Synthesis and Evaluation of PGM-Selective Ligands

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By

BABALWA SILIZIWE BLOSSOM GXOYIYA

BSc (UCT), BSc. Hons (Rhodes)

Department of Chemistry

Rhodes University

Grahamstown

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Abstract

A series of polydentate PGM-selective, sulfur-containing amide ligands have been synthesized from ω–dibromoalkanes and mercaptoacetanilide. The resulting 3,6-dithiaoctanediamides and 3,7-dithianonanediamides, some of which contain a polymerisable group, were all characterized by high-resolution MS, IR, ^{1}H and ^{13}C NMR spectroscopic methods. Various approaches to the polymerisable ligands were explored, the most efficient proving to be the incorporation of an allyl ether moiety in the mercaptoacetanilide. The corresponding Pd(II) and Pt(II) complexes were also prepared from the metal chloride salts and characterized by elemental analysis and spectroscopic methods. The NMR data indicates that both the *cis*- and *trans*-complexes were formed, while the IR data indicates *cis*- coordination of the chlorine ligands.

Molecularly imprinted polymers (MIP`s), prepared using platinum(II) mercaptoacetanilide and 3,6-dithiadiamide complexes, showed high selectivity for palladium(II) [in the presence of Pt(II), Co(II), Cu(II) and Ni(II)] as determined by ICP-MS analysis. The more kinetically inert Pt(II) ions however, slowly displaced Pd(II), confirming the Pt(II) selectivity of the MIP`s.

Solvent extraction studies were conducted to explore the selectivity of the 3,6-dithiaoctanediamides and 3,7-dithianonanediamides for Pd(II) over Co(II), Cu(II) and Ni(II). The ICP-MS data indicate that, in general, equilibration was achieved within ten minutes and that the longer-chain amides were less selective than the shorter-chain analogues.

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LIST OF ABBREVIATIONS

AIBN	Azobis(isobutyronitrile)
COSY	Correlation Spectroscopy
DDPA	1,12-Dodecanediol-*O,O`*-diphenylphosphonic acid
DEPT	Distortionless Enhancement by Polarization Transfer
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
EGDMA	Ethylene glycol dimethacrylate
EtOH	Ethanol
HMBC	Heteronuclear Multiple Bond Coherence
HMQC	Heteronuclear Multiple Quantum Coherence
ICP-MS	Inductively Coupled Plasma mass spectrometer
LAH	Lithium aluminium hydride
MIBK	Methyl isobutylketone
MIP`s	Molecularly imprinted polymers
PGM	Platinum group metals
SDS	Sodium dodecylsulfate
THF	Tetrahydrofuran
TRIM	trimethylolpropane trimethacrylate
W/O	Water-in-oil
W/O/W	Water-in-oil-in-water

CONTENTS

1. Introduction

The six second- and third-row transition metals in groups 8, 9 and 10 are commonly known as the platinum group metals (PGM`s). These elements, ruthenium, osmium, rhodium, iridium, palladium and platinum, are very rare, platinum being the most common with an abundance of $10^{-6}$ %. The PGM`s are known to be relatively inert and occur as metals, alloys or sulfide ores and are sometimes associated with each other or with base metals such as nickel, copper, silver and gold.[1-5] They are all greyish white in colour and may be isolated as powders when their salts are heated. In fact, almost all compounds of these elements afford the corresponding free metal when heated.[1,2]

1.1. Chemistry of Platinum Group Metals

The PGM`s share some similarities in their chemistry, but there are also certain differences in the relative stability of their oxidation states and the corresponding stereochemistry.

1.1.1. Oxidation States

Certain PGM`s may exist in oxidation states ranging from 0 to +8, but the range is somewhat more limited (0 to +6) for platinum and palladium. Consequently, the chemical properties of Pt and Pd tend to be similar. For palladium the most stable state is +2, while in platinum the +2 and +4 states are the most stable. The divalent states of Pd and Pt have the electronic configurations, $[Kr]d^8$ and $[Xe]d^8$ respectively, and form complexes of all possible types, *i.e* ML_4^{2+}, ML_3X^+, *cis*- and *trans*- ML_2X_2, MLX_3^- and MX_4^{2-}. Pt(II) and Pd(II) generally show a low affinity for F^- and O^- ligands, which are classified as hard bases, but a high affinity for halogens and ligands that can π bond, e.g., R_3P, R_2S, CN^-, NO_2^-, alkenes and alkynes, all of which are classed as soft bases.[1,2] The complexes of the bivalent state are diamagnetic except for the Pd^{2+} ion in PdF_2, which is paramagnetic.[1,2,5] Pd(II) is kinetically more active than

Pt(II). The tetravalent states of Pd and Pt have the electronic configurations, $[Kr]d^6$ and $[Xe]d^6$ respectively, and form complexes of the Werner type, $M(L\text{-}L)_3$ or $M(L\text{-}L)_2X_2$, where L-L is a bidentate ligand and X is a monodentate ligand such as Cl^-.[6] All complexes of tetravalent Pt and Pd are diamagnetic. Unlike Pt(II), Pt(IV) has a low affinity for soft ligands, is reduced to Pt(II) by most phosphine, arsine and thiol ligands and is kinetically inert.[3]

1.1.2. Stereochemistry

Palladium and platinum ions rarely exhibit coordination numbers greater than six. While coordination numbers range from 4 to 6 for divalent platinum and palladium, the most common coordination number is four and is associated with square planar geometry.[1-5] Tetrahedral geometry has been observed for some tetra-coordinate complexes, although no complex with this geometry has yet been isolated.[5] The penta-coordinate states form square pyramidal {e.g. $[Pd(TPAs)Cl]^+$} and trigonal bipyrimidal complexes {e.g. $[Pt(SnCl_3)_5]^{3-}$}.[5]

For tetravalent platinum and palladium ions, however, the most common coordination number is six, and the geometry of the complexes tends to be octahedral or slightly distorted octahedral.[5]

1.2. Uses of Platinum Group Metals

Metallic platinum finds application in:-

i) jewelry;
ii) electrical engineering;
iii) temperature measurements;
iv) chemical engineering, including catalysis; and
v) dentistry and medicine.

1.2.1. Jewelry

The jewelry industry is the largest consumer of PGM`s. Both platinum and palladium alloys are widely used. The palladium is used to discolor gold and the resulting Pd-Au alloy is known as the white gold.[3,7] A palladium alloy containing 4% ruthenium and 1% rhenium is also used in watch making.[7]

1.2.2. Electrical Engineering

Because of their freedom from film formation, platinum and palladium alloys are used in electrical engineering as contact materials, especially where reliability of operation is of high importance.[3,7] Platinum is used to coat missile nose cones and jet engine fuel nozzles, which must perform reliably for a long time at high temperatures.[7] It is also used increasingly in making hard disks for personal computers, as platinum-containing disks show superior data-storage properties.[8] Palladium is used to make multi-layer ceramic capacitors, which are used in computers and mobile phones.[8] Because of their high ferromagnetic properties, cobalt-platinum alloys are used as permanent ferromagnets, like the powerful Co-Pt magnet (composed of 23.3% Co and 76.7% Pt by weight), which has a magnetic strength, B-H (max), twice as large as that of the Al-Ni-Fe-Co magnet, Alnico V.[3,7,9]

1.2.3. Temperature measurements

The purest platinum is used for the construction of high-resistance thermometers and thermocouples. A platinum thermometer is used to define the International Temperature Scale from –182.97°C, the boiling point of oxygen, to 961.78°C, the freezing point of silver.[3,10] Platinum:platinum-rhodium thermocouples are used to accurately measure temperatures above 1000°C.[3]

1.2.4. Chemical Engineering

Platinum and its alloys are used for the construction of components, which are subjected to corrosive materials and high temperatures. In this context, it is interesting

to note that platinum has a high resistance to fluorine compounds, including hydrofluoric acid at high temperature.[3] Platinum alloys are used in the glass industry, as they are the only metallic materials that can withstand exposure to high temperature in a non-reducing atmosphere.[3,11] Platinum also has a wide range of applications in electrode coatings and in catalysis see (**Section 1.2.4.1**) and is finding use as an electrocatalyst in fuel cell applications.[12-14]

1.2.4.1. Platinum- and Palladium-Based Catalysts

The catalyst industry is the second largest consumer of PGM`s and both platinum and palladium are widely used.[15] They are used as homogenous or heterogeneous catalysts in many organic reactions to catalyse hydrogenation, hydrosilylation, isomerisation and hydroformylation.[4] Platinum is also used as a platinum-rhodium alloy in catalytic converters in the motor-car industry.[15]

1.2.4.1.1. Hydrogenation

Palladium and platinum are used as heterogeneous catalysts or, in the form of soluble complexes, as homogeneous catalysts. Unlike Raney nickel, which is used at high temperature and elevated pressure, platinum and palladium catalysts can be used at room temperature and atmospheric pressure.[16,17] In homogenous hydrogenation, both platinum(II) and palladium(II) complexes may be used, but platinum(II) complexes, of the form PtX_2L_2 or $PtHXL_2$, are far more widely used; they are used for the hydrogenation of ethylene and acetylene and, particularly, in the reduction of polyolefins to mono-olefins.[5]

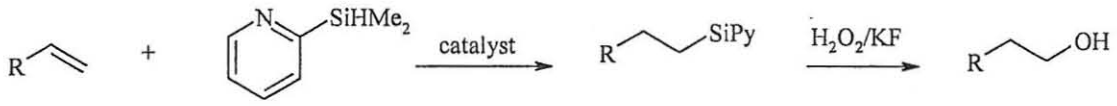
The most widely used heterogeneous palladium catalysts are the palladium-on-carbon (Pd/C) catalysts. They are used in the reduction of a wide range of functional groups, including the reduction of aromatic nitro to aromatic amine, nitrile to amine, acetylene to alkane and alkyl halide to alkane.[16] Platinum dioxide is used for the heterogeneous reduction of alkenes.[16,17]

1.2.4.1.2. Hydroformylation

Both platinum and palladium complexes are used commercially for the hydroformylation of alkenes to afford linear and branched aldehydes. The palladium-catalyzed process, widely known as the Wacker process, uses $PdCl_2$ as a catalyst. The complex $Pt[H(SnCl_3)(CO)(PPh_3)_2]$ is also an active catalyst for the hydrofomylation of 1-pentene and gives a *ca* 20:1 ratio of straight-chain to branched-chain aldehyde when used with synthesis gas (CO/H_2) at 100°C and 3000psi.[5] Platinum dioxide is used in the oxidation of primary alcohols to acids and the oxidation of diols to lactones.[16] Fine platinum wire is used to catalyze the exorthemic oxidation of methanol vapour to form formaldehyde– a reaction which is used commercially in cigarette lighters and hand warmers.

1.4.2.1.3. Hydrosilylation

Hydrosilylation is a very useful tool for generating carbon–silicon bonds from unsaturated carbon – carbon bonds. The silyl group is easily oxidized to the hydroxyl group and this is a very useful method for the synthesis of structurally diverse alcohols from simple precursors.[18]



Metal-catalysed hydrosilylation is also useful for the regio- and stereoselective introduction of carbon-silicon bonds.[18,19] Platinum complexes such as H_2PtCl_6, K_2PtCl_4 and platinum black are used as catalyst for the hydrosilylation of olefins. Although Pt(II) complexes are effective catalysts, Pt(IV) complexes (such as chloroplatinic acid, H_2PtCl_6) are by far the most widely investigated. When used with ethyl alcohol, H_2PtCl_6 is known as the Speier catalyst and is effective at very low concentration (10^{-5}-10^{-8} mol Pt/mol reactant).[5]

1.2.4.1.4. Isomerism

The hydride complexes of Pt(II) and Pd(II) are used in the isomerisation of olefins, especially unconjugated diolefins to conjugated olefins, but palladium complexes tend to be more active in effecting such transformations.[4,5]

1.2.5. Dental and Medical Applications

Both platinum and palladium are used in dentistry as tooth fillings, but palladium is more widely used as it is less expensive. They are also used to make surgical and laboratory instruments, but in medical applications, platinum is more widely used.[3]

Metal-based drugs are used in medicine for various reasons. Thus, the metal centre may participate in redox reactions or undergo stereoselective ligand substitution with biological molecules, while some metal ions are used as radioactive isotopes.[20] The PGM's; ruthenium and platinum, are both used in cancer therapy, but platinum is far more widely used.[21,22] The platinum-based drugs shown in **Figure 1** are used clinically (**1** and **2**) while the others are in clinical trials (**3, 4** and **5**) for the treatment of testicular, ovarian, bladder, head and neck cancers and small-cell lung cancer. Cisplatin **1** has proved to be very successful in the treatment of testicular cancer; carboplatin **2**, however, exhibits reduced toxic side effects, especially nephrotoxicity, compared to cisplatin **1**. Patients develop resistance to both these drugs after long periods of use, and the Pt(IV) drug tetraplatin **3** is in trial to counteract this side-effect.[22] It is expected that the Pt(IV)-based drug JM-216 **4** will be orally administered because of its hydrophobic nature, coupled with the inertness of the Pt(IV) center, renders it easily absorbed.[22] The Pt(II)-based drug **5** is in trial for the treatment of colo-rectal cancer.[23]

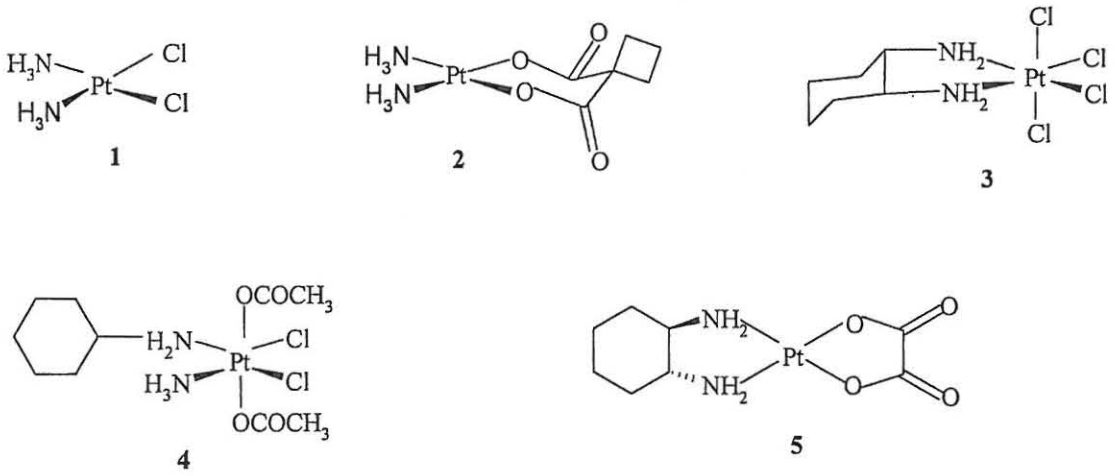


Figure 1: Platinum-based anti-cancer drugs:[22,23] cisplatin **1**; carboplatin **2;** tetraplatin **3**, JM-216 **4** and oxaliplatin **5**.

1.3. Individual Extraction of Platinum Group Metals

Since the PGM`s are scarcely distributed in nature and have a wide range of applications, their market value tends to be very high. Hence, methods of recovering the metals from ores (as primary metals) or from industrial residues (as secondary metals) are of great economic importance.[15,24-26] Two common recovery processes are used. The first, which has been employed for a long time, involves precipitation and filtration. The second method, currently used for the separation of PGM`s from base metals such as iron, nickel, copper and cobalt, involves solvent extraction.[27] In the latter method, complexes are formed between the metals and metal-specific ligands in aqueous or non-aqueous media. The PGM`s are particularly suited for solvent extraction because they have a half-filled *d* subshell and exhibit several oxidation states.[28] These two properties are an added advantage because the former is responsible for complex formation between the metal and the ligand and latter allows for the change in the extraction properties of the metal when the oxidation is made. The solvent extraction approach can be applied using either ion-exchange or liquid-liquid extraction technology.

1.3.1 Extraction of Pt and Pd as Primary Metals

The extraction of PGM`s from various ores is a complicated process and depends on the type of ore. PGM-bearing ores typically contain base metals such as nickel, copper, cobalt and iron. For a long time, the most common procedure involved precipitation and filtration of the individual metals from the ores.[3,5] In this process the ore is crushed, finely ground and then treated by flotation and magnetic methods to separate the mineral sulfides from the nickel concentrate, which contains most of the PGM`s. The nickel concentrate is heated with coke and sodium bisulphate to dissolve the copper sulfide in preference to nickel sulfide. On cooling two layers separate, copper sulfide at the top and nickel sulfide at the bottom. The nickel layer is separated and is electrolytically refined, permitting deposition of the platinum metals on the anode.[3,5]

The platinum metal concentrate is extracted with *aqua regia*, which dissolves most of the gold, palladium and platinum and leaves a residue containing ruthenium, rhodium, iridium and silver chlorides (**Figure 2**). Iron(II) sulfate is then added to the filtrate to precipitate out impure gold, which is purified by the Wohlwill electrolytic process.[5] The solution is then treated with ammonium chloride to precipitate platinum as ammonium hexachloroplatinate(IV) $[(NH_4)_2PtCl_6]$, which is dried and ignited at 1000°C to form a platinum sponge. The impure platinum sponge is dissolved in *aqua regia* and precipitated with sodium chloride and hydrochloric acid as sodium hexachloroplatinate(IV) (Na_2PtCl_6), which is purified by sodium bromate hydrolysis. Re-precipitation with ammonium chloride followed by ignition affords the pure platinum sponge.[3,5]

The filtrate from the ammonium chloride precipitation is treated with excess ammonia and then with hydrochloric acid to precipitate palladium as *trans*-$Pd(NH_3)_2Cl_2$. This salt is slowly ignited at 1000°C to form palladium sponge.

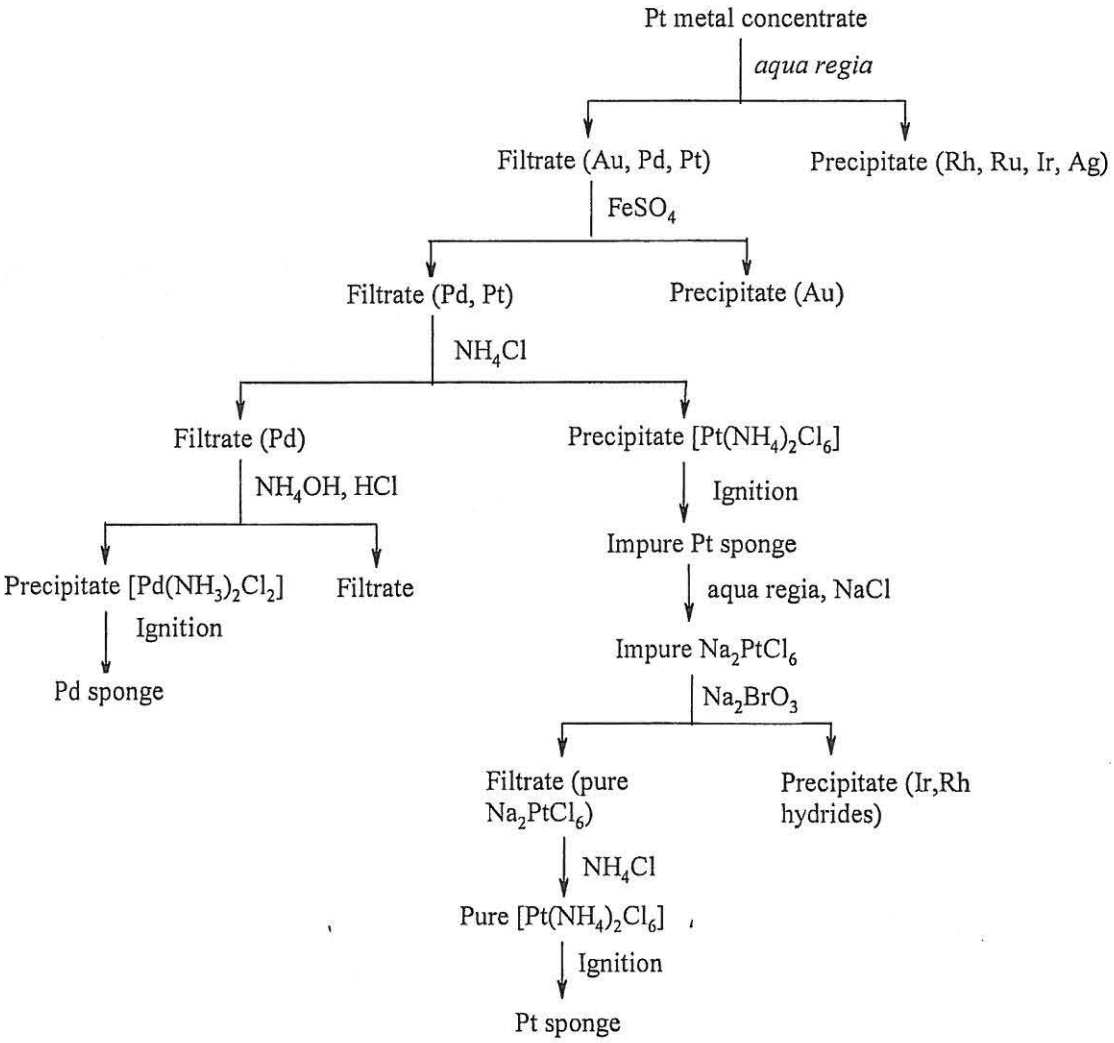


Figure 2: Separation of platinum and palladium from other PGM`s and base metals.[3,5]

Ion-exchangers have also been investigated for separating PGM`s from the base metals that are associated with them.[25,29,30] Silica-based ion-exchangers with polyamine functional groups have been reported to show selectivity for the PGM`s, Pd, Pt and Rh, over the base metals, Cu, Ni and Fe, in industrial base metal refining (BMR) and precious metal refining (PMR). Maximal extraction is achieved when they are employed as continuous extractors.[25]

1.3.2 Extraction of Pt and Pd as Secondary Metals

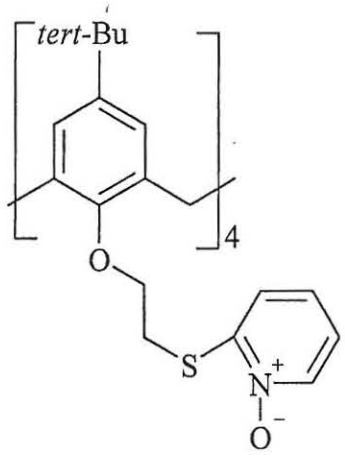
Separation of metal ions such as palladium and platinum from base metals with ion exchangers is effected by the use of either cationic or anionic exchange resins.[29,30] With cationic-exchangers, the base metal ions bind to the resin while Pd and Pt ions pass through the column; in chloride-rich solution platinum and palladium form stable anionic chloro-complexes while, the base metals form cationic complexes. While with anionic-exchangers, the base metal ions pass through the column while the Pd and Pt ions are retained in the column.[29,30] High selectivity for Pt and Pd ions over base metal ions has been reported for strongly basic anion exchangers that contain styrene or acrylic polymers cross-linked with divinyl benzene.[29]

Liquid-liquid extraction has also been employed for the extraction of PGM`s from industrial wastes, using a wide range of extractants, including oxygen-, sulfur-, nitrogen- and phosphorous-containing extractants.[28] Triphenylphoshine and its derivatives has been used as anion-exchange resins to extract platinum(IV) from acidic media.[31] Liquid-liquid extractions of PGM`s from spent catalyst using organophosphine ligands have been reported by Nowottney[15] and Dhadke.[32]

Since the PGM`s are relatively kinetically inert, additives like $SnCl_2$, $SnBr_2$, I^-, SCN^-, Br^-, pyridine, *etc*, are added as catalysts to increase the extractive strength of the ligand.[28,33] Studies of the extraction of palladium, platinum and rhodium using Kelex 100 in toluene have shown that Pd is quantitatively extracted in low acidic medium (<2**M** HCl) while Pt is quantitatively extracted in high acidic medium (6**M** HCl). On addition of the additive $SnCl_2$, rhodium, which is more kinetically inert than both Pt and Pd, is quantitatively extracted over Pt and Pd in both high and low acid medium.[33] *N*-Octylaniline has been reported to be a selective extractant for palladium(II);[34] the selectivity is observed when a 1:1 aqueous ammonia solution is used as the back extraction agent. [34]

Extraction of PGM`s with sulfur containing extractants has been investigated using dialkyl sulfides, disulfides of the type $RSCH_2SR$ and $RSCH_2CH_2SR$ and alkyl sulfoxides.[28] Such extractants have been shown to be selective for palladium and

platinum over the other PGM`s with palladium showing good extractability.[28] Liquid-liquid extraction of palladium(II) with *N*-benzoyl-*N'*,*N'*-diethylthiourea has shown high extraction rates.[35] Liquid-liquid extraction of platinum(II) with cyclic tetrathioethers has been investigated and was observed that tetrathioethers with larger rings were much more efficient than tetrathioethers with smaller rings even though a longer shaking time is required.[36] The calix[4]arene **6** shows particular selectivity for platinum(IV) over palladium(II) and platinum(II).[26]



6

1.4. Molecularly Imprinted Polymers

1.4.1. Definition of Molecularly Imprinted Polymers

MIP technology is concerned with synthetic polymers with specific recognition sites. It has been likened by Shea to "casting a plaster mold of someone's right hand" – a mold which can only fit that person's right hand,[37] or by Mosbach to making molecular locks with specific keys. The technology is based on the concept of enzyme-substrate specificity in biological systems and was first demonstrated by Wulff and co-workers in the early 1970`s.[38,39] The technique involves, initially, polymerization of an assembly of the "print molecule" and the "functional monomer" to give a "highly cross-linked, rigid, glassy polymer" with functional groups placed in specific sites.[39-42] Subsequent removal of the functional monomer then affords the MIP. The assembly can be prepared using two basic approaches, *viz.*, pre-organized or self-organized assembly.

