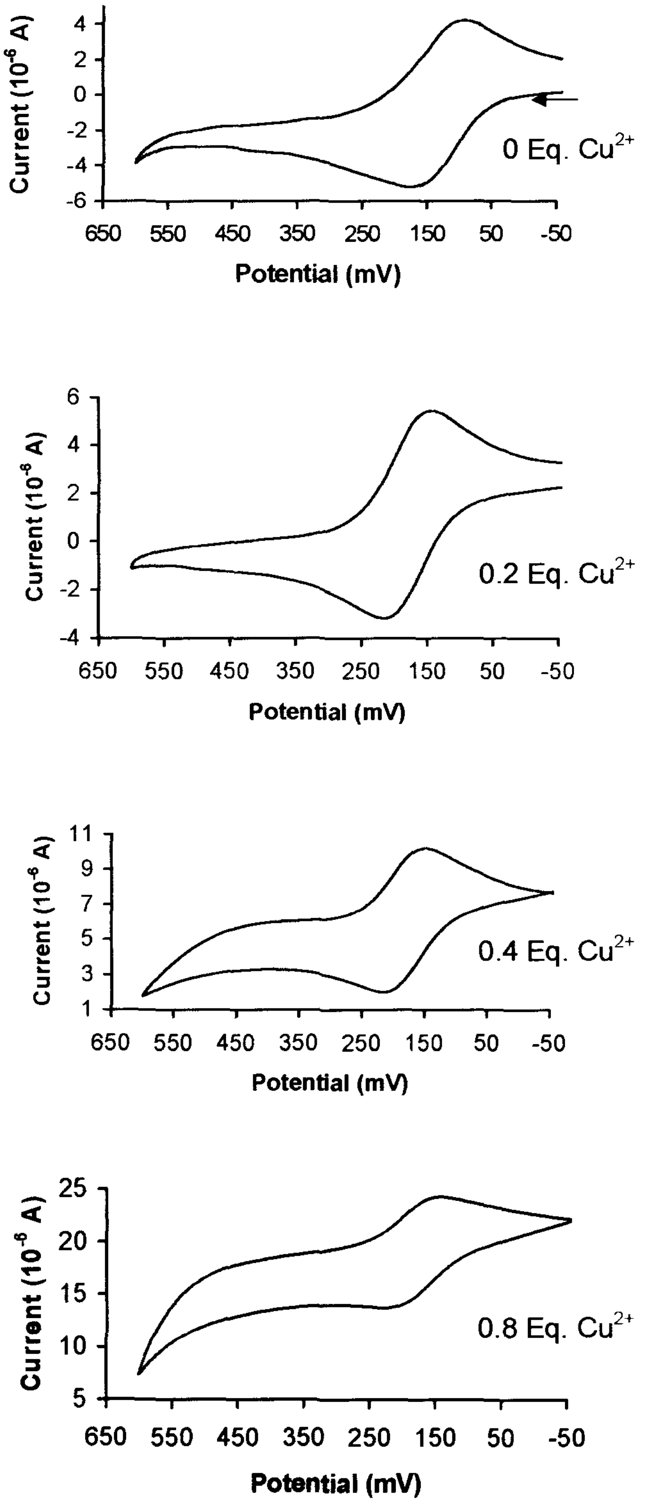

FIGURE 4.9: Electrochemical recognition of Cu^{2+} by (**14**, 1 mM) in acetonitrile. Voltammograms show the continuous shift of the ligand wave during titration with Cu^{2+} solution. The potential is referenced to Ag/Ag^{+} (see Experimental).

It can be seen that the shifts in half-wave potential are much smaller for this ligand compared to receptor **(13)**, where $\Delta E_{1/2}$ values of the order of +180 mV were obtained. The presence of a methylene linker might have decreased the interaction between the donor sulfur atom and the cyclopentadienyl ring or iron centre of the ferrocenyl substituent, resulting in a smaller shift in half-wave potential. In contrast to the behaviour of receptor **(13)**, the receptor **(14)** showed a response to nickel(II) ions.

After addition of 0.4 equivalents of $PhHg^+$ to the solution of receptor **(14)**, a broad anodic wave at *ca.* 200 mV was observed in the voltammogram, unlike the smooth sharp redox waves that were observed in the titration of receptor **(14)** with Cu^{2+}. After addition of 0.8 equivalents of the organomercury ion, two poorly resolved waves appeared (at *ca.* 200 mV, 313 mV) and these were still observed even after 3 equivalents were added (see Figure 4.10, on the next page). As mentioned before for the titration of receptor **(13)** with $PhHg^+$, it is possible that one of the anodic waves observed here was due to the oxidation of the acetate ion.[1] The recognition was dependent on the metal anion salt that was investigated in the experiments. In general, investigations of recognition by receptor **(14)** with metal chlorides were not pursued since no recognition was observed during titration with these metal salts.

Ideally, when the metal solution is added to the receptor solution a receptor–metal complex is formed and the potential of the ferrocenyl redox couple changes to higher potentials. Hence, the current of this wave should also increase.[17] Surprisingly, the current of the redox wave of receptor **(14)**–metal complex decreased continuously as the metal salt solution was added. This behaviour is difficult to explain. This can suggest that during addition of the metal ion to the receptor solution the final solution was diluted, resulting in the decrease in current. Results from three independent experiments using freshly made-up solutions each time showed that the maximum potential shifts took place after addition of a half equivalent of Ni^{2+}, Cu^{2+} or $PhHg^+$. The data suggest a receptor : metal ratio of (2 : 1).