The pre-organized assembly system, introduced by Wulf and co-workers, involves the formation of covalent bonds between the print molecule and the functional monomer.[38,41,43] The self-organized assembly systems, introduced by Mosbach and co-workers, involve the formation of coordinate or non-covalent bonds between the functional monomer and print molecule.[38,41,43]

1.4.2. Preparation of MIP`s

Preparation of an MIP typically requires a "print molecule", a "functional monomer", a cross-linking agent, a solvent system (a "porogen") and a radical initiator.[44]

1.4.2.1. The "print molecule"

The "print molecule", which is sometimes called the template, key or imprint molecule, is the selected target of the imprinting procedure.[44] The "print molecule" can either be a metal ion or an organic compound. Examples of previously used print molecules are listed in **Table 1**.

Table 1: Examples of print molecules employed in MIP synthesis.[38]

Compound Class	Example
Proteins	Immunoglobulin G, serum albumin[37]
Amino Acids	phenylalinine, tryptophan, tyrosine[45,46]
Pesticides	Atrazine[38,47]
Therapeutic Drugs	diazepam, theophiline[48]
Steroids	Cortisone[37]
Nucleotide Bases	Adenine[38]
Metal Ions	Co^{2+}, Zn^{2+}[39,42,49]

1.4.2.2. The "functional monomer"

This is a polymerisable entity, which interacts with the "print molecule". These monomers have specific chemical functionalities such as carboxyl, hydroxyl, amino or aromatic groups, that can bind to the "print molecule" covalently and/or non-covalently. The print molecule determines the nature of the monomer.

1.4.2.3. The cross-linking agent

The cross-linking agent (cross-linker or "molecular glue") is a polymerisable system with two or more groups to which the "functional monomer" can be attached. Many cross-linkers are available, but those common in MIP synthesis are listed in **Figure 3**.

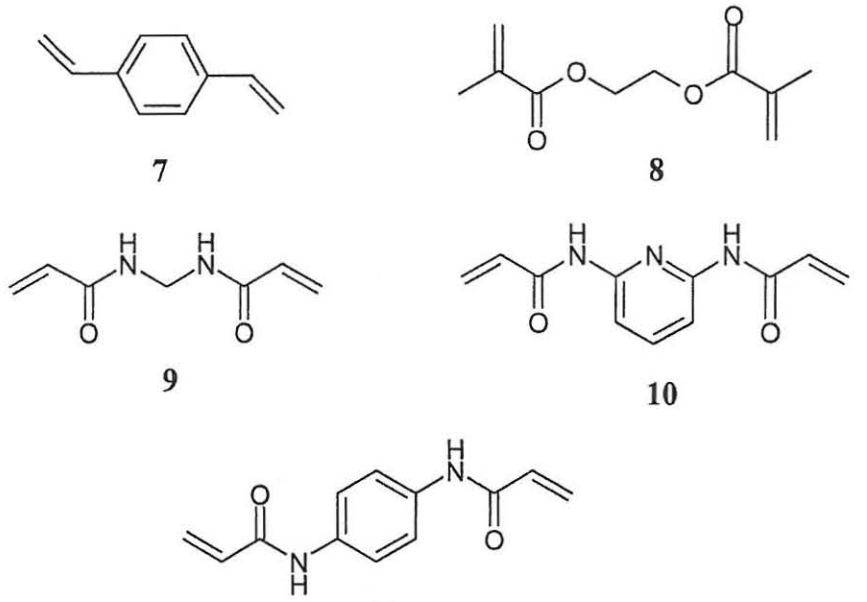
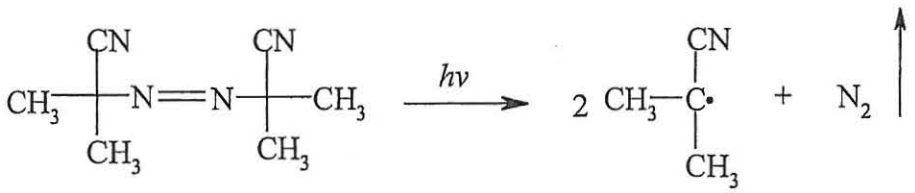


Figure 3: Examples of cross-linkers commonly used in MIP synthesis:- divinylbenzene (DVB) **7;** ethylene glycol dimethacrylate (EGDMA) **8,** bis(acrylamido)methylene **9**, 2,6-bis(acrylamido)pyridine **10** and bis(acrylamido)-*p*-phenylene **11**.

1.4.2.4. The "initiator"

This is a substance used to start the polymerization process, most of which are radically initiated. The most widely used initiator is azobis(isobutyronitrile) (AIBN) **12** because it decomposes at 40°C to form cyanopropyl radicals **13** and is easy to purify.[50]



12 **13**

Scheme 1: Formation of cyanopropyl radicals from AIBN. [50]

1.4.2.5. The porogen

This is the solvent in which the entire polymerization procedure is performed. It is thus called because one of its functions is to take up space so as to produce a porous material. Examples of such solvents are CH_2Cl_2, $CHCl_3$ and CH_3CN.

1.4.2.6. Preparation of the MIP

Preparation of the polymer involves *in situ* pre-arrangement or complexation of the "print molecule" with the "functional monomer" through covalent bonds, using appropriate chemistry, or non-covalent bonds,[41,43] followed by polymerization in the presence of excess cross-linking agent in a suitable solvent (**Figure 4**). Since the polymerization is typically radically induced, an initiator may be added to the solution to start the polymerization process.

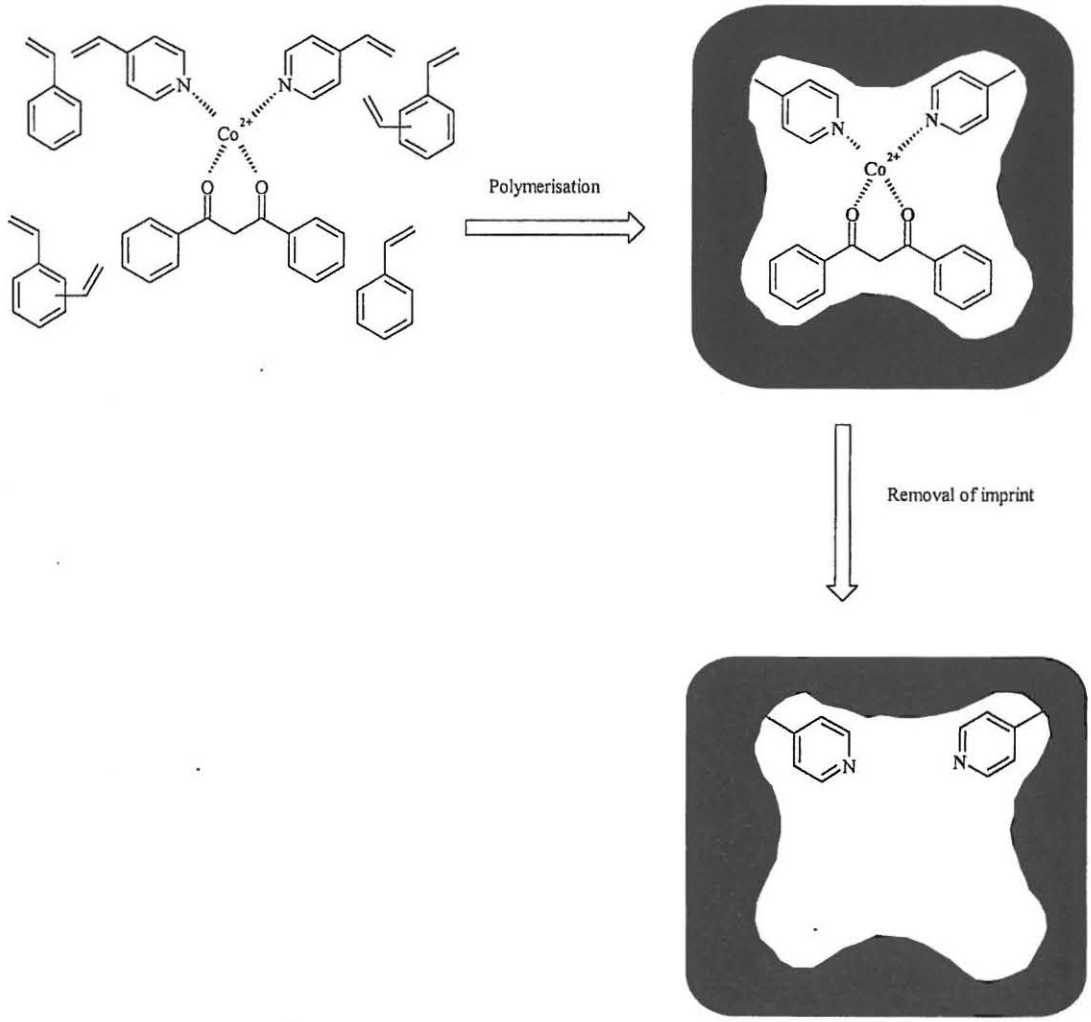


Figure 4: Preparation of a catalytically active cobalt(II) MIP- selective for aldol condensation reactions.[49]

1.4.3 Uses of Molecularly Imprinted Polymers

Since its development some 30 years ago, MIP technology has found use in a wide range of applications. These include:-

i) separation and isolation of various substances
ii) sensors in biosensor-like devices
iii) enzyme/substrate mimics in immuno assay-type analysis and
iv) catalytic applications in organic synthesis.

1.4.3.1 Isolation and separation applications

MIP`s are widely used for the separation and isolation of a wide variety of compounds, including steroids, therapeutic drugs, sugars, metal ions and amino acids.[39] In most cases, MIP`s are used as the stationary phase or sorbent in chromatographic techniques such as high pressure liquid chromatography (HPLC)[51,47] and thin layer chromatography (TLC),[52] or as solid phase extractants (SPE)[41,53,54] for the pre-concentration and separation of racemic mixtures. Shea has reported the use of MIP`s for the chiral recognition of benzodiazepines.[52] The MIP`s were used as stationary phases in HPLC and showed discrimination between enantiomers of the imprinted benzodiazepines as well as enantiomers of structurally similar molecules, which had not been imprinted. Armstrong has reported the HPLC separation of D- and L-phenylalanine anilide using a bubble-fractionating method with phenylalanine anilide imprinted MIP as a collector.[46] The achievement of racemic resolution using MIP`s is attributed to the fact that the polymers are custom made with the exact cavity-shape and the exact arrangement of functional groups for a particular enantiomer.[55,56] The separation of metal ions has also been investigated (See Section **1.4.4**).

1.4.3.2 MIP`s as bio-sensor-like devices

MIP technology is finding application in the construction of biosensor-like devices. The MIP is coated on to the sensor device or electrode and, when the substance of interest interacts with the MIP, a signal, such as fluorescence, is promoted. Fish[57] has

investigated such devices using *N*-(4-vinylbenzyl)-1,4,7-triazacyclononanes (TACN) polymers containing fluorescent groups and coordinated mercury ions. The polymer is expected to shine when mercury ions are encountered in polluted streams. Hirayama and co-workers have prepared a sensor, which can detect acetaldehyde in dilute environmental samples at a threshold concentration of $\geq$ 0.015mmol/L, using a quartz crystal microbalance (QCM) sensor coated with acetaldehyde imprinted polymer.[58]

1.4.3.3 Antibody/receptor binding mimics

MIP`s had their origin in immunology, and Mosbach[48] has reported their use as substitutes for antibodies in immunoassay techniques. MIP`s imprinted with the drugs, theophylline and diazepam, were used as antibody mimics in a competitive binding assay called "molecularly imprinted sorbent assay" (MIA) for determining these drugs in human serum. The MIA method for theophylline proved to be more selective than the MIA method for diazepam, when tested for cross-reactivity with other metabolites.

1.4.3.4 Applications of MIP`s in catalysis and organic synthesis

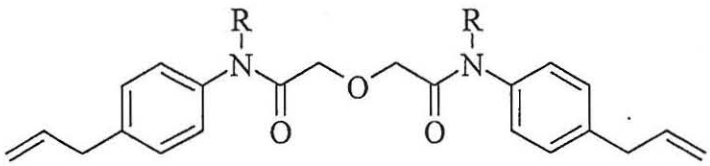
Antibodies are known to act as catalysts in many biological transformations, hence MIP`s which have been developed to mimic antibody activity are now being made to generate substrate-selective catalytic behaviour. MIP`s with predictable catalytic activities (or "plastic enzymes", as described by Mosbach[38]) have been made using a "transition state analogue (TSA)" as the imprint molecule,[38,40,59] while Shea[60] has produced a catalytically active organic MIP for dehydrofluorination reactions. Catalytically-active, metal-containing MIP`s have been reported by Mosbach,[49] who prepared a cobalt-containing polymer imprinted with aldolate TSA to catalyse the entropically unfavoured aldol condensation of acetophenone and benzaldehyde to chalcone. Severin[59,61] has prepared polymers imprinted with an organometallic ruthenium complex TSA to catalyze the asymmetric hydrogenation of aromatic ketones.

Gagné[40] has investigated the use of metal-containing MIP`s in creating chiral cavities with optically active ligands to catalyze asymmetric transformations. The kinetics and

thermodynamics of ligand substitution reactions were investigated on polymers imprinted with Pt(II) complexes. The study revealed that the polymer had different Pt(II)-accessible sites associated with chiral cavities; the less accessible sites were more selective but the more accessible were less selective – an unfavourable situation for asymmetric catalysis. It is predicted that selective poisoning of the more accessible sites could solve the problem.[40]

1.4.4. Metal-selective MIP`s

Molecular imprinting has also been investigated for use in the separation of metal ions from aqueous solutions. Mosbach and co-workers[62] have investigated the separation of calcium(II) from magnesium(II) and other alkali metal ions. Preparation of the metal-selective MIP involved synthesis of the functional monomer, the 3-oxapentanediamide **14b**, complexation of the "print molecule", $CaCl_2$, by **14b**, and polymerization with DVB **7** to afford a highly cross-linked polymer. Removal of the imprinted metal ion gave an MIP, which showed selectivity for calcium(II) over magnesium(II) and other alkali metal ions. 3-Oxapentanediamide derivatives have been known to show selectivity for calcium(II) over magnesium(II), when used as electrically neutral carriers in ion-selective electrodes.



	R
a	H
b	CH_3

14a,b[10]

Murray and co-workers[63] have used MIP technology to prepare a uranyl ion-permeable membrane. The selectivity of the membrane was introduced by imprinting with uranyl ion while permeability was achieved by using polyesters, which interact with the uranyl ions but have long alkyl chains which control the spacing of the active sites. The membrane was prepared using uranyl vinylbenzoate [$UO(VBA)_2$], styrene, DVB, a polyester prepared from 1,6-hexanediol and diglycolic acid, nitrophenyl octyl ether (NPOE) as the plasticizer and AIBN. Competitive experiments showed that the

membrane exhibited selective permeation of $[UO_2]^{2+}$ ions over Ni(II), Cd(II), Cu(II) and Zn(II) ions, while a reference membrane, prepared by imprinting with Ni(II) showed little permeation of UO_2^{2+} but high permeation of the competing ions.

Fish[57] has investigated the use of MIP`s in the extraction of precious metals such as gold and silver from aqueous solution. He prepared the polymers by complexing the desired metal ion, for example zinc or mercury, with two organic ligands [*N*-(4-vinylbenzyl)-1,4,7-triazacyclononanes, (TACN`s)] in a "sandwich" form; cross-linking of the complex resulted in polymer. Washing with strong acid removed the metal ions and empty sites, which can accommodate similar ions, were formed. Grinding the polymer into a fine powder and passing a solution of metal ions through the polymer results in the metal ions being trapped in the polymer, and thus removed from solution.

Fish[57] observed that the ionic radii of the metals, the thermodynamic stability of the interaction between metal ions and the ligand, and the shape of the imprinted site all affect the selectivity of the MIP. Competitive experiments with zinc, copper and other metal ions showed that the Cu(II) ions were trapped more than the Zn(II) ions (157:1). This selectivity was attributed to the thermodynamic stability of the association with Cu(II), since Cu(II) and Zn(II) ions have similar ionic radii. Thus, while both ions will be trapped by the polymer, the association of the TACN with Cu(II) is thermodynamically more stable than the association with Zn(II). Competitive experiments with Cu(II), Fe(III) and other metal ions showed that Cu(II) is trapped more efficiently than Fe(III) (44:1), in spite of the fact that the free TACN ligand prefers Fe(III) ions. This observation was attributed to the shape of the zinc imprinted polymer site; since Cu(II) has a similar radius to Zn(II) it is trapped more efficiently than Fe(III), which has a smaller radius.

Yoshida and co-workers[39,42] have, in the last decade, developed a new imprinting technology called, "Surface Template Polymerisation Technique". This technique was developed with the aim of overcoming the shortcomings of conventional MIP technology, which include slow rebinding kinetics and the difficulty of using MIP`s with water-soluble substances. The polymer is prepared by water-in-oil (W/O) emulsion polymerization (**Figure 5**), and the process requires a "functional

monomer", a "print molecule", an emulsion stabilizer and a cross-linker. The W/O emulsion uses the aqueous-organic interface as the recognition area for the water-soluble imprint molecule.

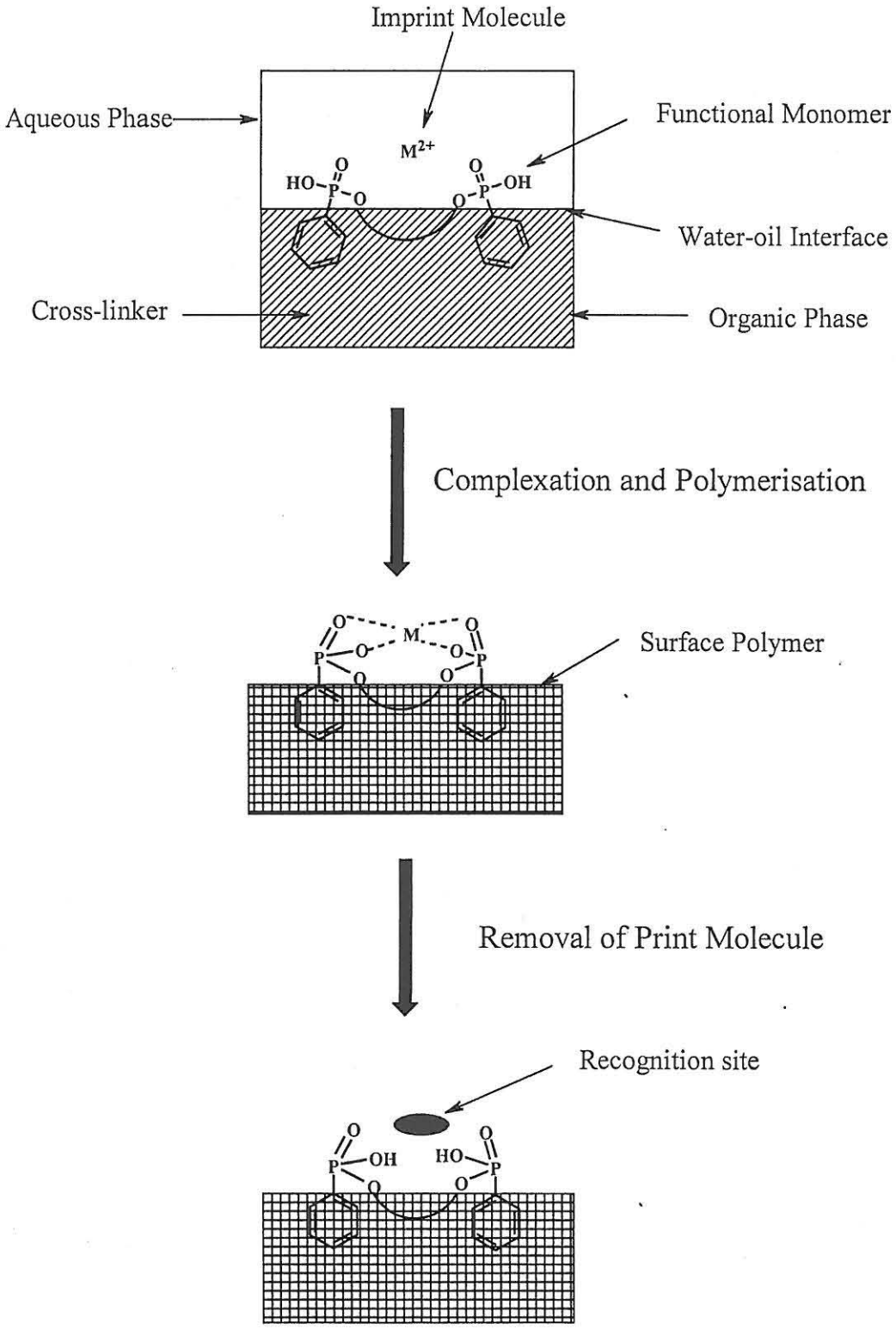
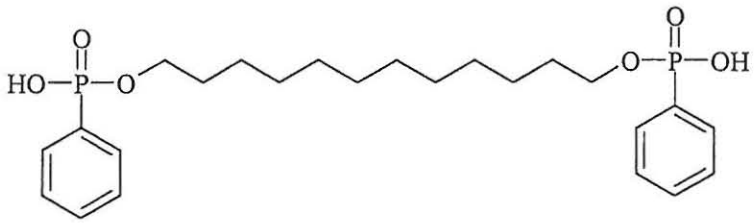
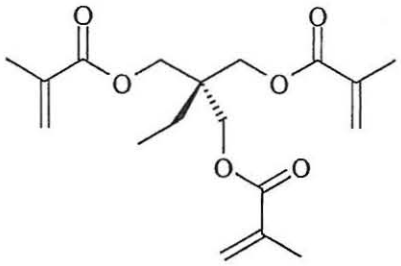


Figure 5: Illustration of surface template polymerisation.[39]

Complexation of the print molecule and the amphilic functional monomer occurs at the interface and the resulting complex, which has a well-ordered pattern is polymerised in such a way that the recognition sites are formed on the surface of the polymer and not in the polymer matrix, as is the case with conventional MIP`s.[40,43] Three factors were observed to increase the template effects of the functional monomer, namely, the presence of a longer alkyl chain which leads to high interfacial cavities, aromatic rings, which form rigid recognition sites, and metal recognition groups, which produce high binding affinity for the target metal ion.[39,42] A zinc-specific polymer has been prepared by Yoshida and co-workers,[42] using W/O and W/O/W emulsions with 1,12-dodecanediol-*O,O`* diphenylphosphonic acid (DDPA) **15** as the functional monomer, trimethylolpropane trimethacrylate (TRIM) **16** as the cross-linker, the dioleyl *N*-ribonyl-L-glutamate (ribatol) **17** as the emulsion stabilizer and sodium dodecylsulfate (SDS) **18** as the dispersion stabilizer (**Figure 6**). Competitive studies with Zn(II) and Cu(II) ions using zinc-imprinted and unimprinted W/O and W/O/W emulsion polymers, showed high selectivity for zinc ions over copper ions in the pH range 1-4. While the un-imprinted polymers showed similar adsorption for both ions, the W/O polymer was more selective than the W/O/W polymer.[39]



15



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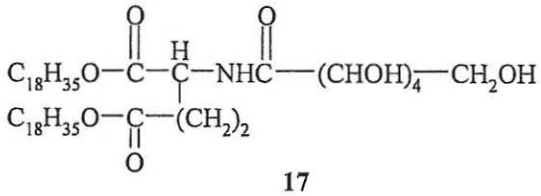

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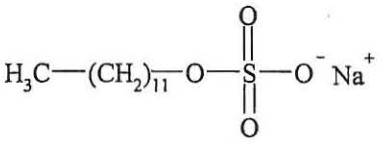


18

Figure 6: Structures of the reagents used in surface template polymerisation; DDPA **15**, TRIM **16**, ribatol **17** and SDS **18**.[42]

1.5 Previous work in the group

Previous work done in our research group has been directed at designing, synthesizing and evaluating biomimetic and metal-selective ligands. Wellington[64] synthesized copper(II) complexes and cobalt(II) analogues, as biomimetic ligands, to model the active site of the enzyme, tyrosinase.

In the development of metal-specific ligands, Hagemann[65] investigated the development of PGM-selective ligands by designing and synthesizing bidentate, tridentate and tetradentate sulfur-containing ligands to selectively chelate platinum(II) and palladium(II) in the presence of base metals. Daubinet[66] synthesized polydentate malonamide derivatives to selectively chelate silver(I) in the presence of base metals, and used computer modelling to explore the mode of coordination of the ligands to the metal; extraction studies showed that the ligands were, in fact, silver(I) selective.

More recently, Tshikudo[67] developed bidentate ligands containing amine and pyridyl moieties, designed to selectively bind nickel(II) in the presence of iron(III) and to contain a vinyl group for the construction of MIP's. Evaluation of these MIP's confirmed their selectivity for nickel(II), with equilibration being achieved within five minutes.

1.6 Aims of the Present Study

The PGM`s have a wide range of application and, in nature, they usually occur with gold, silver and the major base metals nickel, copper, iron and cobalt.[27] It is economically important that the PGM`s should be recovered and recycled in high yield and purity. Traditionally, separation and purification of the PGM`s has been achieved by precipitation and filtration, but there are limitations, such as co-precipitation, associated with this method.[3,5] More recently, solvent extraction techniques have been employed in the separation and purification of these metals. This methodology uses metal-selective ligands to form complexes between the metal and the ligands thus facilitating separation of the PGM`s from the base metals.

The obvious importance of the PGM`s and the need to explore alternative separation techniques promoted the present investigation, the specific aims of which have included the following.

i) Synthesis and characterization PGM-selective sulfur-containing amide ligands, including polymerisable systems.

ii) Characterisation of the corresponding palladium(II) and platinum(II) complexes using spectroscopic and X-ray crystallographic methods.

iii) Preparation and evaluation of platinum(II)-selective MIP`s.

iv) Evaluation of the sulfur-containing amide ligands in solvent extraction applications.

2. Discussion

In the following discussion attention is given to:- the design, synthesis and characterization of monomeric and dimeric PGM-selective ligands (section 2.1); the design, synthesis and characterization of polymerisable ligands and their use in the preparation of PGM-selective MIP`s (section 2.2); complexation of the various ligands with palladium and platinum (section 2.3); and, finally, solvent extraction studies (section 2.4).

2.1. Monomeric and Dimeric PGM-Selective Ligands

2.1.1. Ligand Design

The ligands which are used in industry as extractants for the solvent extraction of metal ions are organic soluble, easy to synthesize and relatively cost effective. Our ligand systems were designed with similar objectives. The ligand systems targeted in this study contain a secondary amide function and a sulfur donor atom. This system was designed to complex platinum or palladium with the sulfur donor atom, for which they have high affinity, because both platinum and palladium are classified as soft acid and sulfur atom is a soft base. The targeted ligand systems **19** and **20** incorporate the following structural features:

i) S and N atoms for metal chelation;
ii) an aromatic ring to increase the lipophilicity of the ligand;
iii) an amide functionality for platinum and palladium selectivity;
iv) an R group to fine-tune N-donor capacity ; and
v) additional sulfur donors for multi-dentate coordination with the metal center(s).

Retrosynthetic analysis **Figure 7** indicates disconnection of the initially targeted ligands **19** to the readily available precursors, which in fact, provided the basis for our synthetic efforts. The synthesis thus involved two phases, *viz.*, i) formation of the monomeric

mercaptoacetanilides **21**; and ii) condensation of the two monomeric mercaptoacetanilide molecules with ω-dibromoalkanes **22** to afford the target ligands **19** and **20**.

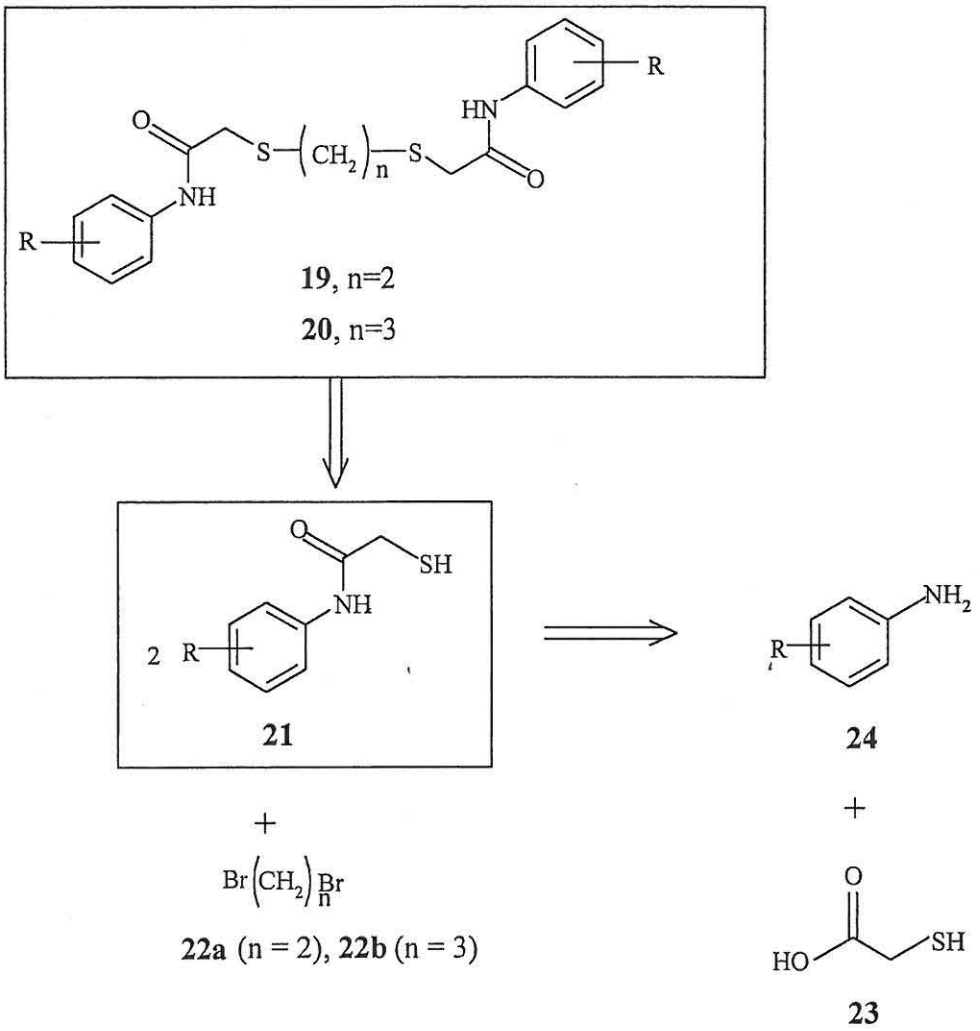
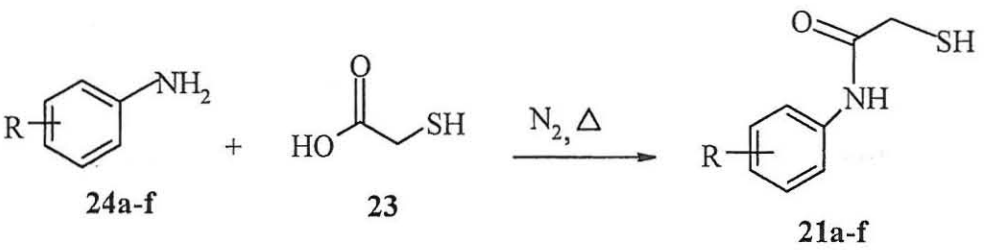


Figure 7: Retrosynthetic analysis of the targeted ligand **23** and **24**

2.1.2. Synthesis of the Mercaptoacetanilide Monomer Units

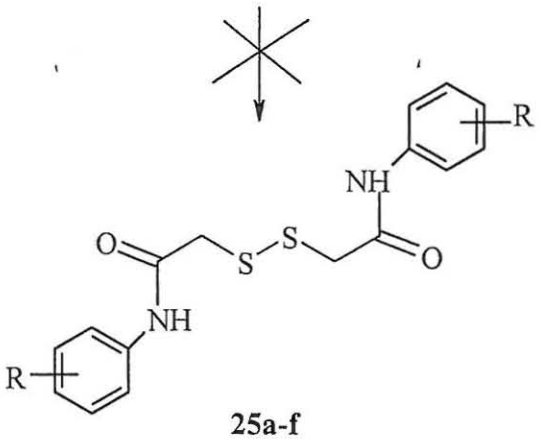
The mercaptoacetanilides **21a-f** were prepared following the method described by Hagemann,[65] which involves heating mercaptoacetic acid **23** and the appropriate aniline **24a-f** as a 1:1 mole ratio mixture under a gentle stream of dry nitrogen (**Scheme 1**). The nitrogen helps to prevent oxidation of the mercaptoacetanilides **21a-f** to the disulfides

25a-f and to remove the water formed during the reaction. The nitrogen flow is, however kept low so as to prevent loss of the reactants in the gas stream and a consequent reduction in yield. The crude mercaptoacetanilides **21a-f** were purified by recrystallization from ethanol-water mixtures and the pure products were generally isolated in moderate yields (40 - 60%; **Table 2**). The structures of the mercaptoacetanilides were verified by spectroscopic analysis. The infrared spectra all show a sharp NH band at *ca* 3300 cm^{-1}, a weak SH band at *ca* 2570 cm^{-1} and a sharp amide carbonyl band at *ca* 1660 cm^{-1}.



24a-f **23** **21a-f**

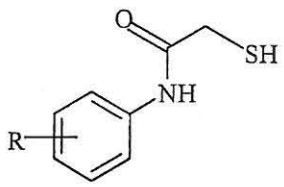
Compound	R
a	H
b	*p*-OCH_3
c	*o*-OCH_3
d	*m*-Cl
e	*o*-Cl
f	*o*-CH_3



25a-f

Scheme 2: Synthesis of mercaptoacetanilides

Table 2: Data for the mercaptoacetanilides **21a-f**



Compd.	R	Yield [a]/%	Mp [b]/°C	ν_{NH}/cm^{-1}	ν_{SH}/cm^{-1}	ν_{CO}/cm^{-1}
a	H	42	110-114 (110-111)	3300	2573	1648
b	*p*-OCH_3	56.8	116-120 (118.5-119.5)	3283	2575	1652
c	*o*-OCH_3	54	64-66 (64-66)	3324	2557	1669
d	*m*-Cl	49.7	82-84 (70-73)	3293	2545	1655
e	*o*-Cl	27	54-56 (56-59)	3256	2557	1659
f	*o*-CH_3	46	80-82 (88-90)	3356	2526	1651

[a] Isolated material. [b] Following recrystallisation from ethanol/water (2:1) mixture; lit.[65] values in parentheses.

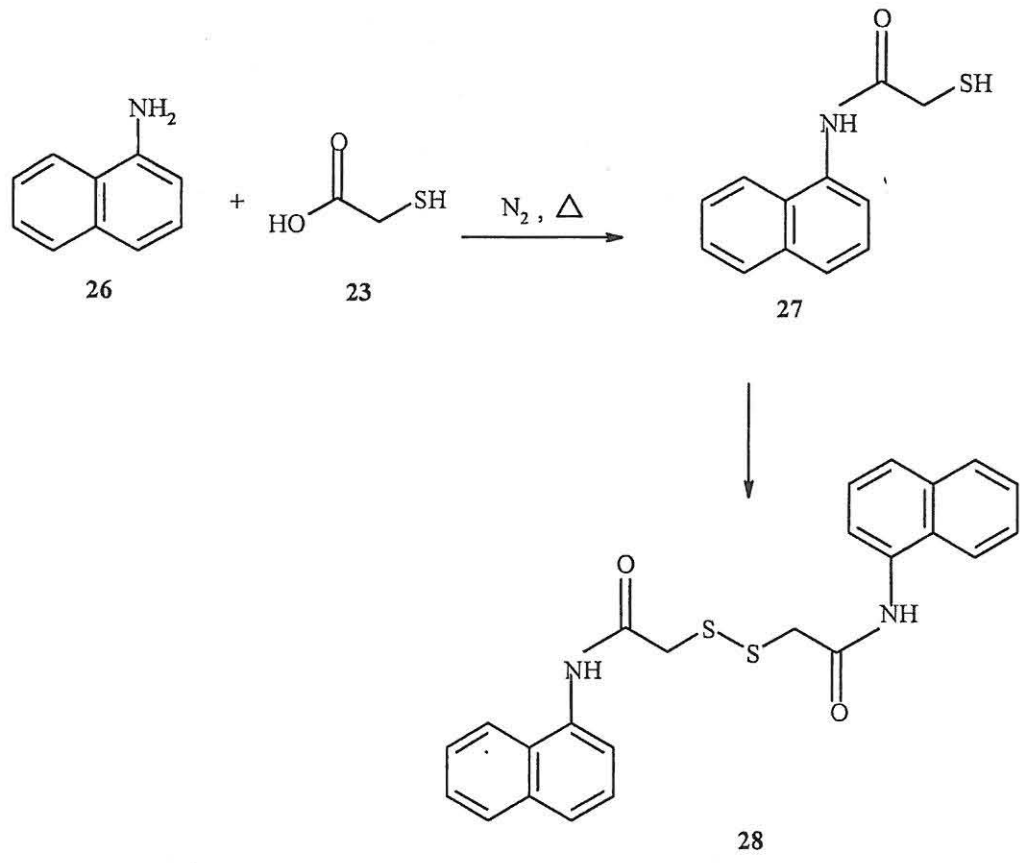
Table 3: ^{1}H NMR and ^{13}C NMR Chemical shift data (ppm) for the mercaptoacetanilides **21a-f**

Compound	R	δ_H[a] SH	δ_H[a] NH	δ_C[a] CH_2	δ_C[a] CO
a	H	2.01	8.45	29.0	167.6
b	*p*-OCH_3	2.00	8.37	29.0	166.9
c	*o*-OCH_3	2.02	9.00	29.4	167.0
d	*m*-Cl	2.02	8.48	29.1	167.1
e	*o*-Cl	3.01[b]	9.67[b]	27.8[b]	168.9[b]
f	*o*-CH_3	2.02	8.51	29.1	167.1

[a] In $CDCl_3$. [b] In DMSO-d_6

The ^{1}H NMR spectra (illustrated for compound **21d** in **Figure 8a**) all show a broad singlet in the region δ 8-9ppm, due to the amide proton and a triplet at *ca* 2 ppm due to the thiol proton, while the ^{13}C NMR spectra (illustrated for compound **21c** in **Figure 8b**) all show a signal at *ca* 29 ppm due to the methylene carbon and a signal at *ca* 167ppm due to the carbonyl carbon.

Attempts were made to prepare a bulkier ligand, containing naphthyl rather than phenyl groups. 1-Aminonaphthaline **26** was therefore treated with mercaptoacetic acid in a 1:1 mole ratio and the mixture was heated under reflux for 3h in a stream of dry nitrogen. Unfortunately, under these conditions, the mercaptoacetanilide **27** was oxidized to form the disulfide **28** (**Scheme 3**). The ^{1}H NMR spectrum of the disulfide **28** reflected the absence of the thiol proton, a triplet at *ca* 2ppm.



Scheme 3: Attempted synthesis of 2-mercapto-*N*-α-naphthylethanamide 27.

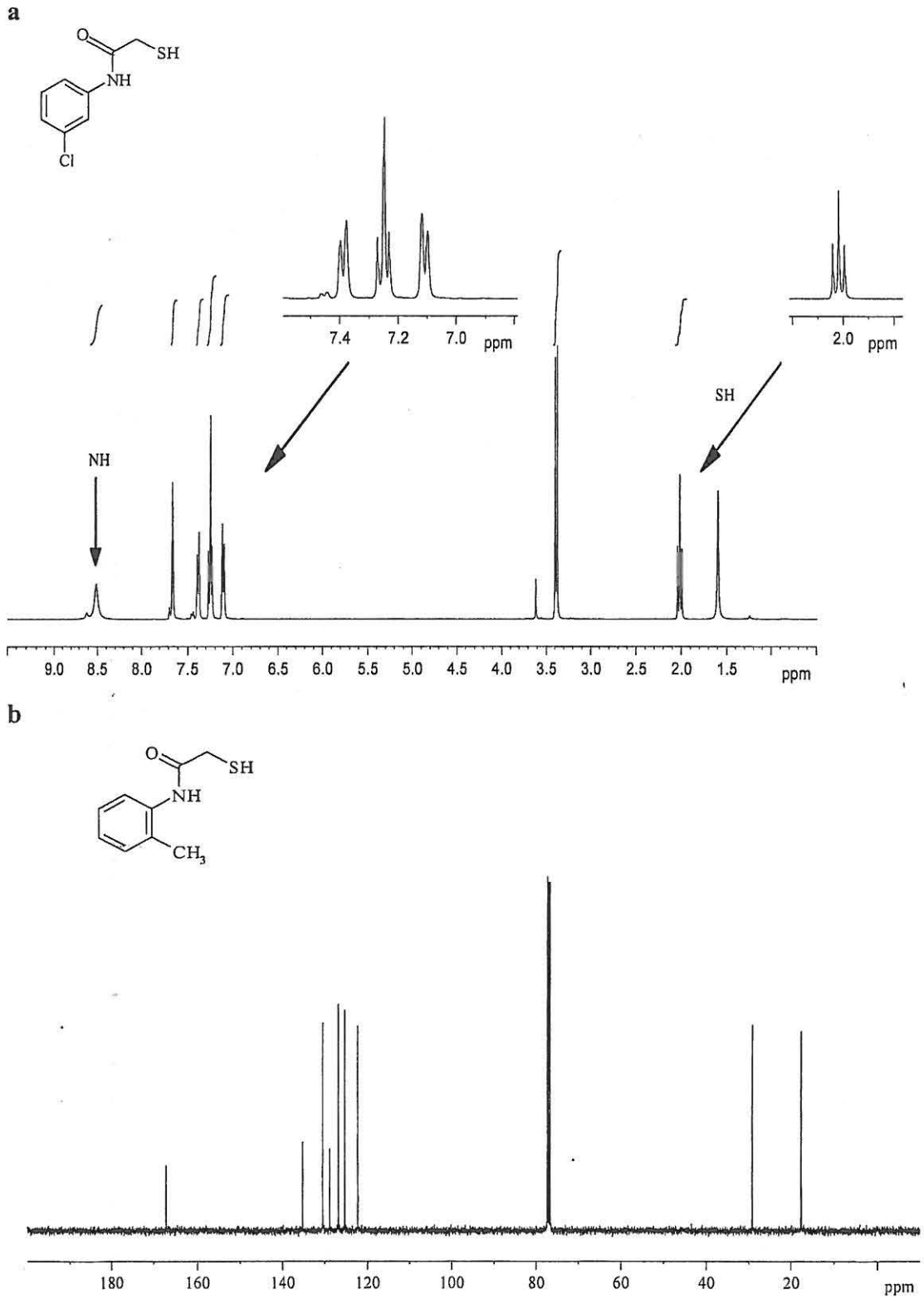
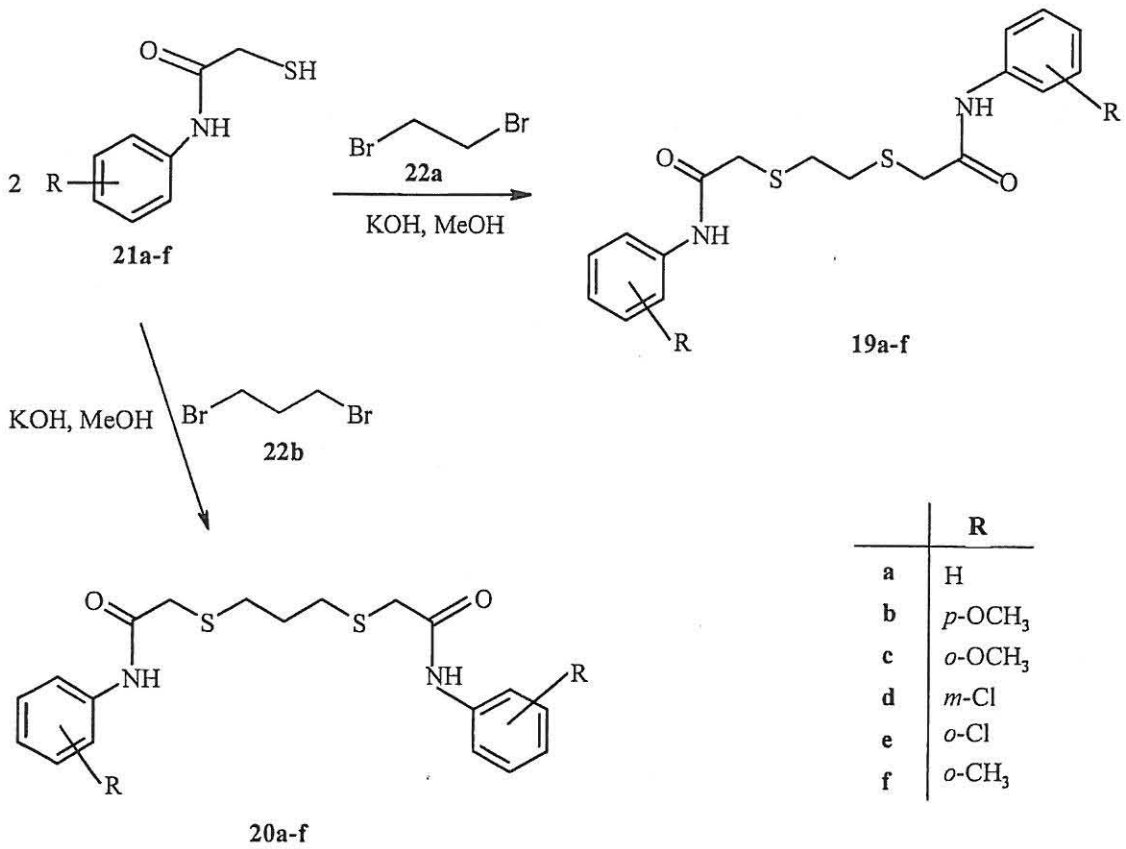


Figure 8: a) 400MHz ^{1}H NMR spectrum for the mercaptoacetanilide **21d** in $CDCl_3$. b) 100MHz ^{13}C NMR spectrum of the monomer ligand **21f** in $CDCl_3$.