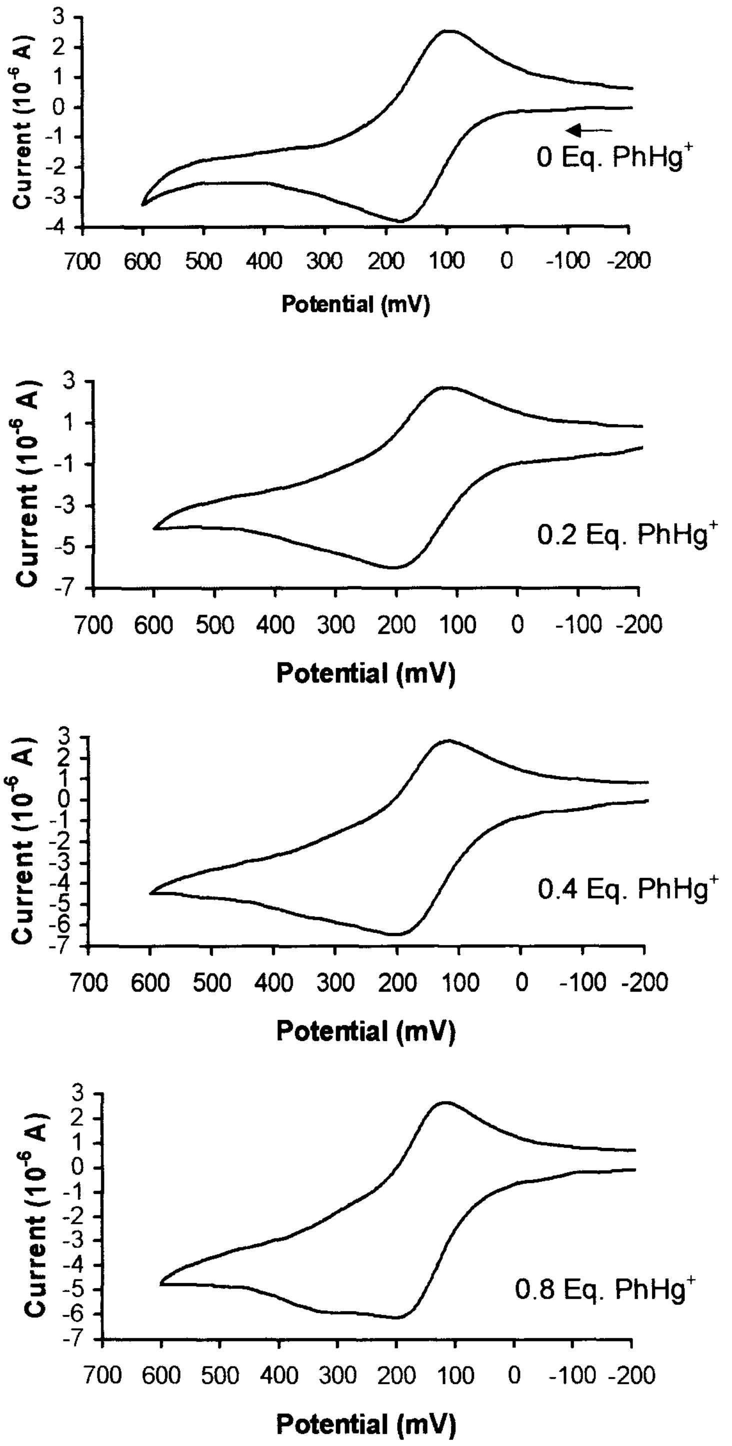

FIGURE 4.10: Electrochemical recognition of $PhHg^+$ by (**14**, 1 mM) in acetonitrile. Voltammograms show the continuous shift of the ligand wave during titration with $PhHg^+$ solution. The potential is referenced to Ag/Ag^+ (see Experimental).

We cannot strongly suggest the receptor : $PhHg^+$ ratio of 2 : 1 as observed from the data because of the inaccuracy associated with the determination of the maximum potential shift of receptor–metal complex [the oxidation potential of the anodic wave was possibly due to two species, i.e. oxidation of acetate ion and the ferrocenyl substituent of receptor (**14**)], thus resulting in the inaccurate values of receptor : metal ratio. Since during titration of the receptor with copper ions an oxidation of the binding site of the receptor rather than coordination was shown to be likely (see Section 4.5), it would then mean that all the initial receptor was oxidised after addition of half an equivalent of Cu^{2+} ions (thus the maximum potential shift was observed after addition of this number of equivalents). This possible oxidation process will be discussed in Section 4.5. Titration curves of $E_{1/2}$ versus number of equivalents of metal ion added to the receptor solution are shown in Figures 4.11, 4.12, or 4.13 for Cu^{2+}, $PhHg^+$ or Ni^{2+}, respectively.

Different colour changes of the receptor solution were also observed when the original red-brown solution of compound (**14**) was titrated with different individual metal ion solutions. For example, the colour of the receptor solution changed slightly to clear red, dark grey or pale green when the receptor was titrated with phenylmercury, nickel or copper ions, respectively (pictures of flasks containing solutions of free receptor (**14**) and with added Cu^{2+} or $PhHg^+$ ions are shown in Figure 4.14).

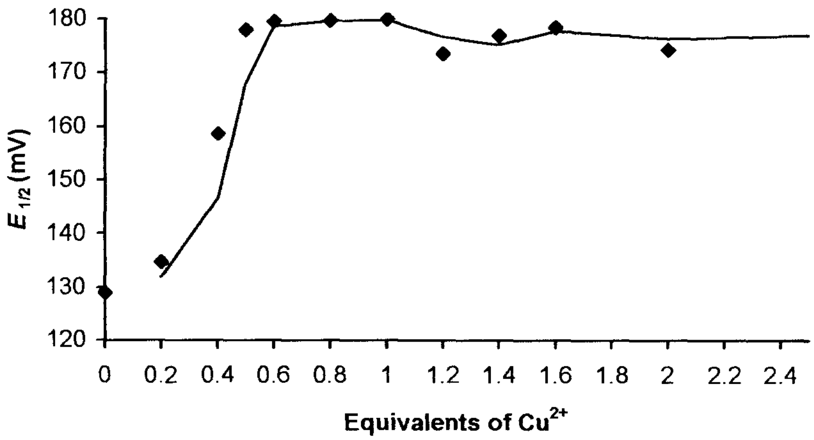

FIGURE 4.11: Titration curve of the equivalents of Cu^{2+} to a reagent (**14**) solution (1 mM). Maximum potential shift takes place after addition of a half equivalent of Cu^{2+} solution. suggesting receptor : metal ratio of 2 : 1.

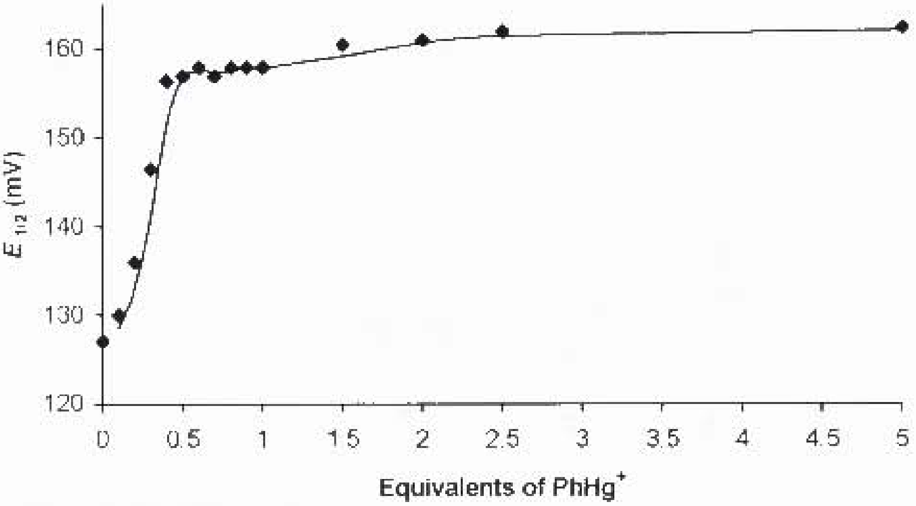

FIGURE 4.12: Titration curve of the equivalents of $PhHg^+$ to a reagent (**14**) solution (1 mM). Maximum potential shift takes place after addition of a half equivalent of $PhHg^+$ solution, suggesting receptor : metal ratio of 2 : 1.

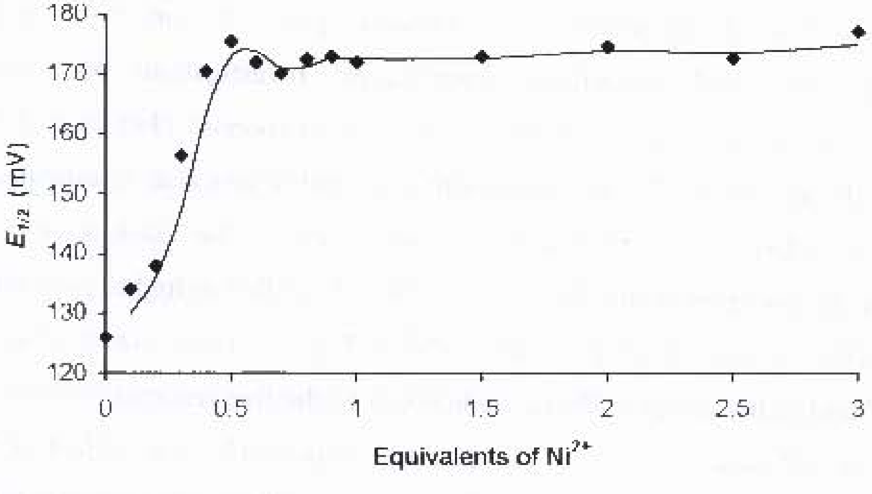

FIGURE 4.13: Titration curve of the equivalents of Ni^{2+} to a reagent (**14**) solution (1 mM). Maximum potential shift takes place after addition of a half equivalent of Ni^{2+} solution, suggesting receptor : metal ratio of 2:1.

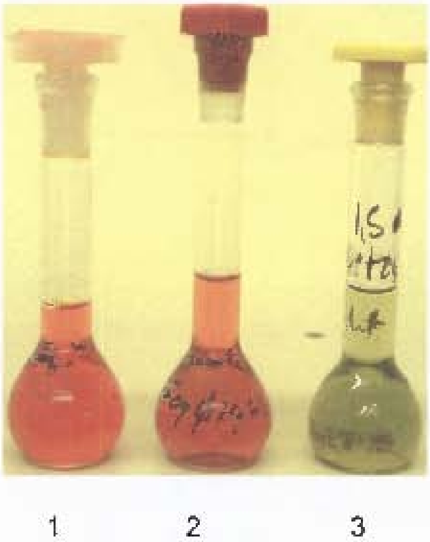

FIGURE 4.14: Solutions of receptor **(14)** during titration with various metal ions in acetonitrile: (1) Solution of *S*-ferrocenylmethyldithizone **(14)**, (2) Solution of **(14)** + 2.5 molar equivalent of Hg^{2+}, (3) Solution of **(14)** + 2.5 molar equivalent of Cu^{2+}.

It was pointed out in Chapter 1 that receptors of this type, in which the colour of their original solutions changes when titrated with different metal ions are important for qualitative analysis of samples of interest; in suitable cases quantitative analysis may also be achieved, e.g. by visible absorption spectroscopy. Investigations of possible protonation of the coordinating atoms of the binding site of receptor **(14)** by hydrated metal ions were also conducted. For comparison this possibility was also investigated in titrations of receptor **(14)** with non-hydrated metal ion solutions. The redox wave of the ferrocenyl couple of this receptor initially at $E_{1/2}$ = 136 mV shifted to higher potential at $E_{1/2}$ = 218 mV after addition of a Lewis acid (HBF_4). The new redox waves observed after addition of acid to the receptor–$PhHg^+$ complex or to the free receptor solution had very different potential values of $E_{1/2}$ = 358 or 218 mV, respectively (see Table 4.2). The colour of the solutions turned maroon on addition of acid. These were similar to the observations made during addition of acid to solutions of receptor **(13)**, thus it cannot be concluded that the protonation type recognition was taking place during titration of receptor **(13)** or **(14)** with metal salts. The smaller potential shifts observed during titration of receptor **(14)** with metal salts suggest that the recognition in the binding event is taking place by through-space communication. This is because the methylene linker increases the distance between the binding event and the ferrocenyl substituent of the transducer. In similar vein we can suggest that similar coordination modes, as discussed in Section 4.2 (see Figure 4.7, considering methylene link between sulfur and cyclopentadienyl ring) are taking place for receptor **(14)**–metal complexes (metal = Ni^{2+}/ Cu^{2+}). The coordination modes listed in Figure 4.8 are most probable for receptor **(14)**–$PhHg^{-}$ complex, but with the information presently available it is not possible to be more specific.

4.4 INVESTIGATION OF THE INTERACTION OF THE NEW RECEPTORS WITH METAL IONS USING UV-VIS SPECTROSCOPY

The interactions between receptors **(13)** or **(14)** with metal ions were investigated by UV-Vis spectroscopy using the same solvent conditions [acetonitrile containing tetrabutylammonium perchlorate (TBAP)] as in the electrochemical recognition experiments. Upon addition of the equivalents of the metal ion solution the colour of the receptor **(13)** solution changed from an initial red-orange to yellow. The absorbance of the receptor band originally at 410 nm decreased continuously with a shift to slightly longer wavelengths (see Figure 4.15). No new band(s) were observed for the receptor–metal complex. This is surprising since the solutions of various metal complexes of dithizone or dithizone derivatives are intensely coloured. These metal complex solutions usually absorb between 400 – 500 nm in the UV-Vis spectrum.[10]