2.1.3. Synthesis of the Dimeric Ligands

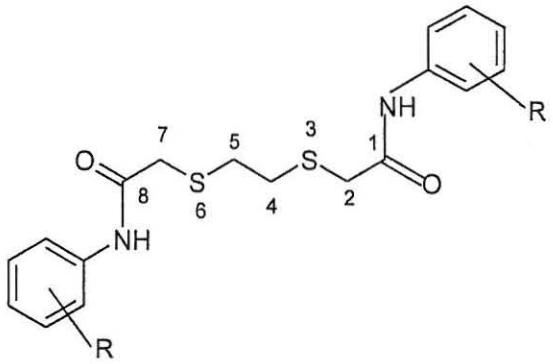
Having obtained the monomeric ligands **21a-f**, attention could be given to the formation of the targeted ligands **19a-f** and **20a-f** respectively. This involved coupling of the mercaptoacetanilides **21a-f** (**Section 2.1.2**) with 1,2-dibromoethane and 1,3-dibromopropane in methanolic potassium hydroxide, following the method described by Hagemann[65] (**Scheme 4**). Purification was achieved by recrystallization from ethanol and, in some cases, by both flash chromatography and recrystallization. The diamide products **19a-f** were isolated in reasonable yields (30-60%), except for the ligand **19d** which was isolated in low yield, (< 20%; **Table 4**). The structures of the ligands were verified by spectroscopic methods. The IR data in all cases show an NH band at *ca* 3300cm^{-1} and a sharp amide carbonyl band at *ca* 1655cm^{-1}. The ^{1}H NMR spectra (illustrated for compound **19a**; **Figure 9a**) show a broad signal in the region δ 8–9ppm due to the amide NH and two sharp methylene singlets at *ca* 2.9ppm and 3.4ppm, integrating for four protons each. The absence of an SH band at *ca* 2500cm^{-1} in the IR spectra and a corresponding signal in the ^{1}H NMR spectra confirms the coupling of alkyl halide **22a** with the mercaptoacetaniledes **21a-f** through sulfur instead of nitrogen. While the ^{13}C NMR spectra (illustrated for compound **19b; Figure 9b**) shows an extra signal in the methylene region δ30-40ppm.



	R
a	H
b	*p*-OCH_3
c	*o*-OCH_3
d	*m*-Cl
e	*o*-Cl
f	*o*-CH_3

Scheme 4: Synthesis of diamide ligands 19a-f and 20a-f

Table 4: Data for the 3,6-dithiaoctanediamide ligands **19a-f**



Compound	R	Yield [a]/%	Mp. [bo]C	ν_{NH}/cm^{-1}	$\nu_{C=O}/cm^{-1}$
a	H	43	160-162 (150-152)	3305	1650
b	*p*-OCH_3	48	178-182 (163-165)	3292	1654
c	*o*-OCH_3	60	138-142 (137-140)	3293	1661
d	*m*-Cl	17.5	120-122 (114-117)	3317	1658
e	*o*-Cl	29.7	176-178 (165-167)	3273	1656
f	*o*-CH_3	32.5	178-184 (176-178)	3274	1651

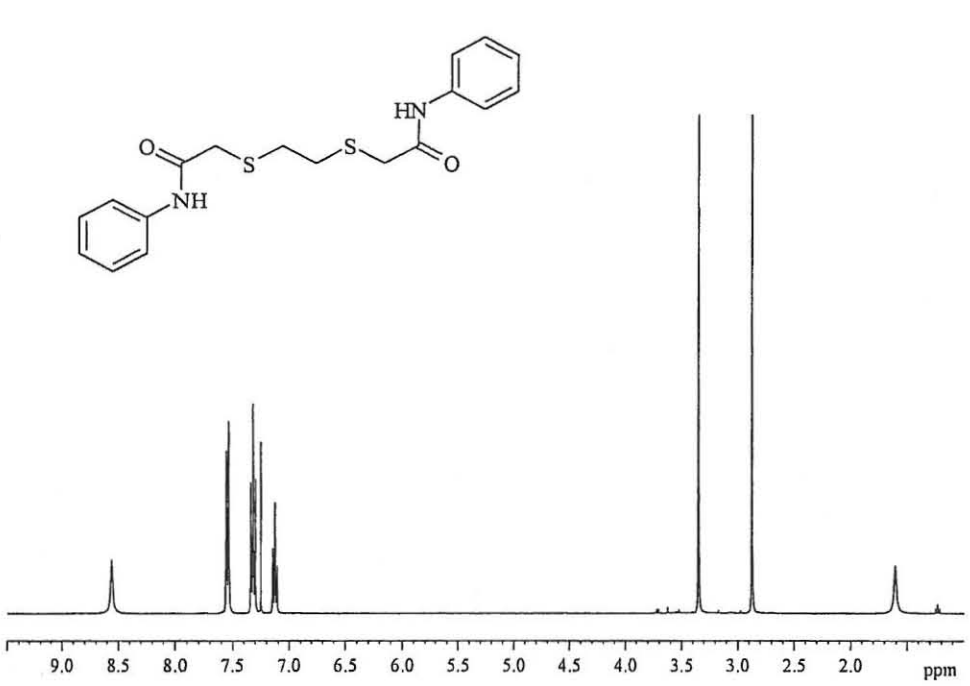
[a] Isolated material. [b] Following recrystallisation from ethanol/water mixture; lit.[65] values in parentheses

Table 5: ^{1}H NMR and ^{13}C NMR chemical shift (ppm) data for the 3,6-dithiaoctanediamide ligands **19a-f.**

Compound	R	δ_H [a]NH	δ_H [a]H-2	δ_H [a]H-4	δ_C [a]C-2	δ_C [a]C-4	δ_C [a]C=O
a	H	8.52	3.35	2.87	36.6	32.0	167.1
b	*p*-OCH_3	8.44	3.33	2.87	36.5	32.0	166.9
c	*o*-OCH_3	9.05	3.41	2.89	37.3	32.5	166.3
d	*m*-Cl	10.28[b]	3.35[b]	2.90[b]	35.1[b]	31.4[b]	168.3[b]
e	*o*-Cl	9.16	3.44	2.92	37.3	32.4	166.5
f	*o*-CH_3	8.44	3.41	2.92	36.9	32.4	166.5

[a] In $CDCl_3$. [b] In DMSO-d_6

a



b

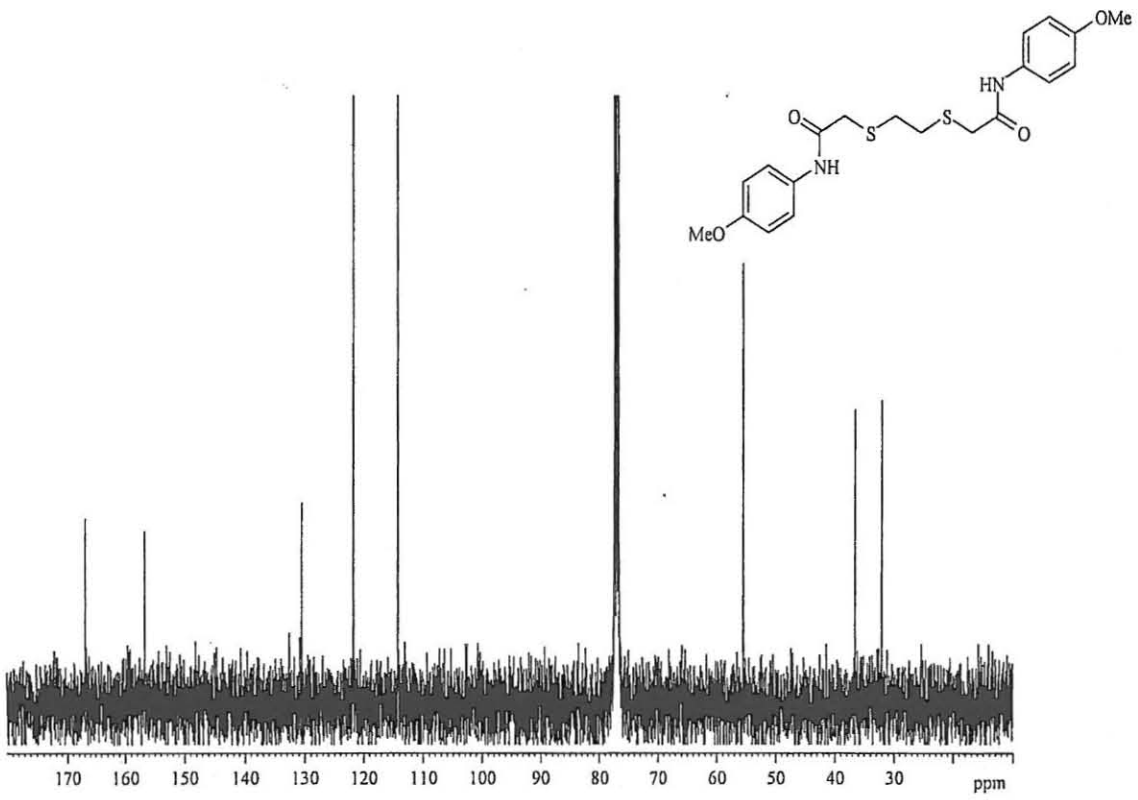
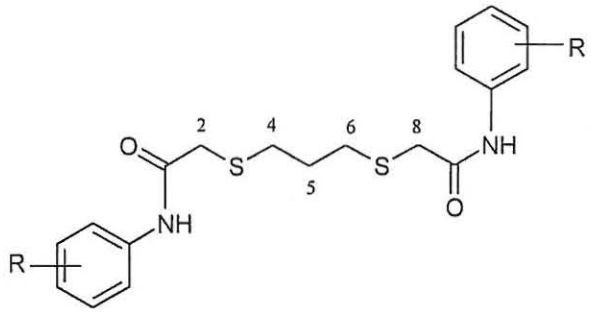


Figure 9: a) 400MHz ^{1}H NMR spectrum of compound **19a** in $CDCl_3$. b) 100MHz ^{13}C NMR spectrum of compound **19b** in $CDCl_3$.

The diamide products (**20a, c, f**) were isolated in moderate to good yields (37-73%), while compounds (**20b, d, e**) were isolated in poor yields (3-17%; **Table 6**). The low yields observed for the latter compounds might be due to the fact that they were purified by both flash chromatography and recrystallisation with consequent loss of the product. The diamides were characterized by IR and NMR spectroscopy; the IR spectra show a band at *ca* 3300cm^{-1} assigned to the amide NH and another at *ca*. 1600 cm^{-1} assigned to the amide carbonyl. The ^{1}H NMR shows a sharp singlet at *ca* 3.35ppm, a triplet at *ca* 2.71ppm and a quintet at *ca* 1.95ppm, which have been assigned to the methylene protons at positions 2 and 8, 4 and 6, and 5 respectively (**Table 7**). The ^{13}C NMR and the DEPT-135 spectra show three methylene signals at *ca* 28.0, 31.5 and 36.9ppm, which have been assigned to carbons 5, 4 and 6, and 2 and 8 respectively (**Table 7**). The absence of an SH band in the IR spectra and an SH signal in the ^{1}H NMR spectra again supports coupling through sulfur rather than nitrogen.

Table 6: Data for the 3,7-dithianonanediamide ligands **20a-f**



Compd.	R	Yield[a]/%	Mp.[b] °C	ν [d]NH/cm^{-1}	ν[d]C=O/cm^{-1}
a	H	73	94-96 (109.5-111)[68]	3250	1656
b	*p*-OCH_3	3.2	130-134 (139)[69]	3297	1652
c	*o*-OCH_3	36.7	-[c]	3326[e]	1661[e]
d	*m*-Cl	3.7	96-98	3338[e]	1647[e]
e	*o*-Cl	17.2	126-128	3296	1662
f	*o*-CH_3	37.5	116-118	3230	1656

[a] Isolated material. [b] Following recrystallisation from ethanol/water mixture; lit. values in parentheses. [c] Isolated as viscous oil, [d] IR spectra recorded for KBr discs. [e] IR spectra obtained for nujol mull.

Table 7: ^{1}H NMR and ^{13}C NMR chemical shift data (ppm) for the diamide ligands **20a-f**

Compd.	R	δ_H[a]NH	δ_H[a]H-2	δ_H[a]H-4	δ_H[a]H-5	δ_C[a]C-2	δ_C[a]C-4	δ_C[a]C-5	δ_C[a]C=O
a	H	8.58	3.34	2.71	1.95	36.8	31.4	28.0	166.9
b	*p*-OCH_3	8.44	3.33	2.71	1.96	36.7	31.5	28.0	166.6
c	*o*-OCH_3	9.16	3.29	2.66	1.88	36.9	31.2	27.9	166.3
d	*m*-Cl	8.57	3.36	2.70	1.95	36.8	31.4	27.9	168.3
e	*o*-Cl	9.29	3.40	2.75	1.97	37.4	31.7	28.2	166.7
f	*o*-CH_3	8.59	3.38	2.74	1.98	36.9	31.6	28.2	166.5

[a] In $CDCl_3$

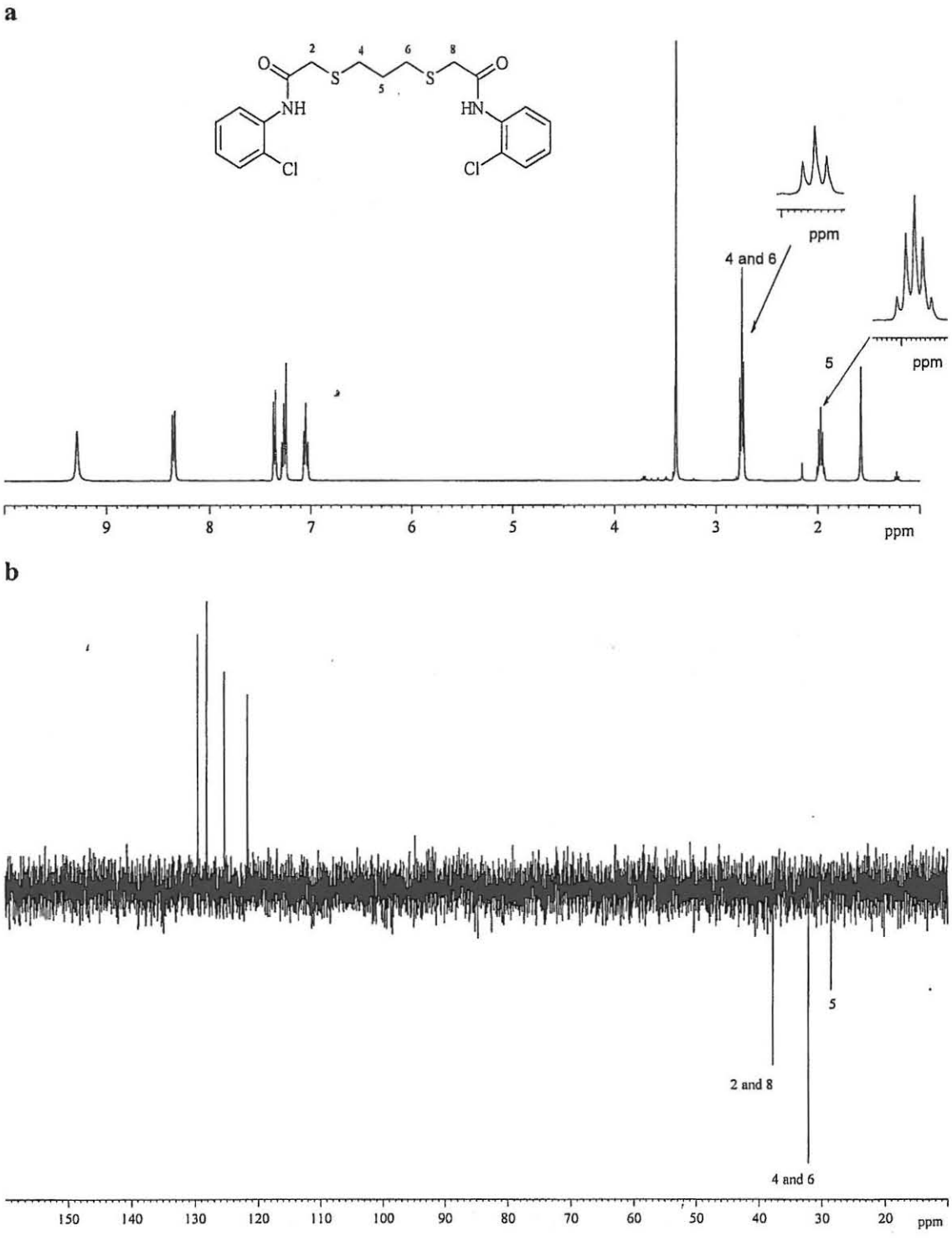


Figure 10: a) 400MHz ^{1}H NMR spectrum of compound **20e** in $CDCl_3$. b) 100MHz DEPT-135 spectrum of compound **20e** in $CDCl_3$.

2.2. Polymerisable Ligands for the Construction of PGM-Selective MIP`s

2.2.1. Ligand Design

The ligand systems targeted in this study contain not only the structural features present in the monomeric and dimeric systems discussed above (**Section 2.1.1**), but in addition, a polymerisable group. More specifically, the ligands incorporate the following features:

i) S and N donor atoms for metal chelation, the latter as an amide nitrogen to enhance platinum and palladium selectivity;

ii) An allyl group for co-polymerisation; and

iii) An aryl substituent to fine-tune electronic and steric effects in the ligand.

These features are evident in the targeted ligands TL1 and TL2 illustrated in **Figure 11**.

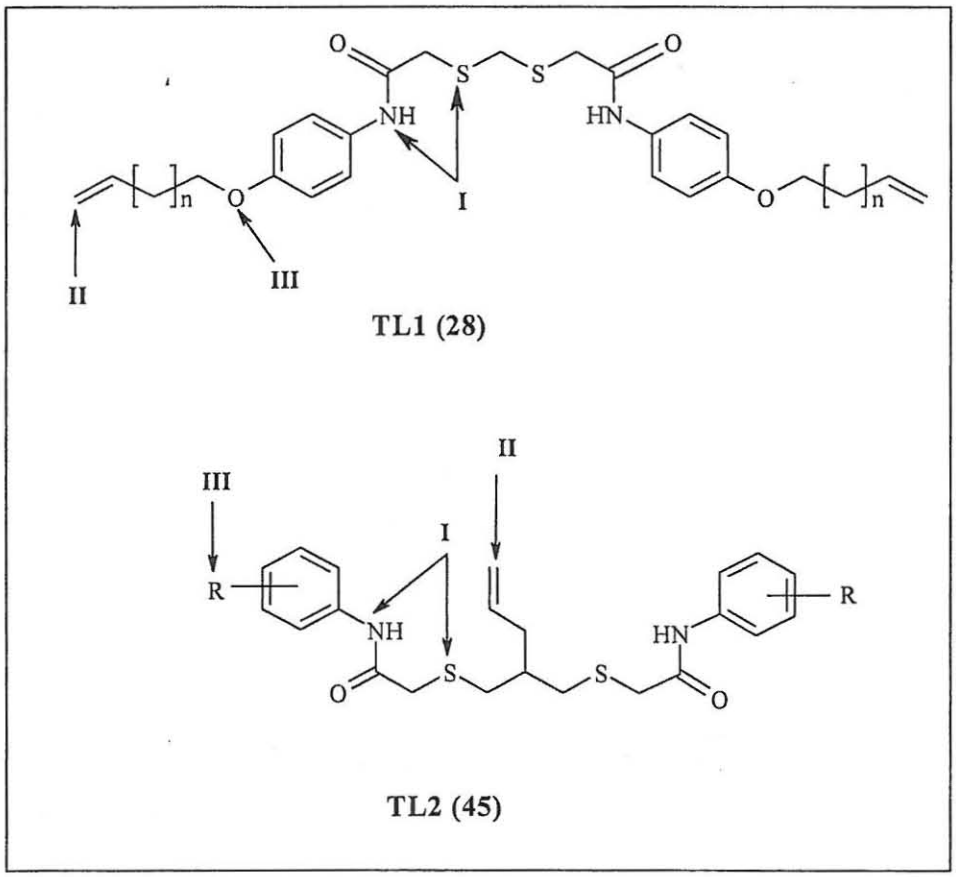


Figure 11: The proposed dimeric ligand systems **TL1** and **TL2**

2.2.2. Synthesis of the alkenyloxyacetanilide systems

2.2.2.1. Retrosynthetic Analysis to the Alkenyloxyacetanilide Systems TL1

Retrosynthetic analysis was used to establish reasonable synthetic pathways to the target ligand **TL1** using readily available precursors. The analysis outlined in **Figure 12** provided the basis for our synthetic efforts. In this approach to the synthesis of ligand **28,** the commercially available aminophenol **33** would be reacted with an alkenyl group to form the alkenyloxyanilines **31** (n=0) and **32** (n=1). The anilines could then be coupled with mercaptoacetic acid **23** to form the mercaptoacetanilides **29** and **30** (see **Section 2.1.2**), which following reaction with the commercially available dibromide **22a** would afford the targeted ligand **28.**

2.2.2.2. Synthesis of 4-Alkenyloxyaniline

The first attempt to synthesize a 4-alkenyloxyaniline involved allylation of 4-aminophenol **33** with allyl bromide **34** in ethanolic potassium hydroxide at room temperature for 24h (**Scheme 5**). Addition of water and extraction with diethyl ether afforded a black oil, which gave three spots on TLC analysis, subsequently shown to correspond to compounds **31, 35** and **36.** The infra-red spectrum of the oil showed a very strong broad band in the hydroxyl and primary amine stretching region *ca* 3300cm^{-1}. Flash chromatography of the mixture afforded a number of fractions, but none of them were pure. Distillation under reduced pressure finally afforded a small quantity of the pure allyloxyaniline **31,** as yellow oil, which turns black on standing.