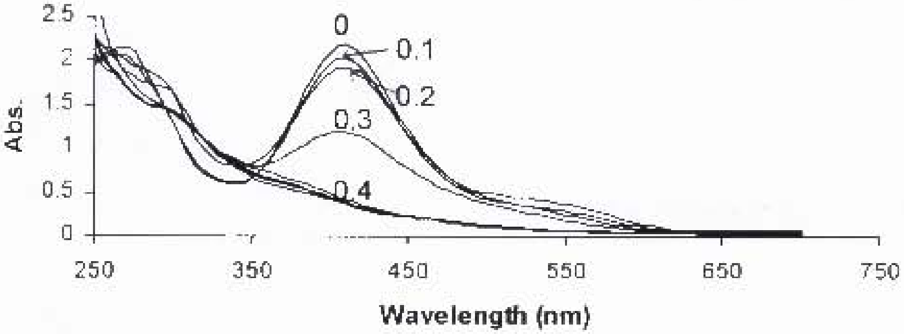

FIGURE 4.15: The UV-Vis spectrum of *S*-ferrocenyldithizone (**13**) titrated with 0.1 M solution of Cu^{2+}. The numbers show the equivalents of Cu^{2+} ions added.

It is possible that under these conditions something contrary to the formation of a receptor–copper complex is taking place; a process like oxidation of the formazan binding site to form the nearly colourless tetrazolium salt. In contrast to the electrochemical experiments, where the receptor wave disappeared after addition of 0.8 equivalent of metal solution, the band due to the ligand disappeared after addition of 0.4 metal ion equivalents. It was also observed that from addition of 0.5 or more equivalents of Cu^{2+} solution a new, broad, weak intensity band at *ca.* 700 nm appeared, which increased continuously in absorbance (this band is not shown in Figure 4.15, where the absorbance scale is too large to reflect the weak d–d transition). The band corresponds to the transition for distorted octahedral Cu^{2+} (d^9) complexes as described by the Jahn–Teller distortion phenomenon. This confirms that the salt solution was in excess from addition of 0.5 equivalents of Cu^{2+} since all the receptor was consumed. Previously, researchers found that these two different techniques of UV-Vis spectroscopy and cyclic voltammetry can only be used to estimate the receptor–metal ratios as they have different time scales for measurements.[7,18]

In the case of titration with phenylmercury(II) cation, the original receptor band decreased in absorbance until after addition of 0.2 equivalent of $PhHg^+$ to the receptor solution (see Figure 4.16, red curves on the spectrum). From addition of 0.3 equivalents of $PhHg^+$ a new band was observed at longer wavelengths (see Figure 4.16, black curves on the spectrum). Surprisingly, the absorbance of this band increased until a total of 2.5 equivalents or more of $PhHg^+$ had been added (see Figure 4.16, green curve in the spectrum). This behaviour is difficult to explain since if this new band was due to the receptor–metal complex, it should be constant at a certain maximum absorbance as the receptor will be completely consumed in the solution. However, it is safe to conclude that oxidation of the formazan binding site to form tetrazolium salt was not taking place during titration of receptor **(13)** with $PhHg^+$.

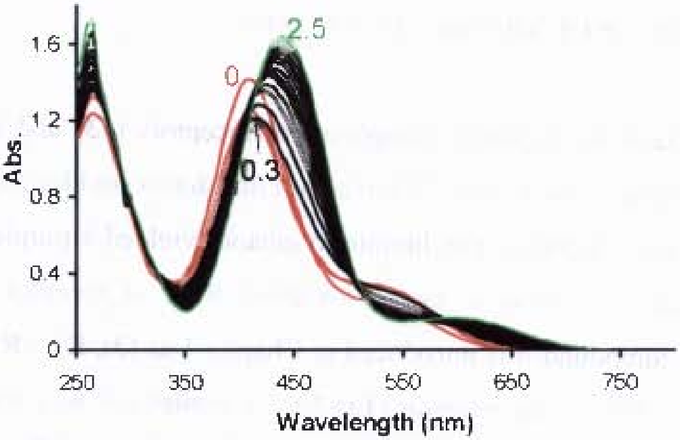

FIGURE 4.16: The UV-Vis spectrum of *S*-ferrocenyldithizone (**13**) titrated with 0.1 M solution of $PhHg^+$. The numbers shows the equivalents of $PhHg^+$ ions added

Similar results were obtained when the interaction of receptor (**14**) and metal ions were investigated. Upon addition of the equivalents of the copper(II) ion solution, the colour of the receptor (**14**) solution changed from an initial red-orange to yellow. In this case, the absorbance of the ligand band originally at 415 nm decreased continuously with a shift to slightly longer wavelengths (see Figure 4.17). The band due to the receptor disappeared after addition of 0.6 Cu^{2+} ion equivalents. No new additional band(s) were observed for the receptor–metal complex. Titrations with other metal ions for this investigation were not performed.

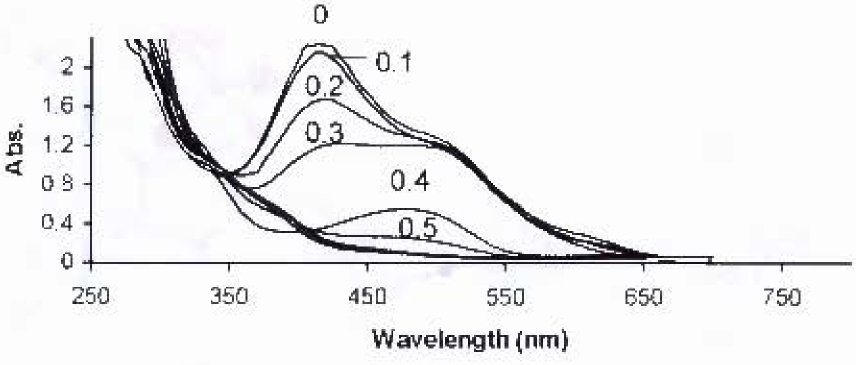

FIGURE 4.17: The UV-Vis spectrum of *S*-ferrocenylmethyldithizone (**14**) titrated with 0.1 M solution of $Cu(ClO_4)_2.6H_2O$. The numbers shows the equivalents of Cu^{2+} ions added.

4.5 ATTEMPTED SYNTHESIS OF METAL COMPLEXES

Experiments for the synthesis of the metal complexes of receptors **(13)** and **(14)** were performed using various metal salt solutions. The reaction of *S*-ferrocenyldithizone with a half-molar equivalent amount of copper perchlorate in ethanol yielded a purple product. This product was unexpectedly found to be the oxidised form of receptor **(13)**, the tetrazolium salt [this new compound was introduced in Chapter 1 as **(3)**, $R^1 = R^2 = Ph$, $R^3 = S(\eta^5\text{-}C_5H_4)Fe(\eta^5\text{-}C_5H_5)$] and not the receptor **(13)**–Cu^{2+} complex (as was discussed in Section 4.2). A single crystal was obtained and analysed by X-ray diffraction. The compound crystallised in the orthorhombic crystal system with the space group of *Pbca*. An N–N bond has formed to make a tetrazolium ring and the phenyl groups are partially out of plane in opposite senses [see Figure 4.18 (b)]. Some crystallographic data are summarized and shown in Tables 4.3 (a) and (b) on the next page. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a chloroform solution. This reaction gave the same product even when compound **(13)** was reacted with equal or excess amounts of copper perchlorate or copper chloride solutions (for long reaction times). Oxidation of formazans in air or in the presence of the copper ions has been previously observed.[19]

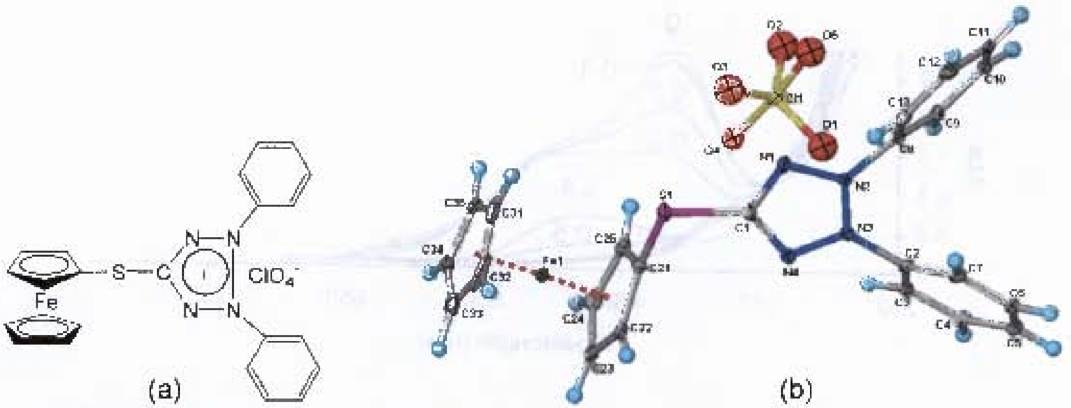

FIGURE 4.18: (a) Chemical structure and (b) molecular structure of the oxidised form of *S*-ferrocenyldithizone **(13)**, the tetrazolium salt with the perchlorate as an anion. The ClO_4^- ion is disordered and the axial oxygens (O4 and O5) were modelled with site occupancy factor (s.o.f) at 0.5 and the other oxygens (O1, O2 and O3) at s.o.f = 1.

TABLE 4.3 (a): Selected bond lengths (Å) and angles (°) for 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate

Atoms	bond length (Å)	Atoms	bond angle (°)
S(1)-C(1)	1.746(9)	C(1)-S(1)-C(21)	103.3(5)
S(1)-C(21)	1.759(10)	N(4)-C(1)-S(1)	128.0(7)
N(1)-N(2)	1.329(10)	N(1)-C(1)-S(1)	118.7(7)
N(1)-C(1)	1.348(10)	N(3)-N(2)-C(8)	128.8(7)
N(2)-N(3)	1.315(10)	N(1)-N(2)-C(8)	120.5(7)
N(2)-C(8)	1.461(11)	N(2)-N(3)-N(4)	110.6(7)
N(3)-N(4)	1.324(10)	N(2)-N(3)-C(2)	126.1(7)
N(3)-C(2)	1.467(11)	N(4)-N(3)-C(2)	123.4(7)
N(4)-C(1)	1.343(12)	N(3)-N(4)-C(1)	103.0(7)
		N(4)-C(1)-N(1)	113.3(8)
		N(2)-N(1)-C(1)	102.6(7)
		N(3)-N(2)-N(1)	110.6(7)

TABLE 4.3 (b): Crystal data and structure refinement for 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate

Empirical formula	$C_{23}H_{19}ClFeN_4O_4S$
Formula weight	538.78
Temperature	133(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, *Pbca*
Unit cell dimensions	a = 11.5692(4) Å, α = 90°
	b = 18.1768(5) Å, β = 90°
	c = 21.3099(7) Å, γ = 90°
Volume	4481.3(2) Å^3
Z, Calculated density	8, 1.597 Mg m^{-3}
Reflections collected/unique	38863/3911 [R(int) = 0.1075]
Goodness of fit on F^2	1.144
Final R indices [I>2sigma (I)]	R_1 = 0.1085, wR_2= 0.2217
R indices (all data)	R_1 = 0.1419, wR_2 = 0.2351

The colour of the solution of *S*-ferrocenyldithizone in ethanol changed from red–brown to green upon addition of an organomercury salt solution. Unfortunately, no solid compound was isolated in the reactions of receptor **(13)** with various organomercury salts. Variation of the experimental conditions,[14,20] including boiling the reaction mixtures under reflux, resulted in no success. Addition of water to the ethanol reaction mixture yielded a green precipitate and after filtering, a green, fluffy powder was obtained. The solid material was taken up in chloroform for purification and the removal of the solvent from the solution resulted in a green oil. No precipitates were formed upon adding a non-polar solvent such as hexane or diethyl ether. Purification of this oil by column or flash chromatography resulted in a red-brown decomposition product characteristic of the starting material compound **(13)**. The ^1H NMR spectrum of this oily green material showed all the protons in the ferrocenyl and phenyl regions together with the NH proton signal. A similar spectrum was obtained even after reaction of equivalent amounts of the receptor and different mercury salt solutions. It is possible that the complex was not stable and the metal dissociated back in the solution. The ethanol solution of Ni^{2+} with receptor **(13)** was heated under reflux in order to facilitate the reactivity of this metal ion. During the reaction the colour of this solution changed from red-brown to grey assuming the formation of receptor–metal complex. No precipitates were observed after addition of water to the solution. The colour of the extracted layer from the solution with dichloromethane was red-brown during attempted separation of the product. This suggested that the receptor **(13)**–Ni^{2+} complex (presumably forming in the solution) was not stable and the metal ion dissociated back to the aqueous layer. Similar results were obtained when various nickel salts were employed.

Compound **(14)** was also reacted with various metal salts. For all reactions performed, a red-orange solid precipitated immediately out of the reaction mixture during the addition of the metal salt solution to the solution of compound **(14)** in ethanol. The ^1H NMR spectra showed the disappearance of the ferrocenyl protons which suggested the decomposition of the original compound **(14)**. Different reaction conditions resulted in no success.