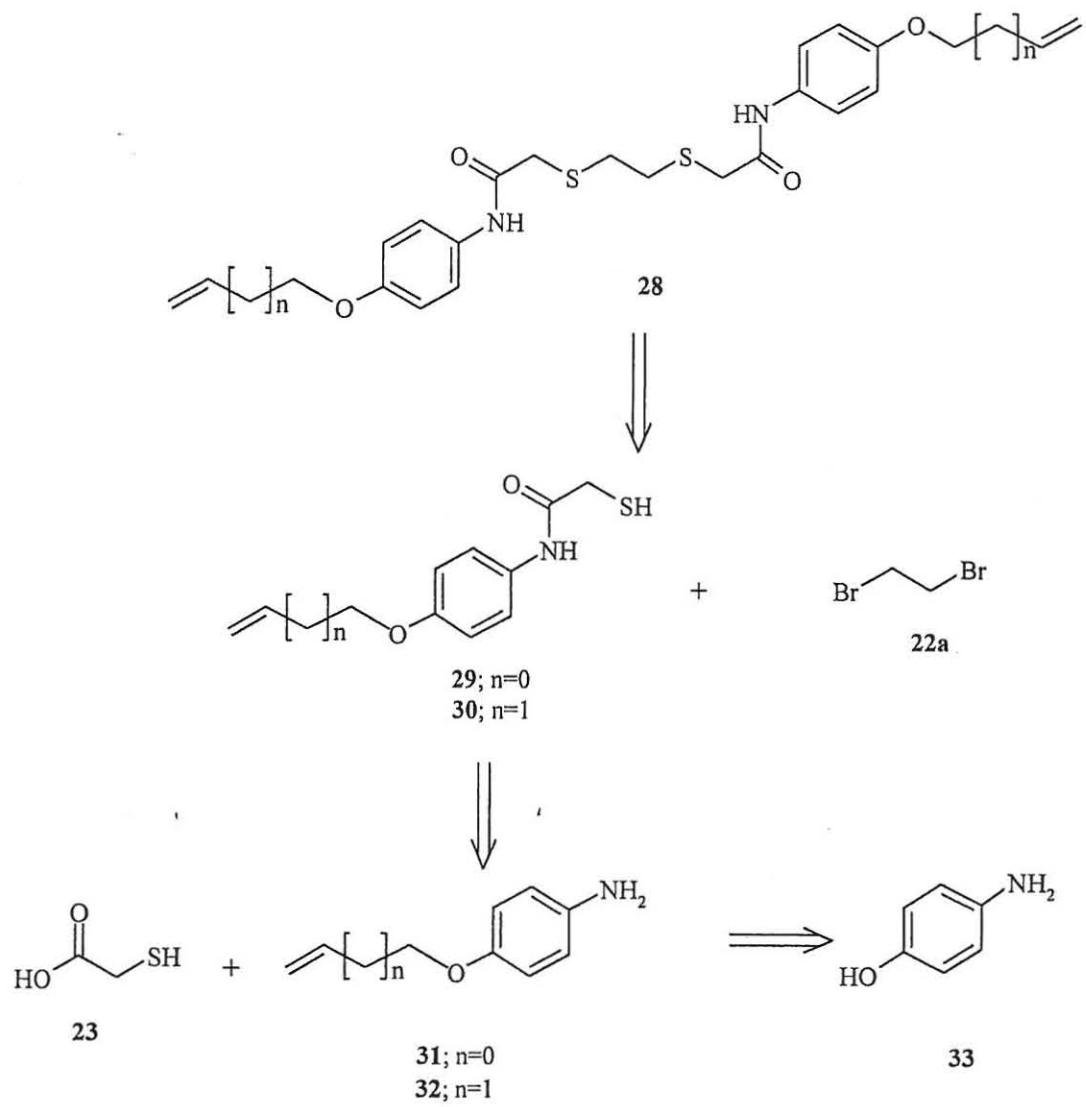
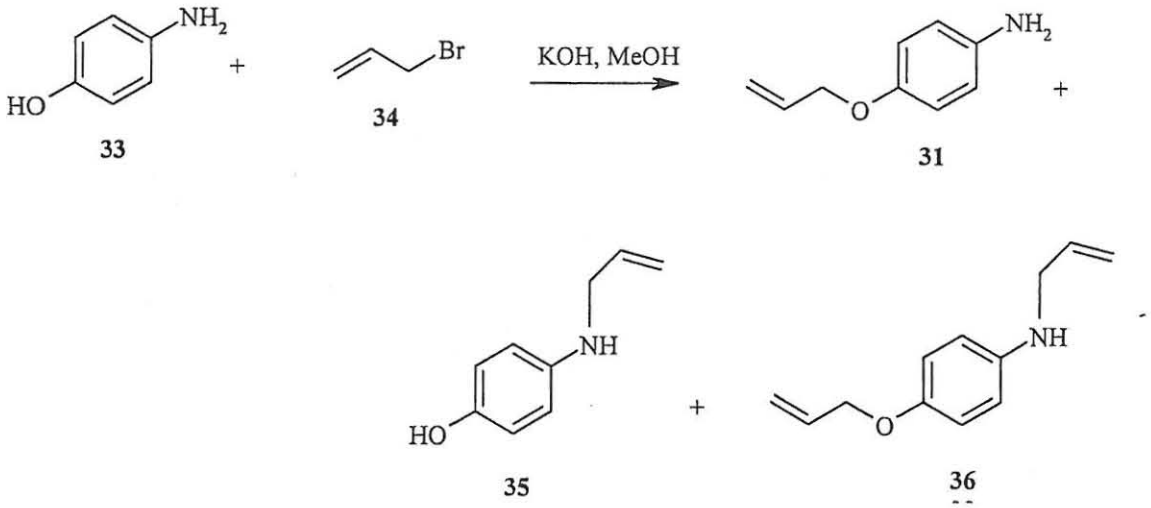
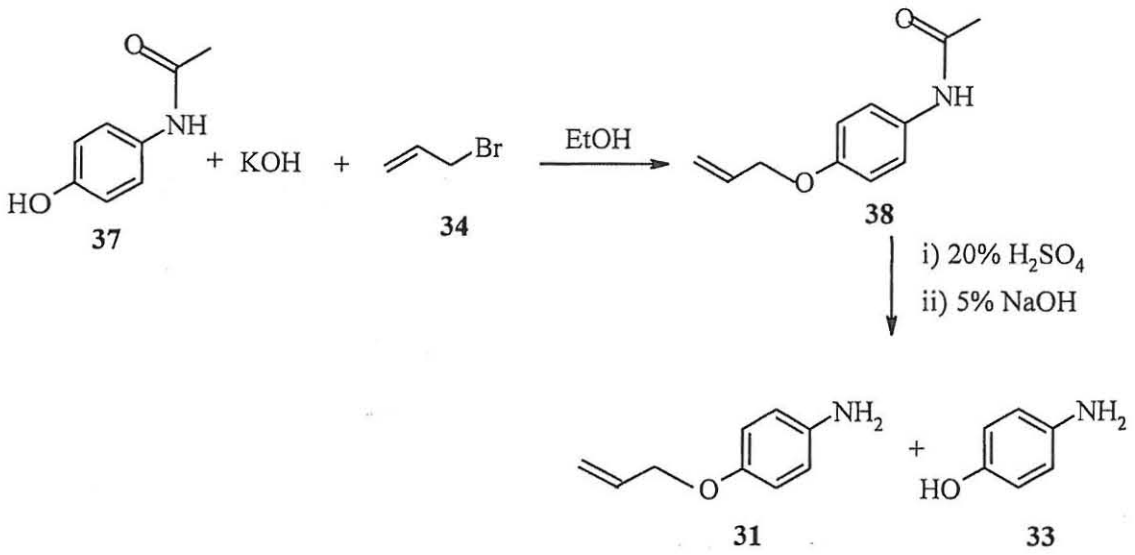


Figure 12: Retrosynthetic analysis of the targeted ligand **28.**



Scheme 5: Synthesis of allyloxyaniline 31 from 4-aminophenol 33.

An alternative approach to the 4-allyloxyaniline **31** was then explored, *viz.*, a method described by Buu-Hoi *et al.*[70] (**Scheme 6**), which involves treating a cold solution of *p*-acetamidophenol **37** and potassium hydroxide in aqueous ethanol with allyl bromide, and boiling the mixture under reflux for 1h. Addition of water to the reaction mixture precipitated solid material, which was recrystallised from aqueous ethanol to afford the acetanilide **38**. Acid hydrolysis of the acetanilide with 20% sulfuric acid and extraction into ether gave the allyoxyaniline **31**, in low yield, together with 4-aminophenol **33**. Gutekanst *et al.*,[71] also prepared the allyloxyaniline **31** using a similar method, in which the acetanilide **37** was stirred with allyl bromide in ethanol for 8h; the residual oil, after removing the solvents, was then dissolved in benzene and crystallized by the addition of petroleum ether (bp. 60-80°C).



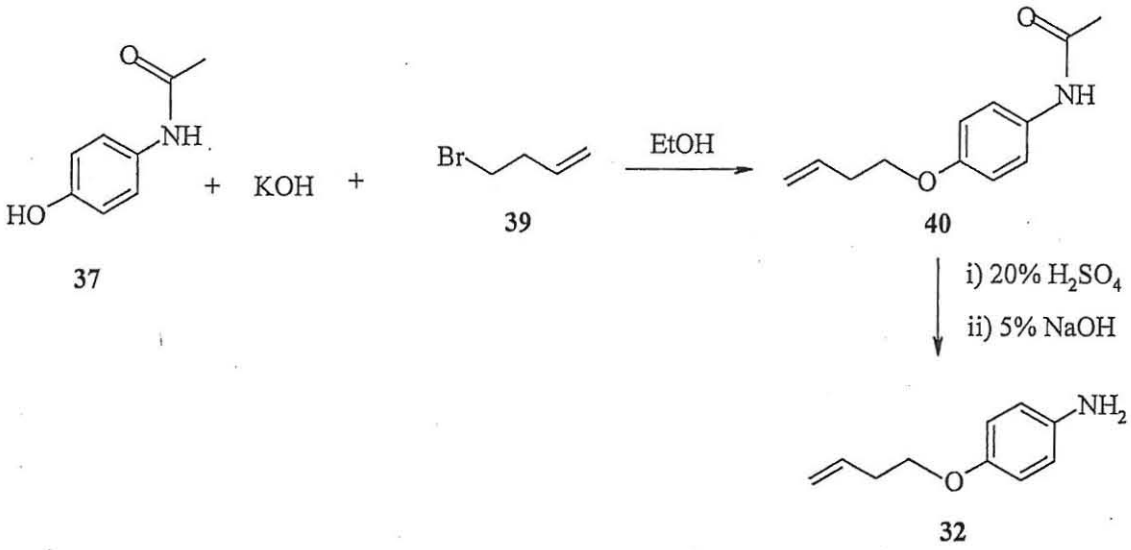
Scheme 6: Synthesis of 4-allyloxyaniline from acetamidophenol 37.

The isolation of 4-aminophenol **33** as a by-product in the hydrolysis of the allyloxyacetanilide **38** reflects the susceptibility of allyl ethers to hydrolysis,[72-73] and it was decided to use 3-butenylbromide **39** as the alkenyl halide (**Scheme 7**). This approach also proved to be unsatisfactory as the yield of the butenyloxyaniline **32** was even lower than the yield of the allyloxyaniline **31 (Table 8)**.

Table 8: Data for the alkenyloxyanilines **31** and **32**

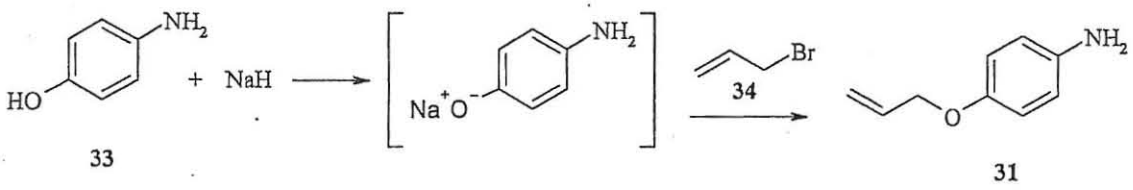
Compd.	Yield [a]%	Bp. °C	$\delta_H NH_2$/ppm
28	49	110/0.05mmHg	3.41
29	21.5	120/0.1mmHg	3.31

[a] Isolated as oils after distillation *in vacuo*.



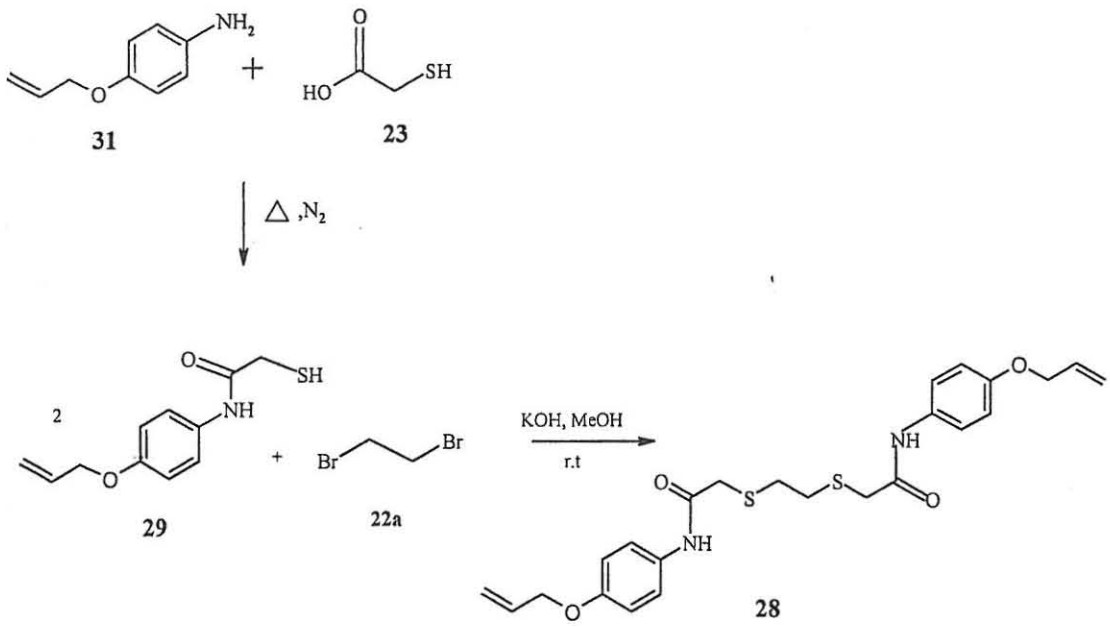
Scheme 7: Synthesis of 4-butenyloxyaniline.

In yet another approach, a stronger base was used to form the phenoxide ion from 4-aminophenol **33**. Sodium hydride in dry THF was used to generate the phenoxide ion, which was then reacted with allyl bromide to form the 4-allyloxyaniline **31** (**Scheme 8**). The reaction mixture was boiled under reflux for an hour before adding allyl bromide, but this method produced 4-allyloxyaniline **31** in yields of less than 10%. Further variations on this general theme were then explored. 3-Butenylbromide **39** was used, instead of allyl bromide, together with two base/solvent systems, *viz.*, sodium hydride in dry THF and butyllithium in dry DMF. Unfortunately, in both cases, the 4-butenyloxyaniline **32** was not produced; instead black oils were obtained, ^{1}H NMR analysis of which failed to show signals corresponding to the expected product.



Scheme 8: Synthesis of 4-allyloxyaniline 31.

The dimeric ligand **28** was finally prepared as shown in **Scheme 9** using the 4-allyloxyaniline **31** isolated from the acetanilide **38** (**Scheme 6**). The alloxymercaptoacetanilide **29** was obtained in good yields (40%) by treating 4-allyloxyaniline **31** with mercaptoacetic acid, following the method described in **Section 2.1.2**. The mercaptoacetanilide **29** was then coupled with 1,2-dibromoethane to form the dimeric ligand **28** in reasonable yields (36%), following the method described in **Section 2.1.3**. However attempted synthesis of the corresponding mercaptoacetanilide **30** from the 4-butenyloxyaniline **32** and mercaptoacetic acid was unsuccessful due to hydrolysis of the butenyl ether.



Scheme 9: Synthesis of the dimeric ligand 28.

Table 9: Data for the allylated ligands **28** and **29**

Compd.	Yield [a]%	Mp.°C	δ_H [b]NH/ppm	δ_C [b]C=O/ppm	ν [c] NH/cm^{-1}	ν [c]C=O/cm^{-1}
28	35.6	120-124	8.53	167	3300	1654
29	40	102-104	8.43	167	3295	1657

[a] Recrystallized from aqueous ethanol. [b] In $CDCl_3$. [c] KBr discs.

The ^{1}H NMR spectra for the ligands **28** and **29** (illustrated for the monomer **29** in **Figure 13a**) show a multiplet at *ca* 6ppm assigned to the vinyl methine proton and a pair of doublets at *ca* 5.3ppm assigned to the methylidine protons for both compounds. The doublet at *ca* 3.3ppm assigned to the thiomethylene protons, becomes a singlet on coupling to the halide **22a** in compound **28**. The ^{13}C NMR spectra (illustrated for the dimer **28** in **Figure 13b**) show three methylene carbons in the up-field region (<70ppm) for compound **28** and, as expected, two methylene carbons for compound **29**.

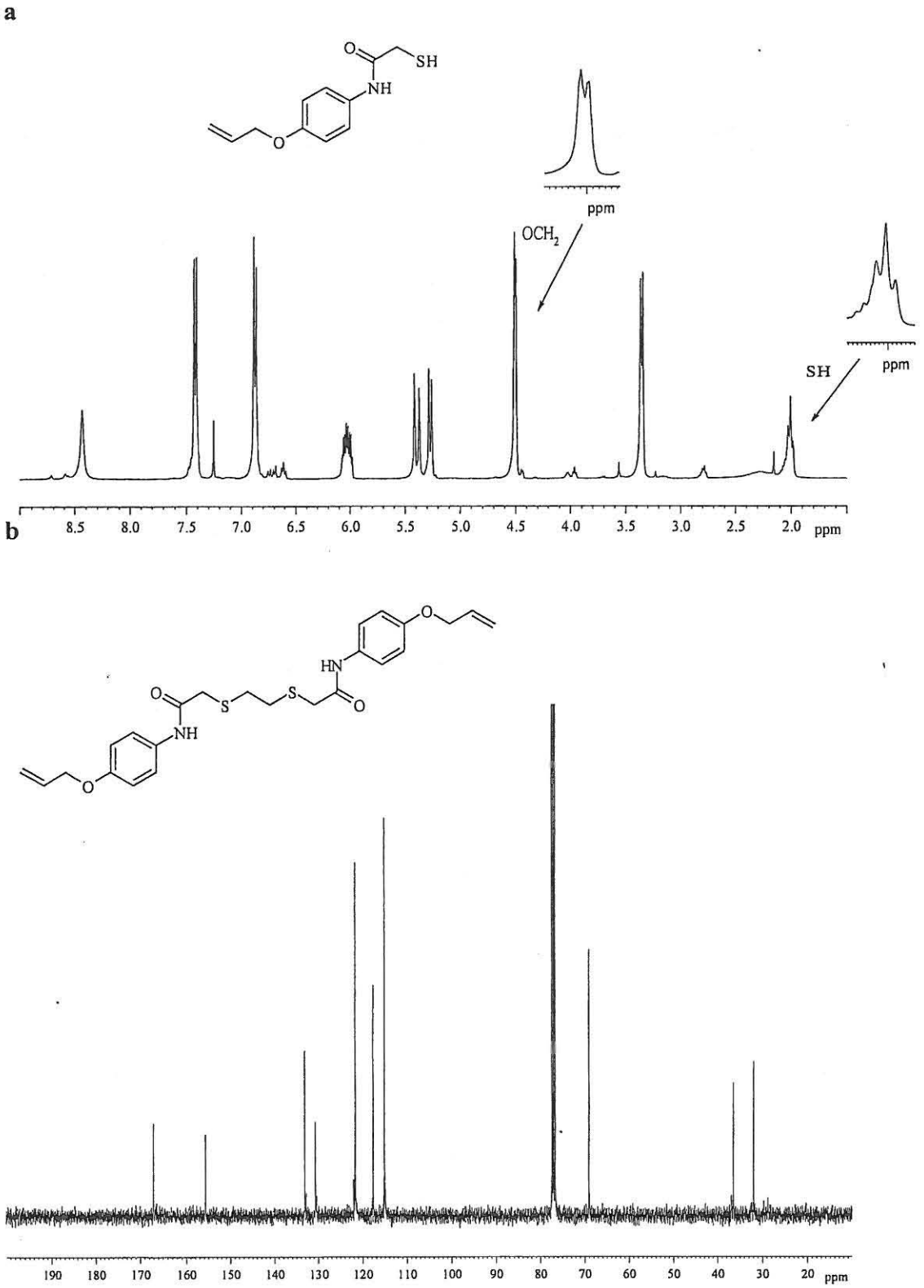


Figure 13: a) 400MHz ^{1}H NMR spectrum of compound **29** in $CDCl_3$. **b)** 100MHz ^{13}C NMR spectrum of compound **28** in $CDCl_3$.

2.2.3. Synthesis of the malonate-derived ligand system

2.2.3.1. Retrosynthetic Approach

Retrosynthetic analysis was used to establish reasonable synthetic pathways to the target ligands using readily available precursors. The analysis outlined in **Figure 14** illustrated the basis for our synthetic efforts. Thus it was expected that diethyl malonate **41** could be allylated to form the allyl malonate **42** which could then be reduced to form the diol **43**. Subsequent bromination or chlorination would afford the dihalide, **44** (X = Br, Cl), which could be coupled with the mercaptoacetanilides **21a-f** to afford the dimeric system **45**.