4.6 CONCLUSIONS

The results show that the two new receptors do electrochemically interact with the metal ions Cu^{2+}, $PhHg^{+}$ and $MeHg^{+}$, while Ni^{2+} was only detected by receptor **(14)**, though the mechanism of interaction is uncertain and certainly different for Cu^{2+} compared with the organomercury ions. Experiments performed by UV-Vis spectroscopy showed that there was an interaction between the metal ions and the receptors in acetonitrile solutions. *S*-Ferrocenyldithizone showed new waves with significant electrochemical shifts to higher potentials in the presence of metal ions. The shifts, however, do not differ much for different metal ions that were analysed. This factor makes this ligand non-selective towards mercury and copper ions, and also non-specific towards either aliphatic or aromatic organomercury ions under the conditions where the experiments were performed. Slow reactions of nickel with the reagent might have resulted in the absence of the new signal during titration with receptor **(13)**, however, this factor made the receptor to be selective towards copper in the presence of nickel ions.

S-Ferrocenylmethyldithizone **(14)** showed small electrochemical shifts in the presence of the metal ions. The type of recognition of metal ions, though not fully understood, was different to that of compound **(13)** with metal ions. The redox shifts were also not much different for various metal salt solutions, thus this receptor was also not selective towards different metal ions and not specific to organomercury ions. No new signal was observed when each receptor **(13)** or **(14)** was titrated with metal chlorides or organomercury chlorides. Generally, the factors discussed in the above paragraphs show a drawback for the development of the multi-responsive analytical method by one reagent. For example, if the receptor is to be immobilised on the electrode surface for the analysis of different metal ions in solution, one cannot distinguish which metal is giving a signal.

The detection of metals at very low concentrations (less than 10 mg L^{-1}) will be difficult, since at these concentrations the colour of the receptor–metal solutions were the same. The possible spectrophotometric method which can be applicable both in the qualitative (by visual colour observation) and quantitative analysis of metal ions is the titration of the ligand solution by the metal salt solutions at higher concentrations (greater than 10 mg L^{-1}). At these concentrations different metal ions give different colours of the solutions of the receptor–metal complexes. The types of recognition are not fully understood; however, during titration of the solutions of receptor **(13)** or **(14)** with Cu^{2+} the formazan group was most likely oxidised to form a tetrazolium salt. The potential of the ferrocene/ferrocenium couple of the tetrazolium salt and that obtained during titration with metal ions were not very different. The small differences can be accounted by the fact that in both cases the chemistry of the formazan binding site was changing causing a similar oxidation effect on the ferrocene/ferrocenium couple. This makes it difficult to differentiate between these processes. Numerous attempts to obtain the single crystal structures of the metal complexes by X-ray diffraction as an additional method for the understanding of the modes of recognition were unsuccessful.

In addition to the above conclusions, it is important to mention that though the main aim of this research project was focused on the recognition of the transition metal ions by these new organometallic analytical reagents, the possible applications of *S*-ferrocenyldithizone (a formazan) in the analyses of biological systems were also considered. The ability of this reagent to be oxidised makes it possible to be applied in the analytical systems such as the investigation of the anti-oxidative activity of compounds such as polyphenols.[21-26]

This can provide an alternative voltammetric method in such studies compared to the known available methods in which reagents such as 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical[21,22] and dichlorofluorescein-diacetate (DCFH-DA)[23] are used in spectrophotometry and fluorimetry, respectively. The oxidised form of *S*-ferrocenyldithizone, the tetrazolium salt, might also be applicable in the investigation of the viability of cells in various biological studies compared to the use of the well known salt 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT).[27,28]

To this end, preliminary experiments were conducted in dimethyl sulfoxide. Equal amounts of the new 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate were added to test tubes containing increasing concentrations of yeast cell culture. The mitochondrial enzyme (NADH) present inside the living cells reduces the salt to a formazan which absorbs in the UV-Vis region. The increase in absorbance at 415 nm was directly proportional to the concentration of the reduced form of the tetrazolium salt. This confirmed that the salt was reduced by the enzyme present in the cells.

4.7 EXPERIMENTAL

4.7.1 *Experimental details*

All the instrumental techniques used here, such as cyclic voltammetry, ^{1}H and ^{13}C NMR, UV-Visible spectroscopy, melting point determinations and details of materials and solvents were the same as those described in Section 2.6.1 of Chapter 2 and are not repeated here.

X-ray single crystal data was collected at 133(2) K on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, 54 kV, 22 mA). Data were reduced and scaled using DENZO-SMN software.[29] The structure was solved and refined using the program SHELX97.[30]

4.7.2 *Electrochemical recognition of the metal ions*

Both metal ion and ligand solutions were prepared in anhydrous acetonitrile with 0.1 M [n-Bu_4N][ClO_4] as supporting electrolyte. The scan rate used was 100 mV s^{-1} in all experiments. The concentration of the species under study was always *ca.* 1 mM (in 10 cm^3 of solvent). All titrations were performed using solutions of suitable concentration to allow delivery of one equivalent per 100 μL. The titrant solution was transferred using a micro-syringe. These solutions were prepared in the same acetonitrile electrolyte solution.

Caution: Extreme care must be taken when handling the very toxic methylmercury(II) salts. Only small quantities should be used, all operations should be conducted in an efficient fume-hood, and suitable protective clothing should be worn, including rubber gloves and face mask. All residues containing methylmercury(II) should be separately bottled and professionally treated by a waste management authority.

4.7.3 *Interaction of the new receptors with metal ions using UV-Vis spectroscopy*

Unless otherwise stated, all solutions were 1×10^{-5} M in sample, prepared with anhydrous acetonitrile containing 0.1 M $[n\text{-Bu}_4\text{N}][\text{ClO}_4]$. The instrument was zeroed against this electrolyte solution before each run. All titrant solutions were prepared so as to deliver carefully one equivalent per 100 μL using a micro-syringe. During each titration the reagent was added to 3 cm^3 of solution, this being thoroughly mixed before measurements were taken. Care was taken to avoid any losses of the solution during the procedure. In cases of interest, a portion of the final solution from the voltammetric titration was diluted in the ratio of 1 : 100 with acetonitrile electrolyte solution and an absorption spectrum recorded.