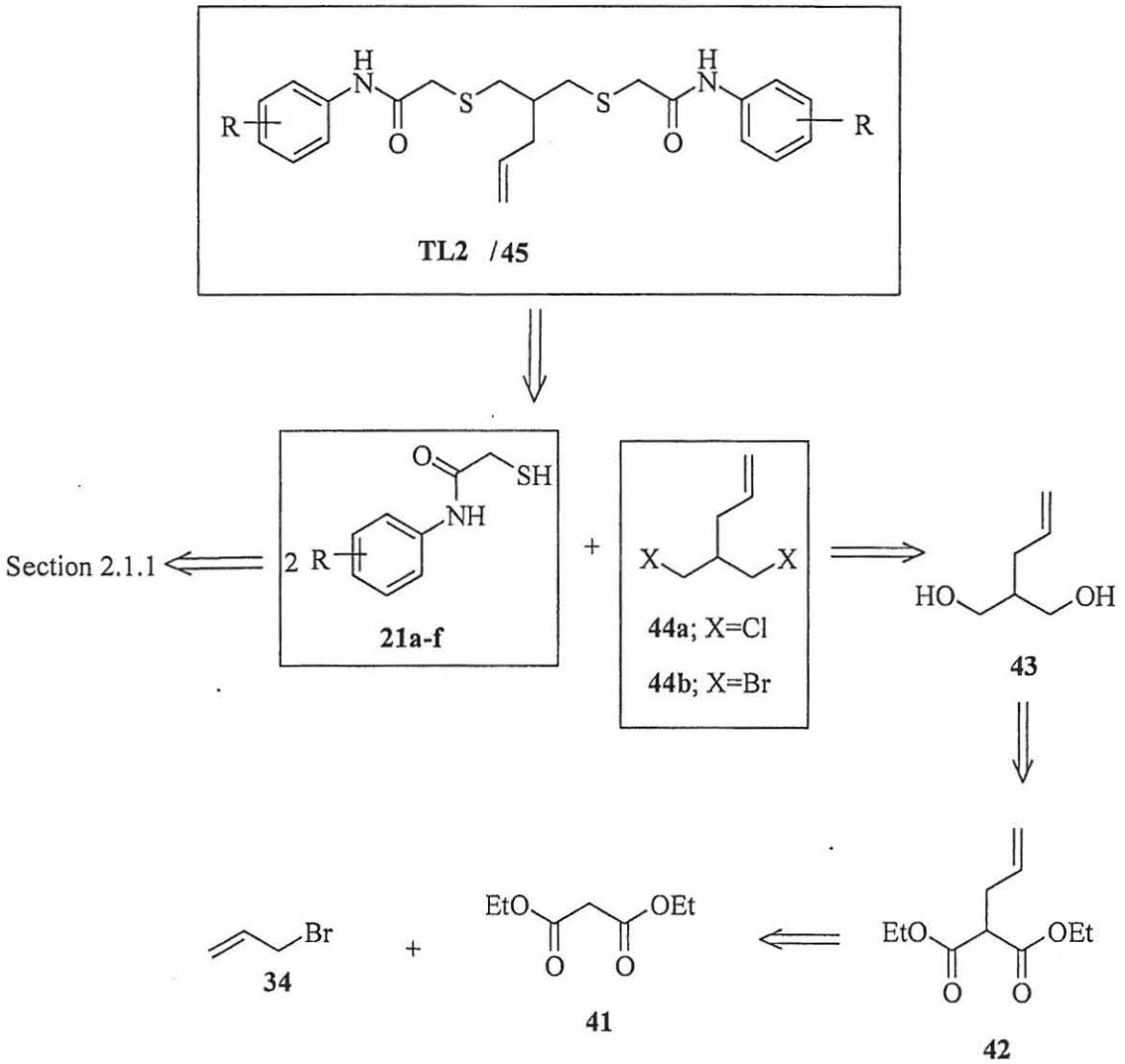
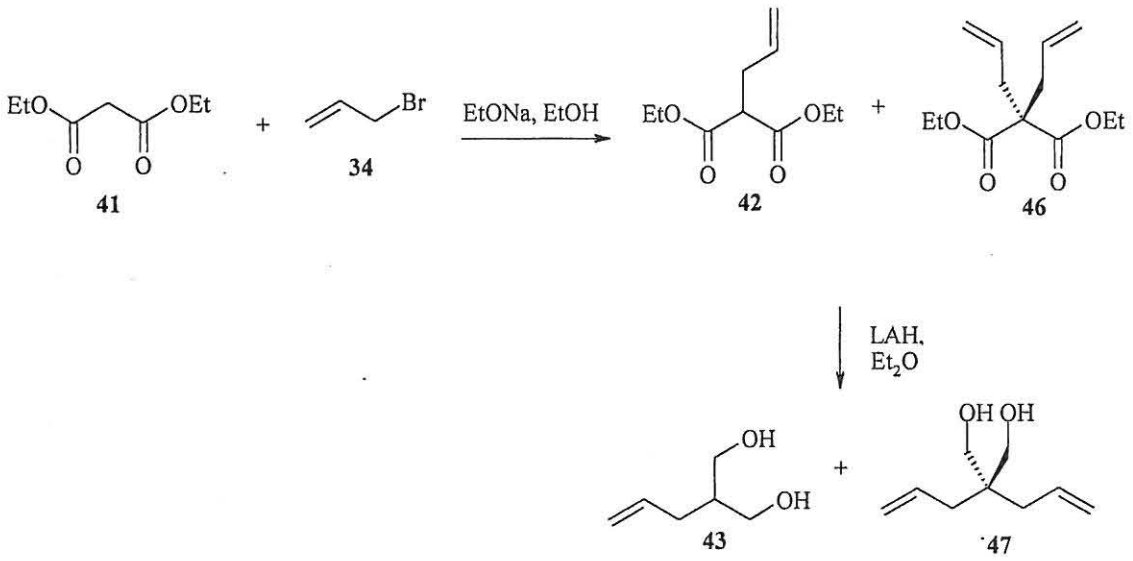


Figure 14: Retrosynthetic analysis of the target ligand system **TL2/45.**

2.2.3.2. Synthetic Approach

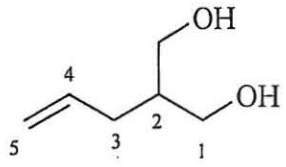
The first step in the synthesis of the malonate-derived ligand system involved allylation of diethyl malonate **41** with allyl bromide in the presence of sodium ethoxide (prepared *in situ* by reacting sodium metal with dry ethanol) to form diethyl allylmalonate **42** in 66% yield (**Scheme 10**), following the method described by Vogel[17] and Linstead and Rydon.[74] Purification of the crude material was achieved by distillation under reduced pressure. The structure of compound **42** was verified by spectroscopic methods. The ^{1}H NMR spectrum showed a multiplet in the region δ 5.5-6ppm, which was assigned to the vinylic methine proton, while the triplet at *ca* 3ppm was assigned to the other methine proton. The ^{13}C NMR and the DEPT-135 spectra showed additional signals for the vinylic methylene and methine carbons, which were initially assumed to be due to tautomerism. However, following reduction monoallylated and diallylated alcohols **43** and **47** were isolated, and the additional signals were then attributed to the mixture of the monoallylated and the diallylated diesters **41** and **46**.



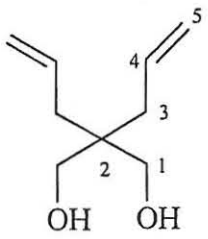
Scheme 10: Allylation and reduction of diethyl malonate.

The reduction of the malonate esters **42** and **46** to the corresponding diols **43** and **47** proved to be a challenge. The reduction was first attempted with lithium aluminium hydride (LAH) in diethyl ether, and the mixture was boiled under reflux for 30min, following the method described by Kharasch and Büechi;[75] the excess LAH was destroyed by the addition of water, aqueous NaOH and water.[16,50] The resulting product was shown by TLC to be a mixture of three compounds, which were separated by flash chromatography, the NMR analysis of the fractions confirmed the presence of the malonate ester **42** in large quantities, and the monoallylated and diallylated in small quantities. In the second attempt, the malonate ester **42** was stirred for a longer time and the solvent was changed to THF. Unfortunately, a mixture was again obtained, but the diol **43** was present in higher yield. In the third attempt, the malonate ester **42** was refluxed for even longer in diethyl ether, and the quantity of LAH was doubled, resulting in an improved yield (55.6%) of the required diol **43**; **Table 10.**

Table 10: Data for the formation of the reduction products **43** and **43**



43



47

Yield[a]%				
Compd. 43	**Compd. 47**	**Solvent**	**Time (h)**	**LAH:42[b]**
6.3	19.7	Et_2O	0.5	1:1
35.1	23.4	THF	2.30	1:1
55.6	22	Et_2O	9	2:1

[a] Chromatographic material, [b] mole ratio.

The structures of the diols were verified by NMR spectroscopy. The ^{1}H NMR of the monoallylated diol **43** shows a pair of double doublets in the region δ 3.6-3.8ppm integrating for 4 protons. These were assigned to the diol methylene protons. The observed splitting is attributed to the fact that the methylene protons are diastereotopic; internal rotation does not produce conformers having a plane of symmetry and, hence, the observed magnetic non-equivalence in the protons.[76]

The structure of the diallylated diol was confirmed using ^{1}H NMR, ^{13}C NMR, COSY, DEPT-135 and HETCOR experiments. The ^{1}H NMR spectrum of the diol **47** differs from that of the diol **43**, revealing a four-proton singlet at 3.49ppm and the absence of a multiplet at *ca* 1.8ppm. The ^{13}C NMR shows five carbon signals, which were indicated by the DEPT-135 experiment to comprise three methylene carbons and one methine carbon. The COSY experiment shows correlations between the 3- and 5-protons, and between the 4- and 5-protons. The HMBC spectrum shows that the 3-methylene protons correlate to all the carbons in the compound, while the HMQC and the DEPT-135 spectra confirm that there is only one quaternary carbon.

The third step in the synthesis of the ligand system **45** involved halogenation of the diol **43** to form the dihalides **44**. The halide **44a** was prepared by adding thionyl chloride to a solution of the diol **43** in pyridine and boiling the mixture under reflux for 3h (**Scheme 11**). Extraction with diethyl ether afforded a brown oil, which was purified by distillation *in vacuo* to produce the dihalide **44a** as a colourless oil. The dihalide was characterized by ^{1}H NMR analysis and the data agreed with the proposed structure.

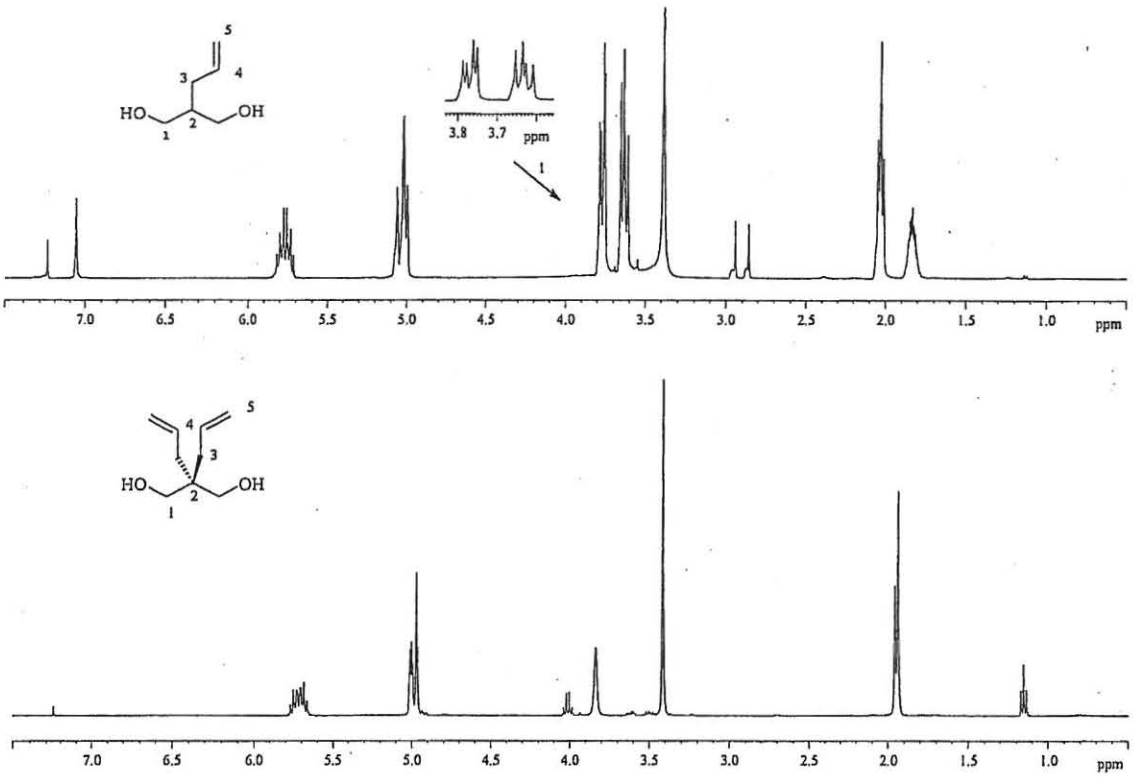
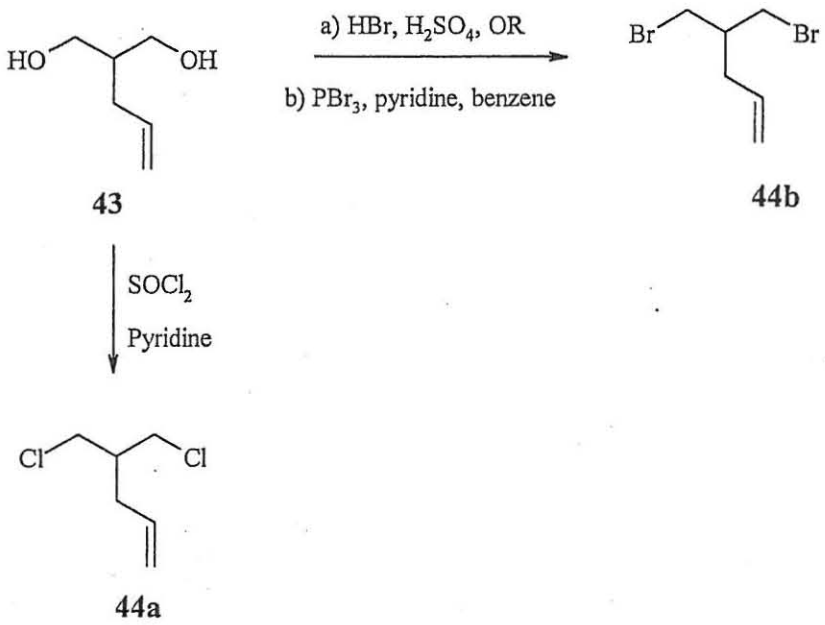


Figure 15: 400MHz ^{1}H NMR spectra of the diols **43** and **47** in $CDCl_3$.

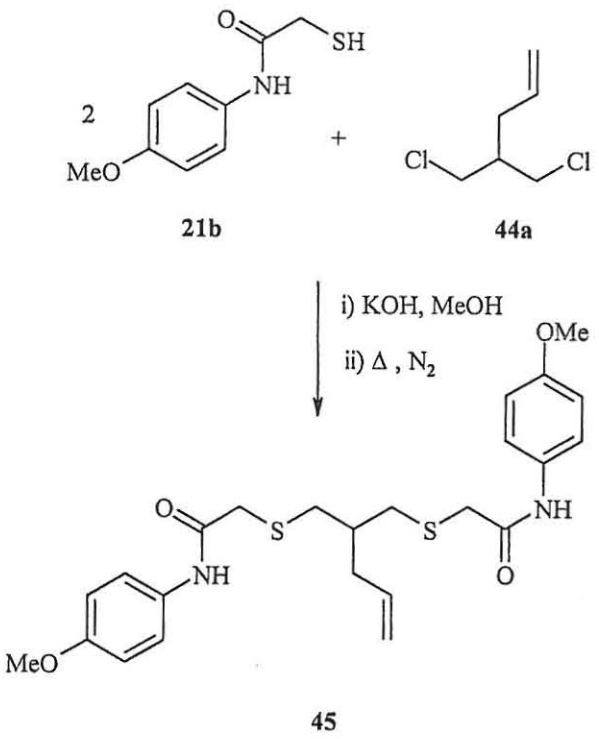


Scheme 11: Synthesis of dihalides 44a and 44b.

In an attempt to prepare the dibromo analogue **44b**, 2-allyl-1,3-propanediol **43** was treated with a boiling mixture of hydrobromic acid and sulfuric acid for 3h under reflux. The resulting mixture was extracted with diethyl ether and the crude residue was distilled *in vacuo* to produce a colourless oil boiling at 50-52°C/0.5mmHg. While the ^{1}H NMR spectrum of the oil did not show signals corresponding to the expected product, low- and high-resolution mass spectrometry gave masses, which correspond to the expected product. It was thus assumed that the required product **44b** was formed in very small quantities.

In a further attempt to prepare the dibromo compound **44b**, the method described by Karasch and Büechi[74] was followed using PBr_3 in pyridine. The resulting product was purified by distillation under reduced pressure, but the fraction boiling at 56-58°C/1mmHg was shown by ^{1}H NMR not to contain the desired product. The residue, however was shown to contain the dibromo compound **44b**, and further purification by PLC and HPLC failed to produce the pure product instead a fraction containing the desired product was obtained.

The last step was to couple the halide with the mercaptoacetanilides **21a-f**. In the first attempt the mercaptoacetanilide **21a** was coupled with the halide following the method described in **Section 2.1.2**. The dimer **45** was not formed instead the mercaptoacetanilide **21a** oxidized to form the disulfide product **25a**. In the second attempt the mixture was stirred for a week but still the disulfide product was formed. The dimer **45** was finally prepared by boiling the mercaptoacetanilide **21b** under reflux for 3h while keeping the reaction mixture under stream of nitrogen, and then stirring at room temperature for 24h (**Scheme 12**). The crude product was purified by column chromatography and the dimer ligand **45** was obtained as a yellow oil in 10% yield. The ligand **45** was characterized by NMR and mass spectroscopic methods.



Scheme 12: Synthesis of the dimer ligand 45.

2.2.4. Preparation of the Molecularly Imprinted Polymers

A major objective of the project has been to prepare platinum-selective MIP`s, the first phase having been to prepare polymerisable PGM-selective ligands. With the compounds **28** and **29** in hand as functional monomers, attention could be given to generating the corresponding MIP`s (**Scheme 13**).

2.2.4.1. Mixing

The first step in preparing an MIP is to mix the "functional monomer" and the "print molecule". The "functional monomers" **28** and **29**, dissolved in MeOH, were therefore mixed with an aqueous solution of the "print molecule" (K_2PtCl_4) in a 1:1 molar ratio to afford the corresponding Pt complexes. The mixtures were then stirred at room temperature for 24h, after which the aqueous methanol was removed by means of Pasteur pipette, and the residual precipitates were dissolved in DMF.

2.2.4.2. Polymerisation

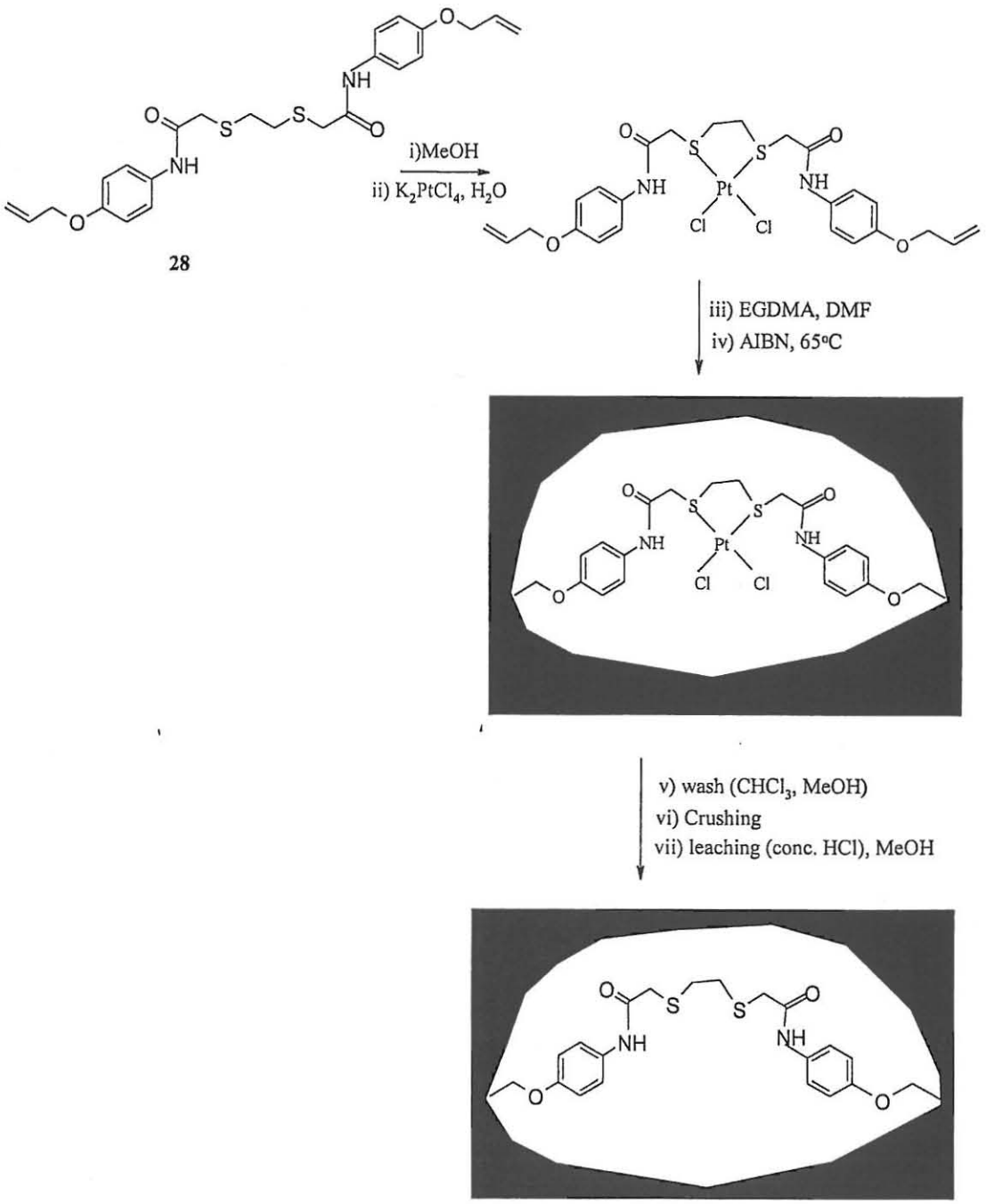
A large excess of the cross-linking agent EGDMA was then added under nitrogen to the functional monomer-print molecule complexes in DMF in a 20:1, (cross-linker: functional monomer) molar ratio. A small amount of the initiator, AIBN, was then added, and the mixtures were heated to 65°C to start the polymerization process. After 4h a yellow solid was formed in the case of functional monomer **28**, and a yellowish green solid in the case of the functional monomer **29**.

Reference polymers were also prepared with each of the functional monomers using the same method, but the "print molecule" was not included in the complexation step.

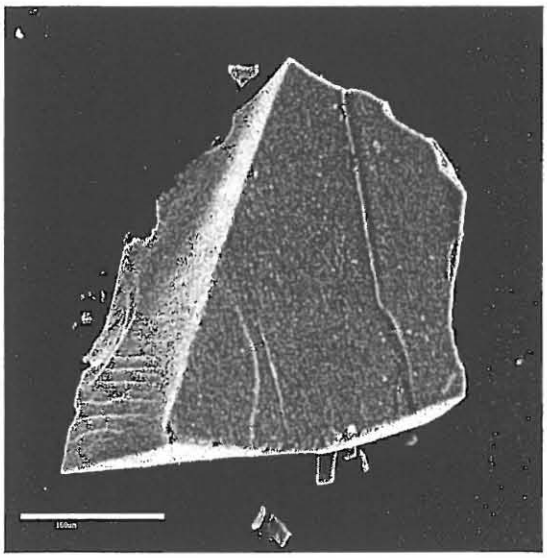
2.2.4.3. Removal of print molecule

The solid material was washed, in each case, with chloroform and then with MeOH to remove any unreacted "functional monomer." The solids were then dried *in vacuo* and crushed to fine powders using a pestle and mortar. The powders were washed with conc. HCl with the aid of suction filtration and then soaked in conc. HCl overnight. Further washing with conc. HCl, followed by MeOH, produced a cream powder for the monomer **28** and a pale yellow powder for the monomer **29** after drying *in vacuo* for two days. The reference (blank) polymers were obtained as cream powders.

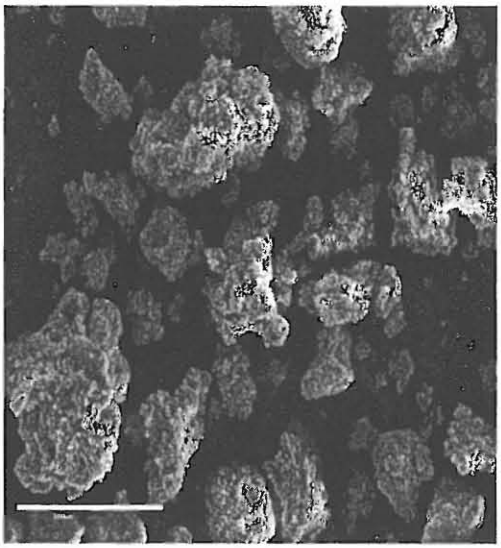
Scanning Electron Microscopy (SEM) was used to examine the physical appearance and dimension of the fine polymer particles. The dried imprinted and unimprinted polymer particles were dusted onto a conductive double-sided adhesive tape on SEM specimen tubs. The dusted particles were then coated with gold using a Balzero Union coating device and the samples were viewed under the Scanning Electron Microsope. The picture **a** in **Figure 16** clearly shows a smooth surface for the blank polymer while pictures **b** and **c** in **Figure 16** shows a rough surface with numerous cavities in the imprinted polymers.



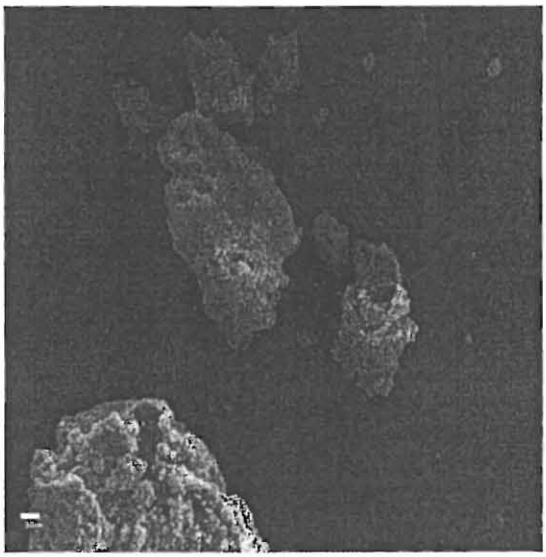
Scheme 13: Preparation of a platinum selective MIP



a



b



c

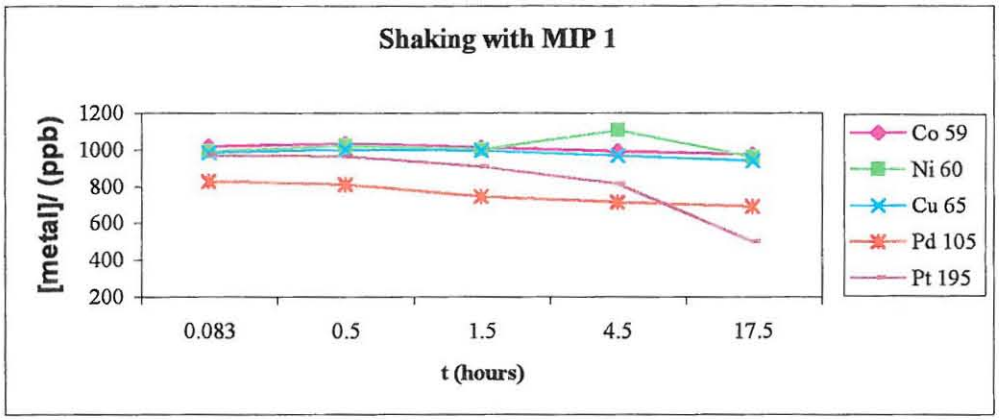
Figure 16: Scanning Electron Micrographs of; **a**) reference (**blank 1**) polymer (300 x magnification); **b**) fine particles of the imprinted polymer, **MIP2** (330 x magnification); and **c**) the imprinted polymer **MIP2** (370 x magnification).

2.2.5. Evaluation of the extraction efficiency of the MIP`s

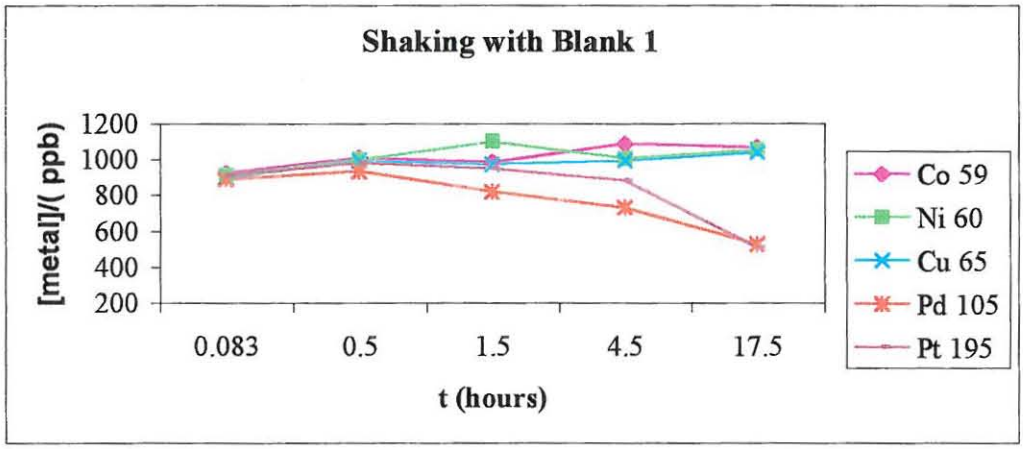
Evaluation of the platinum imprinted polymers was carried out, firstly, by mechanically shaking the polymers with a concentrated solution of cobalt(II), copper(II), nickel(II), palladium(II) and platinum(II) ions in 2% aq. HCl. In a second approach, MIP particles were used as the stationary phase in column separations.

In the first method, the MIP`s were shaken for several hours with the metal salt solution in 2% aq. HCl. Samples of the supernatant liquid were removed at various time intervals and subsequently analysed by ICP-MS. It was observed that the MIP prepared using the mercaptoacetanilide ligand **29**, changed colour gradually from pale-yellow to orange. The results from this study show that the MIP`s are very selective for palladium at shaking times of less than 4.5h and after 4.5h of stirring the MIP`s show selectivity for platinum (see **Figure 17a** and **17c**). This is attributed to the fact that, while palladium and platinum have similar ionic radii, the palladium may be held in the polymer cavities, but the palladium is not a perfect fit; hence, as time goes by, the palladium ions are displaced by the perfectly fitting but more kinetically inert platinum ions.

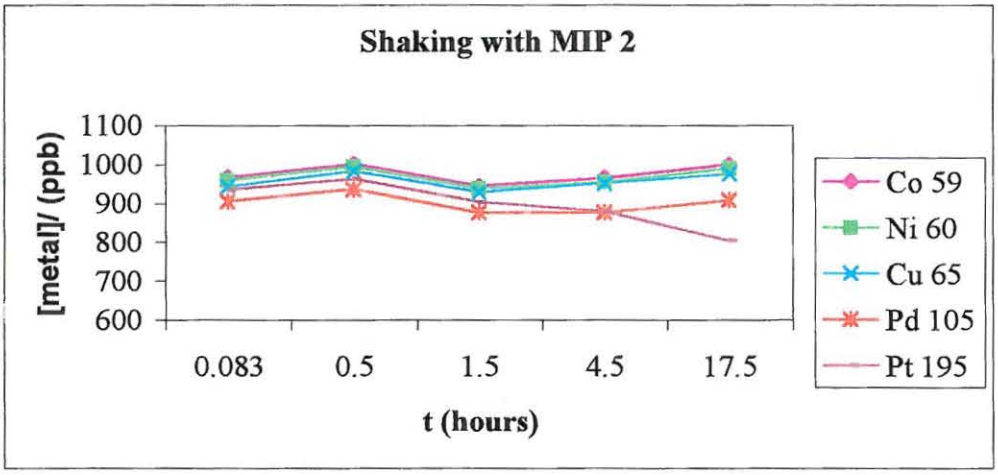
The MIP`s were then used as stationary phases in column separation. A Pasteur pipette was employed as the column and the same metal ion solution used in the shaking experiments was passed through the columns. The ICP-MS data for the eluents show that **MIP1** is very selective for palladium ions while the **blank1** fails to show any selectivity for palladium(II) or platinum(II) ions, **Figure 18**. Clearly equilibration is not achieved under these conditions.



a



b



c

Figure 17: ICP-MS data showing the metal ions present in the metal ion solution after shaking with; **a) MIP1** (prepared from functional monomer **29**); **b)** reference polymer **1**; **c) MIP2** (prepared from functional monomer **28**). (Note: The time axis are non-linear).

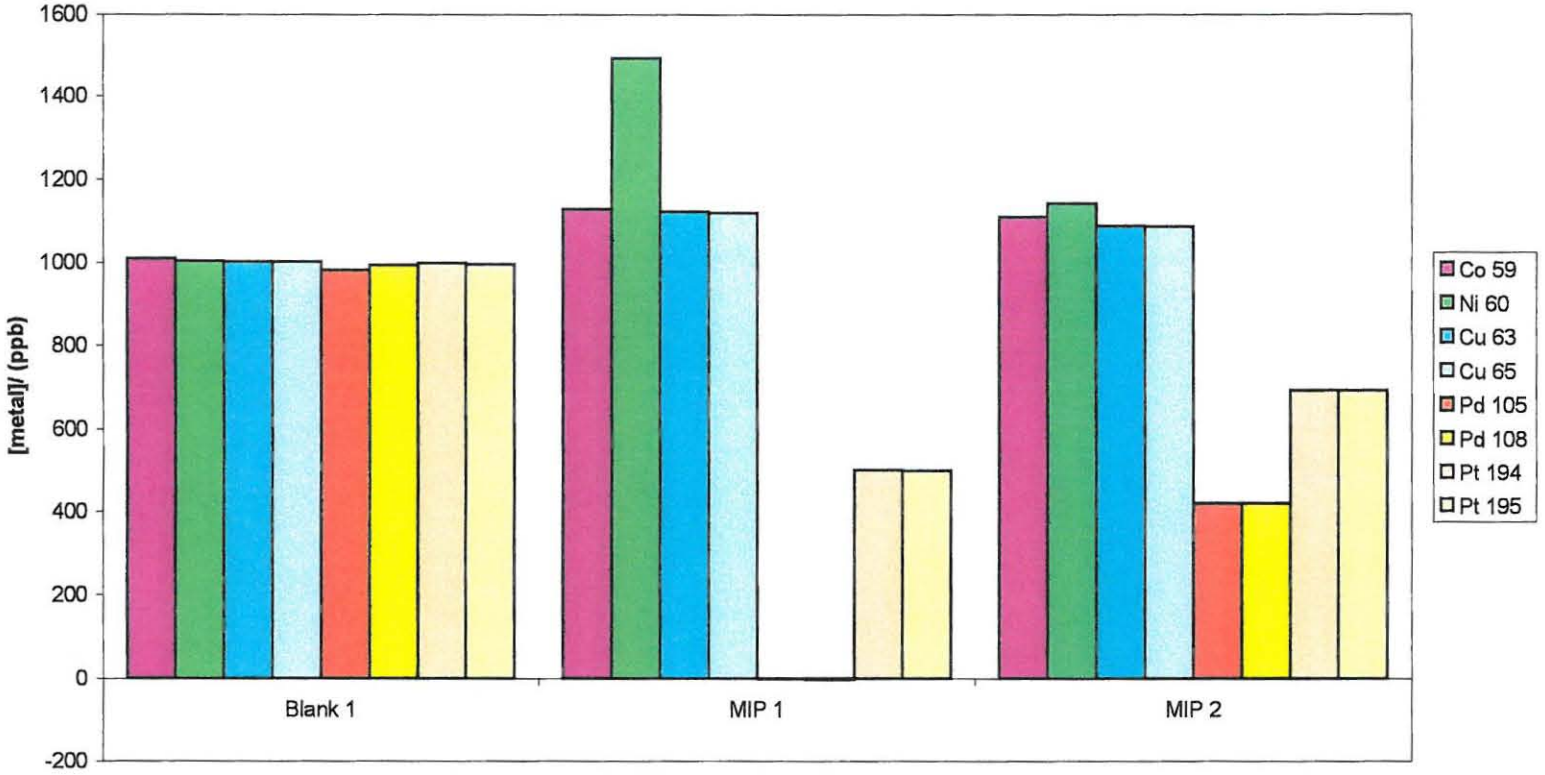


Figure 18: ICP-MS data showing the metal ions present in the metal ion solution after passing through columns containing the reference polymer and the MIP`s: (Note: For **MIP1**, the Pd(II) concentration could not be detected).

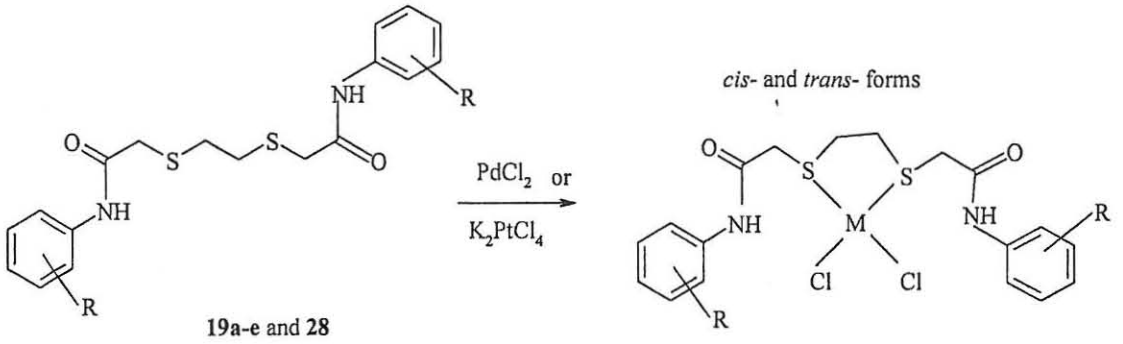
2.3. Complexation Studies

A major objective of this study has been to synthesize and characterize palladium- and platinum-selective sulfur-containing ligands, and to test the selectivity of these ligands in solvent extraction technology.

Coordination of palladium (II) and platinum (II) with sulfur donors is influenced by the type of sulfur donor (thiol or thioether), the substituent on the sulfur donor (in the case of thioethers) and the other ligands coordinated to the metal. It has been reported that the metal-sulfur bond is much stronger for thiols than for thioethers, and that characterization of the complexes is made difficult by the tendency of thiol sulfur to form insoluble bridged polymers with these metals.[3]

The complexes were prepared following the method described by Hagemann[65] by adding the appropriate 3,6-dithiadiamide ligand, dissolved in either MeOH or MeOH-acetone (1:1) to a solution of $PdCl_2$ or K_2PtCl_4 in hydrochloric acid (**Scheme 14**). After stirring for two days and evaporation of the solvent the complexes **48a-f** and **49a, b, c** and **f** were obtained as yellow powders, which were purified by washing with MeOH. Attempts to obtain crystals suitable for X-Ray crystallography were, however, unsuccessful. The complexes were characterized by NMR, infrared and mass spectrometric methods and combustion analysis. The ^{1}H NMR spectra (illustrated for complex **49c**; **Figure 19**) of the complexes show a series of methylene multiplets in the region δ 3.2-4.5ppm attributed to the formation of diastereomeric (*cis* and *trans*) sulfur-sulfur chelates. The two singlets at *ca* 10ppm have been assigned to the NH protons, the presence of which confirms that the metal binds to the ligand through the sulfur atoms alone and not through both the nitrogen and sulfur atoms. The fact that the amide protons are observed as two singlets, suggests the presence of magnetically non-equivalent amide moieties, consistent with the presence of both *cis*- and *trans*-forms of the complex.[77] The *cis*- and *trans*-isomers arise from the configurational stability of the tetrahedral sulfur atoms. In the ^{13}C NMR spectra (illustrated for complex **49b**; **Figure 20**) doubling of the carbonyl carbon and other signals is observed; the four methylene carbons overlap with the solvent signal at

39.4ppm (DMSO-d_6) but are observed in the DEPT-135 experiment. These observations also support coordination through the sulfur atoms to afford the diastereomeric chelates. The mid-IR spectra confirm coordination through sulfur alone as there are no significant changes in the amide and carbonyl frequencies for the free ligands and the complexes. The far-IR spectra indicate that the metal is also coordinated to chlorine ligands as there are metal-ligand vibrations in the frequency region 300-350cm^{-1}, which is the region where Pt-Cl and Pd-Cl stretching vibrations are normally observed.[4,78-80] The shoulder observed *ca* 20cm^{-1} lower than the main band indicates *cis*-geometry in the coordination of the chlorine atoms[4] (for *trans*-geometry a single band would be observed at *ca.* 270 cm^{-1} [81]). The typical Pt-S and Pd-S vibrations are also observed in the region of 400-440 cm^{-1}.[82] The high-resolution mass spectrometric results also agree with the proposed structures.



	R
a	H
b	*o*-OCH_3
c	*o*-Cl
d	*m*-Cl
e	*o*-CH_3
f	*p*-OC_3H_5

Scheme 14: Synthesis of the palladium and platinum complexes 48 and 49.

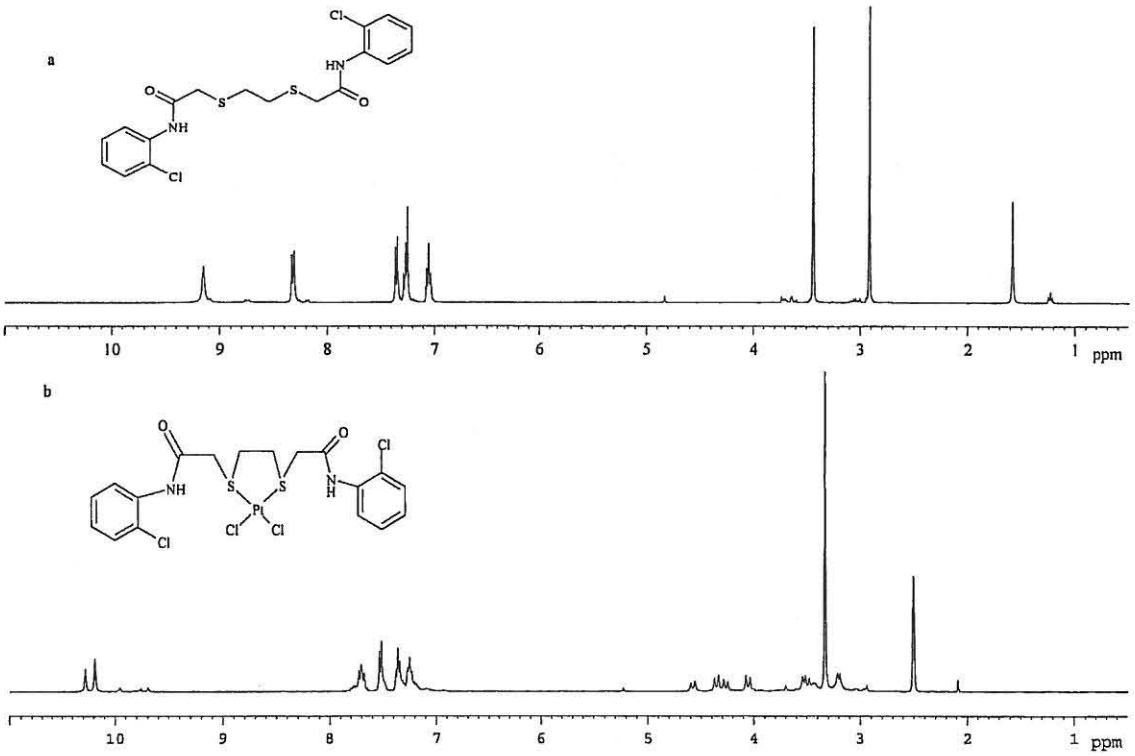


Figure 19: 400MHz ^{1}H NMR spectra of; a) the ligand **19e** in $CDCl_3$ and b) the complex **49c** in DMSO-d_6.

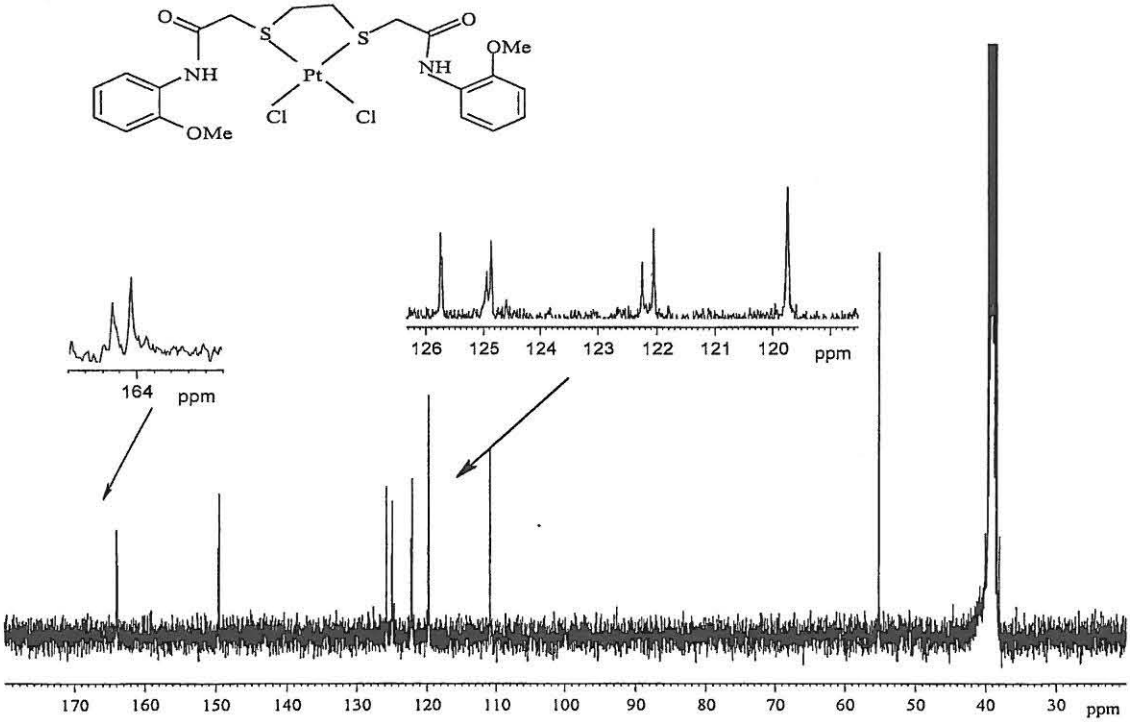


Figure 20:. 400MHz ^{13}C NMR spectrum of the complex **49b** in DMSO-d_6.