4.7.4 *Attempted synthesis of the metal complexes*

Two general methods were followed. In the first one, an ethanol solution of the metal salt (0.035 mmol) was added dropwise to the stirred ligand solution (0.070 mmol) in the same solvent. The stirring was continued for a minimum of 20 minutes; the resultant precipitate was filtered under vacuum and washed successively with ethanol. The tetrazolium salt was discovered when using this method. This experimental procedure was followed also when the analytical reagent was reacted with excess or equal amounts of the metal ion.

The second method was similar to that of Irving and Sahota.[14] The ethanol solution of the metal salt (0.25 mmol) was added dropwise to the stirred solution of the ligand (0.05 mmol) in the same solvent. The solid sodium acetate (0.1 mmol) was added as one portion to the reaction mixture. The stirring was continued for a minimum of 20 minutes.

The product was precipitated by the addition of water to the reaction mixture. The precipitate was filtered under reduced pressure and washed successively with ethanol.

REACTIONS OF METAL IONS AND RECEPTORS FOLLOWING METHOD ONE

Reaction of copper(II) and S-ferrocenyldithizone (**13**)

S-Ferrocenyldithizone (0.03 g, 0.07 mmol) was dissolved in dichloromethane (10 cm^3). To this solution was added dropwise a solution of copper perchlorate (0.01 g, 0.03 mmol) in ethanol (5 cm^3). Blue-black solid precipitated out of the solution within five minutes of the reaction. The reaction mixture was stirred at room temperature for 30 min. The precipitate was filtered and washed with ethanol. The product was purified by recrystallization from dichloromethane-hexane mixture. Crystals suitable for X-ray analysis were grown from slow evaporation of chloroform solution. The product, 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate (**3**), crystallized as blue-black needles. The yield of the product was 45% and the melting point obtained was 224 °C (dec.). Similar results were obtained when using an equivalent or an excess amount of copper perchlorate or copper chloride under the same conditions.

^{1}H NMR ($CDCl_3$) δ_H; 4.30 (5H, s), 4.41 (2H, t, J = 1.90 Hz), 4.72 (2H, t, J = 1.90 Hz) and 7.57 ppm (10H, m). Elemental analysis for $C_{23}H_{19}ClFeN_4O_4S$ [found (calculated)]; C 47.99 (51.27), H 3.67 (3.55), N 8.54 (10.40) and S 5.19 (5.95). Repeated recrystallization attempts did not yield any better microanalysis results; however, the crystal structure analysis was unambiguous.

Reactions of mercury(II) or phenylmercury(II) and S-ferrocenyldithizone (**13**)

A solution of phenylmercury acetate (0.01 g, 0.03 mmol) or mercury acetate (0.01 g, 0.03 mmol) in ethanol (5 cm^3) was added dropwise to the solution of *S*-ferrocenyldithizone (0.03 g, 0.07 mmol) in dichloromethane (10 cm^3). In both cases the colour of the initial solution of *S*-ferrocenyldithizone changed from red-brown to green upon addition of the metal ion solution. The reaction mixture was stirred at room temperature for 30 min. The solvent was then removed under reduced pressure. Recrystallization from various solvent mixtures did not precipitate the product. Purification by flash chromatography on silica or alumina eluting with benzene resulted in the decomposition of the product to the starting materials. Similar results were obtained when using an equivalent molar amount or an excess of the metal ion solutions under the same conditions.

REACTIONS OF METAL IONS AND RECEPTORS FOLLOWING METHOD TWO[14]

Reactions of mercury(II) or phenylmercury(II) and S-ferrocenyldithizone (**13**)

A solution of phenylmercury acetate (0.07 g, 0.25 mmol) or mercury acetate (0.07 g, 0.25 mmol) in ethanol (5 cm^3) was added dropwise to a solution of *S*-ferrocenyldithizone (0.03 g, 0.07 mmol) in ethanol (10 cm^3). Solid sodium acetate (0.03 g, 0.22 mmol) was added as a single portion. In both cases the colour of the initial solution of *S*-ferrocenyldithizone changed from red-brown to green upon addition of the metal ion solution. The reaction mixture was stirred at room temperature for 30 min. Water (30 cm^3) was added to the reaction mixture. A green powdery material precipitated out of the solution. This material was then filtered and washed with copious amount of water to remove the excess salt, then dried under vacuum. ^{1}H NMR spectroscopy of the crude material showed some resonances corresponding to the starting ligand (**13**) but no definite conclusions could be drawn. Recrystallization from various solvent mixtures did not precipitate the product. Purification by flash chromatography on silica or alumina, eluting with benzene, resulted in the decomposition of the product to the starting materials.

Reaction of nickel(II) and S-ferrocenyldithizone (**13**)

A solution of nickel(II) chloride hexahydrate (0.07 g, 0.25 mmol) in ethanol (5 cm^3) was added dropwise to a solution of *S*-ferrocenyldithizone (0.03 g, 0.07 mmol) in ethanol (10 cm^3). Solid sodium acetate (0.03 g, 0.22 mmol) was added as a single portion. The colour of the initial solution of *S*-ferrocenyldithizone remained unchanged after one hour of the reaction process. The reaction mixture was then stirred and heated under reflux for an additional five hours. The colour of the solution turned to grey. Water (30 cm^3) was added to the reaction mixture. No precipitate was observed. Ethanol was removed under vacuum. The solution turned back to red-brown during extraction of the product by dichloromethane from the water layer. Similar results were obtained when various nickel salts were employed under the same conditions.

Reactions of metal ions and S-*ferrocenylmethyldithizone* **(14)**

S-Ferrocenylmethyldithizone (0.03 g, 0.07 mmol) was dissolved in dichloromethane (10 cm^3). To this solution was added dropwise a solution of a metal salt (0.03 mmol) in ethanol (5 cm^3). A red-orange precipitate was observed upon addition of the solution of the metal salt to the receptor solution following each method mentioned above. ^{1}H NMR investigations of this material indicated loss of the ferrocenyl group and it was concluded that the material was a decomposition product. Reactions with the following metal salts were conducted: phenylmercury(II) acetate, mercury(II) acetate, mercury(II) chloride, copper(II) perchlorate, copper(II) chloride and nickel(II) chloride.

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CHAPTER 5

OVERALL CONCLUSIONS

This work was composed of two broad areas of investigation. In the first area the interactions between photochromic and redox properties were investigated for two new mercury dithizonate compounds, namely (*N*,*S*-dithizonato)(ferrocenyl)mercury(II) **(11)** and (ferrocene-1,1′-diyl)bis[(*N*,*S*-dithizonato)mercury(II)] **(12)**. These new photochromic mercury dithizonate compounds containing a ferrocenyl group as a redox-active substituent were successfully synthesised. The supporting evidence for their characterisation was obtained from UV-Vis spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry and cyclic voltammetric data. These data showed that the new compounds were fully characterised and pure, though some difficulty was experienced obtaining satisfactory elemental analyses. Many attempts were made to grow crystals suitable for X-ray diffraction but these were not successful. The new mercury(II) dithizonate compounds prepared in this work were found to be photochromic in various non-polar organic solvents. The data obtained from UV-visible spectroscopy for compounds **(11)** and **(12)** were found to be similar to the spectral data that have been obtained for other known mercury(II) dithizonate complexes. There were no interactions observed between the photochromic and redox properties in either compound, as evidenced from the cyclic voltammetric results.

This study could be expanded and other possible investigations for this potential interaction could be pursued, such as the following: firstly, the preparation of mercury(II) dithizonate complexes with ferrocenyl substituents on mercury and on one of the phenyl groups of dithizone. The interaction between the resulting two redox-active substituents could be investigated in the different photo-isomers of the specific compound. Secondly, various mercury(II) dithizonate complexes with ferrocenyl substituents on both phenyl rings of dithizone could also be interesting to investigate; conjugation in the thiocarbazone chain will allow through-bond interaction between the redox-active substituents which may be either weaker or stronger in the blue or orange forms. Through-space interactions between substituents will also be different in the orange or blue forms; there should be a shorter distance between the redox-active centres in the blue compared to the orange form of the resulting mercury(II) dithizonate compounds. These varying distances could result in different electrochemical interactions between the redox-active centres and these could be monitored by cyclic voltammetry. The preparation of such envisaged new compounds would undoubtedly present some synthetic challenges!

The second area of this work involved the preparation of the new analytical reagents (**13**) and (**14**), with the objective being to investigate the electrochemical recognition of some transition and organotransition metal ions by these new reagents. New dithizone derivatives containing ferrocene were successfully synthesised; the low yields of products might be improved by modifying the synthetic methods which were followed in this work. The derivative with the ferrocene group bonded directly through sulfur [compound (**13**)] was found to exhibit similar isomerisation behaviour to the previously prepared *S*-methyldithizone compounds, while dilute solutions of the dithizone derivative with a methylene group linker [compound (**14**)] was found to decompose upon exposure to sunlight. Characterisation of these compounds was performed by UV-Vis spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, mass spectrometry and cyclic voltammetry. Even after many attempts, crystals suitable for X-ray diffraction were not obtained.

The cyclic voltammetric results showed that the two new receptors do electrochemically recognise the metal ions Cu^{2+}, $PhHg^{+}$ and $MeHg^{+}$, while Ni^{2+} was only recognised by receptor (**14**), though the mechanism of interaction was uncertain and certainly different for Cu^{2+} compared with the organomercury ions. Experiments performed by UV-Vis spectroscopy showed that there was an interaction between the metal ions and the receptors in acetonitrile solutions. *S*-Ferrocenyldithizone (**13**) showed a new wave with a significant electrochemical shift to higher potential in the presence of metal ions. The shifts, however, do not differ much for the different metal ions that were analysed. This factor makes this ligand non-selective towards mercury and copper ions, and also non-specific towards either aliphatic or aromatic organomercury ions under the conditions of the experiments.

S-Ferrocenylmethyldithizone (**14**) showed only small electrochemical shifts in the presence of the metal ions. The type of recognition of metal ions, though not fully understood, was different to that of compound (**13**) with metal ions. The redox shifts were also not much different for various metal salt solutions, thus this receptor was also not selective towards different metal ions and not specific to organomercury ions. No new signal was observed when each receptor (**13**) or (**14**) was titrated with metal chlorides or organomercury chlorides. Generally, the factors discussed in the above paragraphs are not favourable for the development of a multi-responsive analytical method using one reagent. For example, if the receptor is to be immobilised on an electrode surface for the analysis of different metal ions in solution, one would not be able to distinguish which metal was giving the signal.

The spectrophotometric detection of metals at very low concentrations (less than 10 mg L^{-1}) would be difficult, since at these concentrations the colour of the receptor–metal solutions was the same as the free ligand. A possible spectrophotometric method which might be applicable both in the qualitative (by visual colour observation) and quantitative analysis of metal ions is the titration of the ligand solution by the metal salt solutions at higher concentrations (greater than 10 mg L^{-1}). At these concentrations different metal ions gave different colours of the solutions of the receptor–metal complexes.

The precise modes of the receptor–metal interactions are not fully understood; however, during titration of the solutions of receptor (**13**) or (**14**) with Cu^{2+} the formazan group was most likely oxidised to form a tetrazolium salt. The potential of the ferrocene/ferrocenium couple of an authentic sample of the tetrazolium salt and that obtained during titration with metal ions were not very different. The small differences may be accounted for by the fact that in both cases the chemistry of the formazan binding site was changing, exerting a similar influence on the ferrocene/ferrocenium couple. This made it difficult to differentiate between these processes. Numerous attempts to obtain single crystal structures of the metal complexes by X-ray diffraction as an additional method for the understanding of the modes of recognition were unsuccessful.

In the absence of crystal structures of receptor–metal complexes, the solutions of receptors during titration with metal ions might be monitored by mass spectrometry (ESI-MS) to confirm various species forming in the solution. It would also be important to perform titrations and reactions of metal ions with receptors at various pH levels and in various solvents. We showed in this work that the new receptors (**13**) and (**14**) displayed interactions with some metals ions in solution; further derivatives of these receptors might be synthesised to improve selectivity towards various metal ions.

In addition to the above conclusions, the possible applications of *S*-ferrocenyldithizone (**13**) (a formazan) in the analysis of various systems was also considered. The ability of this reagent to be oxidised makes it possible to be applied in analytical systems such as the investigation of the anti-oxidative activity of compounds like polyphenols. This might provide an alternative sensitive voltammetric method in such studies compared to the known available protocols, in which reagents such as the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and dichlorofluorescein-diacetate (DCFH-DA) are used in spectrophotometry and fluorimetry, respectively. The *S*-ferrocenyldithizone reagent should also find applications in the quantitative analysis of electrochemically reducible metal ions such as Cu^{2+}, Au^{3+} and Tl^{3+} by oxidation of the ligand. Finally, we briefly considered a biological application of the new 5-ferrocenylthio-2,3-diphenyltetrazolium perchlorate to the determination of the viability of cells in various drug-activity studies compared to the use of the well-known salt 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT).

Clearly the chemistry of these new receptor ligands is just beginning to be explored, and much remains to be discovered!