2.4 Solvent Extraction Studies

Several studies have been conducted to investigate the extraction of PGM`s with sulfur containing extractants.[28,35,36] It has been shown that dialkyl sulfides, disulfides of the type $RSCH_2SR$ and $RSCH_2CH_2SR$, and dialkyl sulfoxides can extract palladium very well and partially extract platinum but cannot extract practically any of the other PGM`s.[28,35,36] Thiols have been shown to be selective extractants for palladium, the extraction involving the formation of thiolato complexes, with the complex being polymerized in the organic phase.[28]

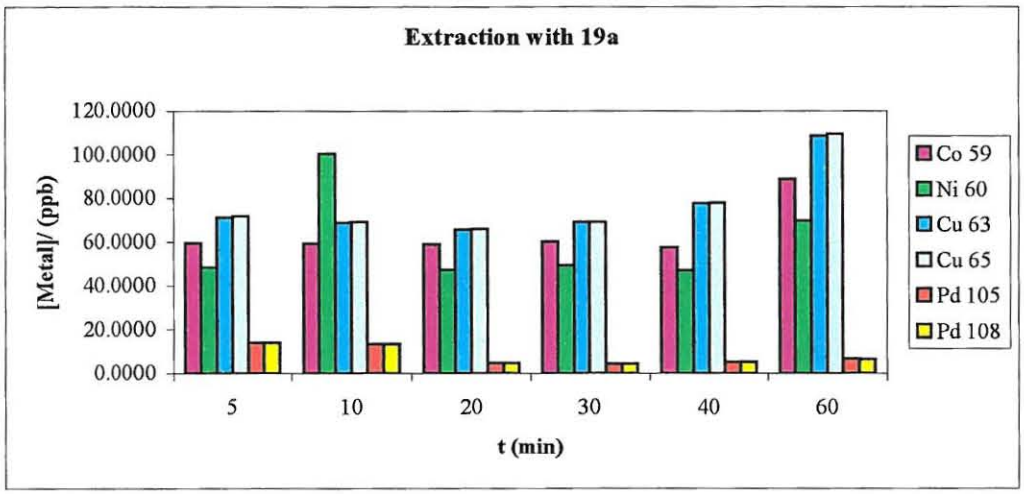
In the present study, the 3,6-dithiaoctanediamide **19a-f** ligands and selected 3,7-dithianonanediamide **20a, c** and **d** ligands were tested as extractants for separating palladium(II) from the base metals: copper(II), nickel(II) and cobalt(II) in 1**M**-HCl, with the metal concentration being 1 x 10^{-3}**M**. Due to the presence of two amide functions, the solubility of the ligands in the chosen organic solvents, toluene and MIBK, was reduced and the solutions were generally warmed to effect total dissolution; the *ortho*-chloro and the *ortho*-methoxy ligands however were readily soluble in these solvents. Equal volumes of each phase (50ml for toluene and 20ml for MIBK) were vigorously stirred together in a 150ml jacketed vessel at 30°C for 1h. Aliquots were removed at 10 minute intervals and the residual aqueous metal concentrations were determined by ICP-MS analysis; the results are shown in **Figures 21** to **25**. Inspection of the ICP-MS data reveals several interesting patterns.

i) The 3,6-dithiaoctanediamide ligands **19a-f** (**Figures 21** to **24**) generally show higher selectivity for palladium than the longer chain 3,7-dithianonanediamide ligands **20 a, c** and **d** (**Figure 25**).

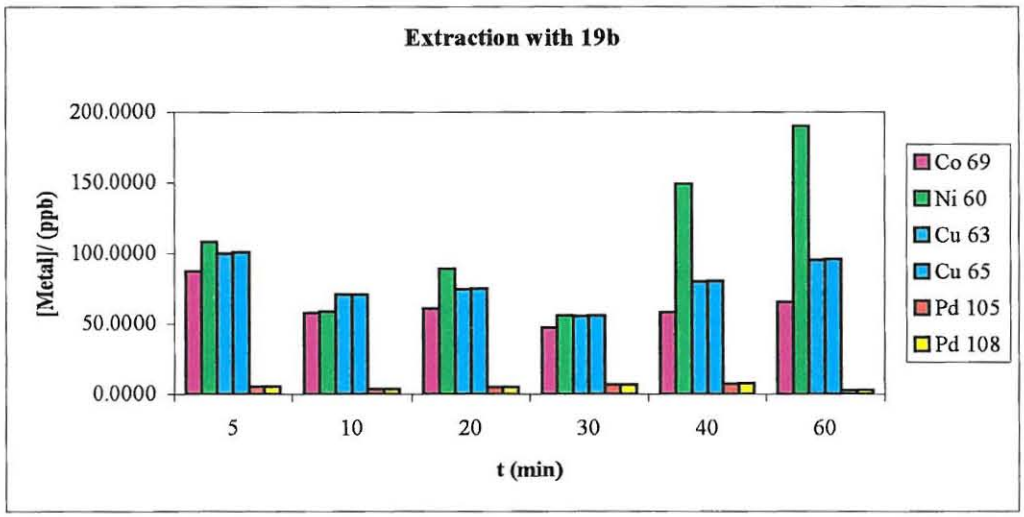
ii) The *ortho*-chloro ligand **19e** in toluene shows much poorer selectivity for palladium compared to the other ligands.

iii) Equilibration is normally achieved within 10 minutes.

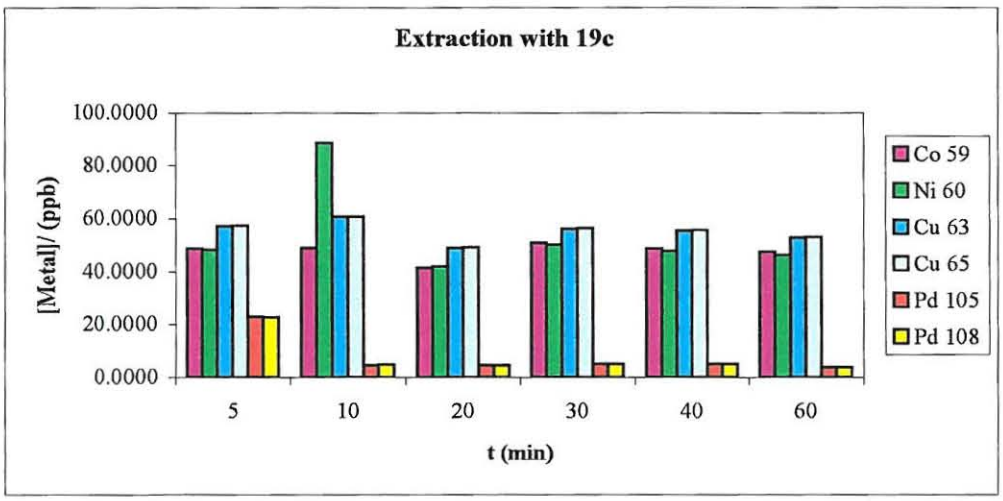
iv) Extraction with the 3,6-dithiaoctanediamide ligands **19a-f** appears to be somewhat more efficient in MIBK (**Figures 23** and **24**) than in toluene (**Figures 21** and **22**).



Compound **19a**

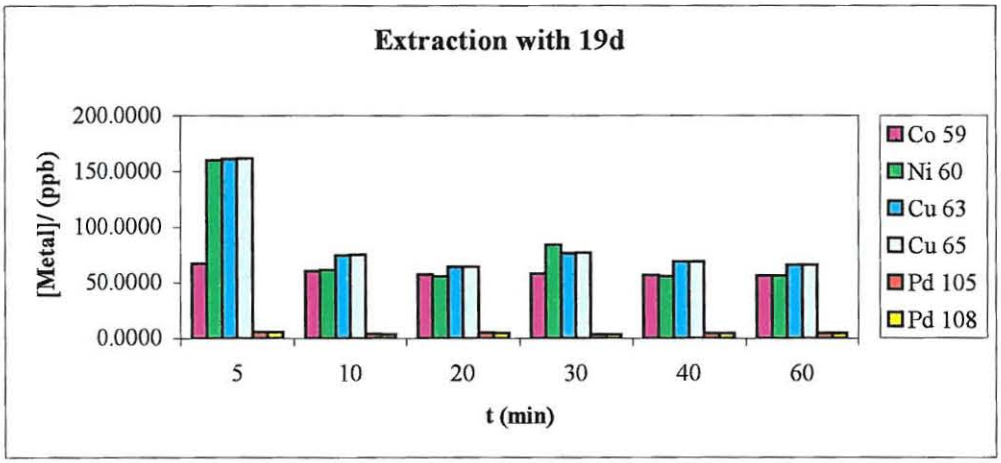


Compound **19b**

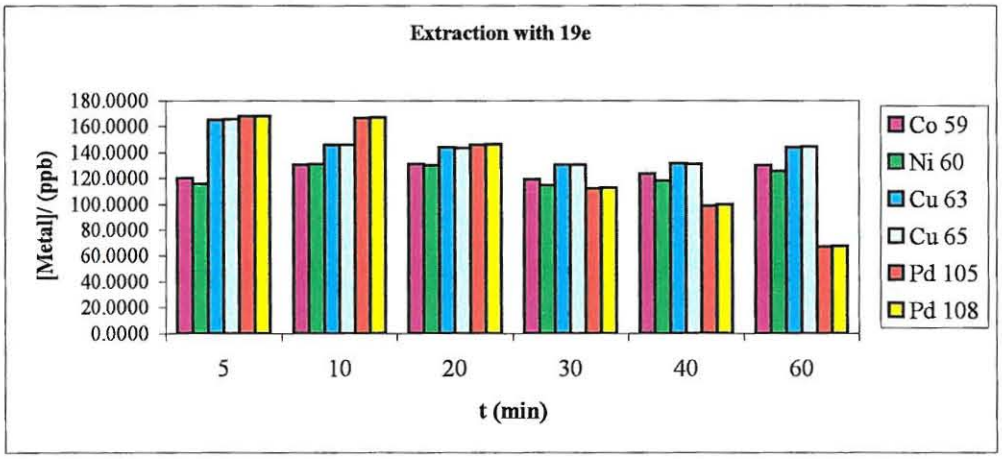


Compound **19c**

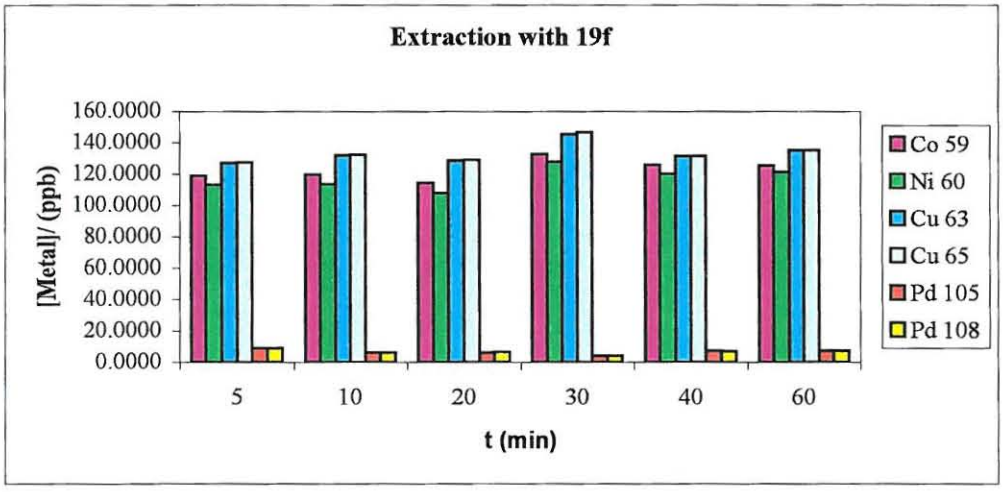
Figure 21: Residual metal concentration in the aqueous phase during competitive extraction with the 3,6-dithiaoctanediamide ligands **19a-c** in toluene.



Compound **19d**

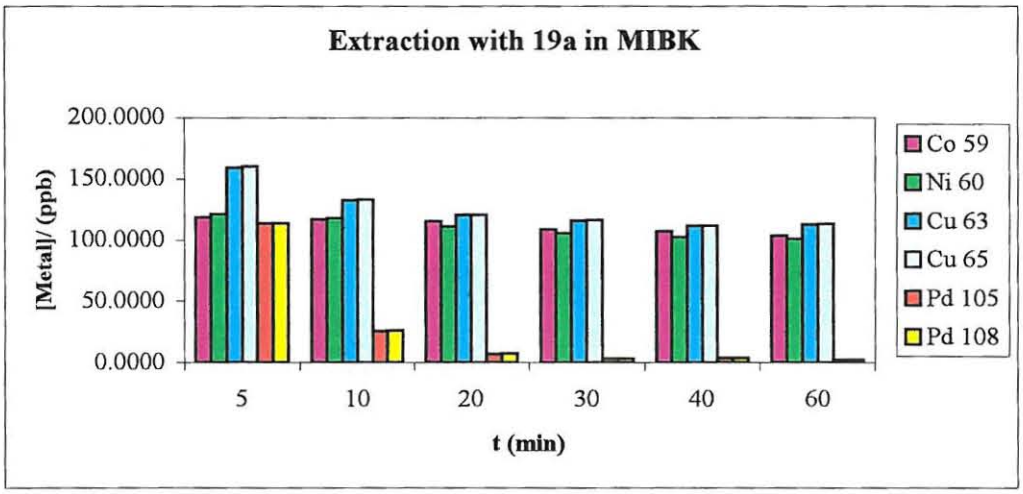


Compound **19e**

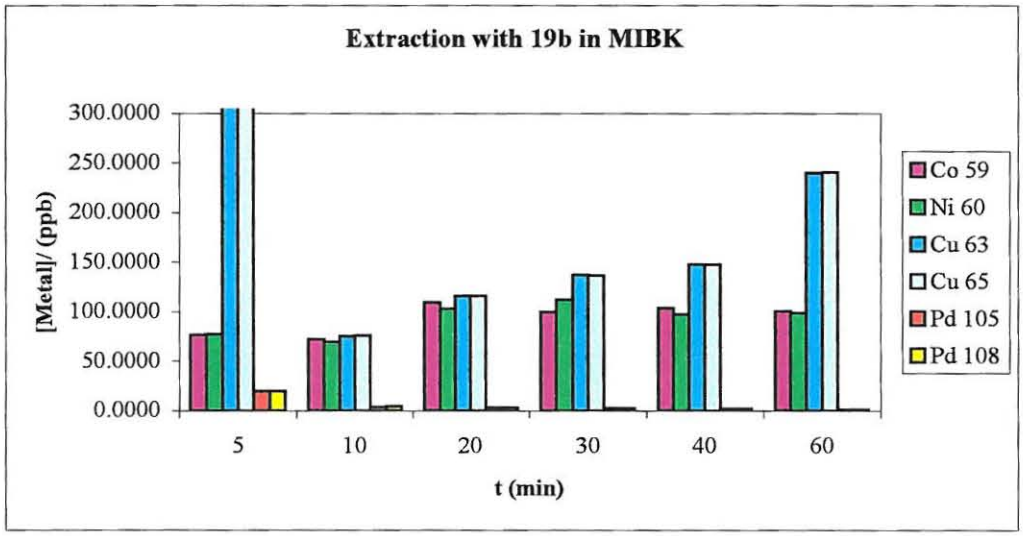


Compound **19f**

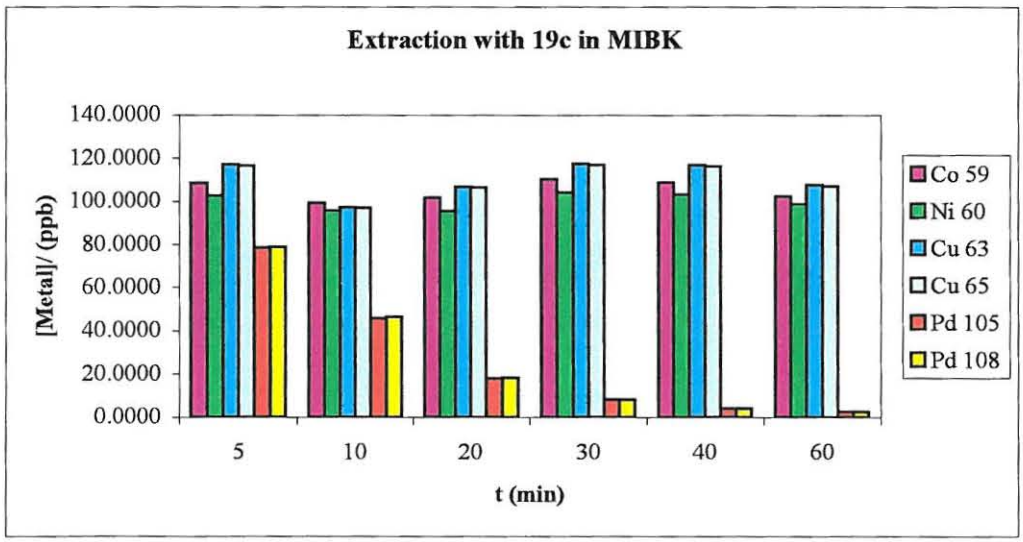
Figure 22: Residual metal concentration in the aqueous phase during competitive extraction with the 3,6-dithiaoctanediamide ligands **19d-f** in toluene.



Compound **19a**

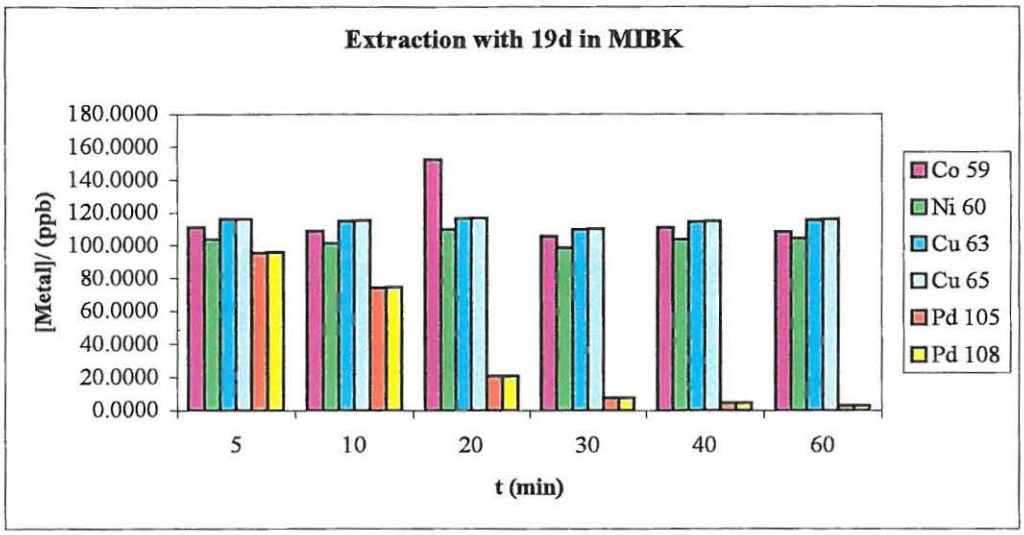


Compound **19b**

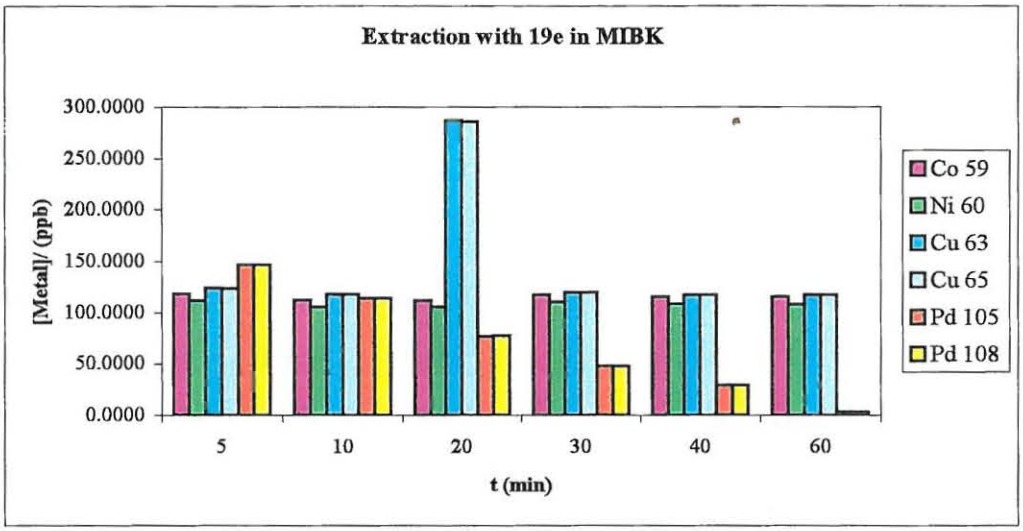


Compound **19c**

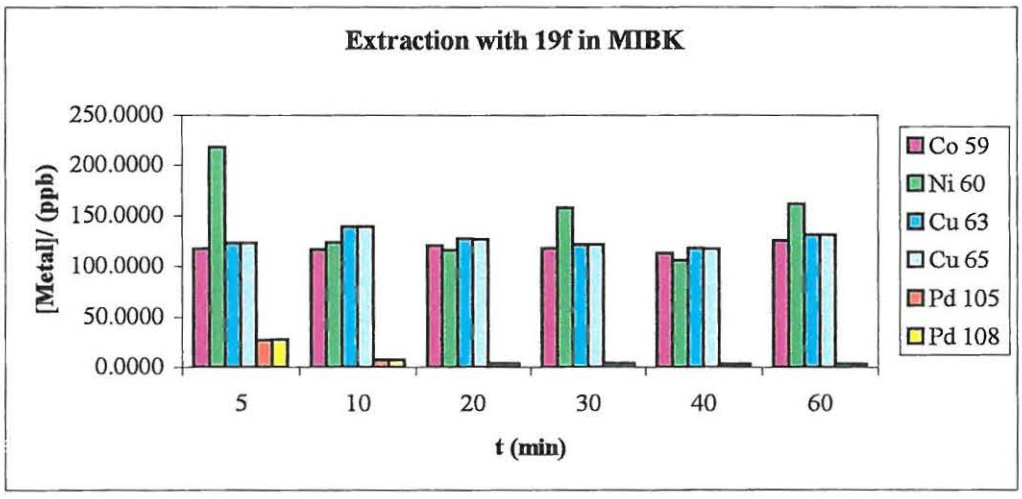
Figure 23: Residual metal concentration in the aqueous phase after competitive extraction with the 3,6-dithiaoctanediamide ligand **19a-c** in MIBK.



Compound **19d**

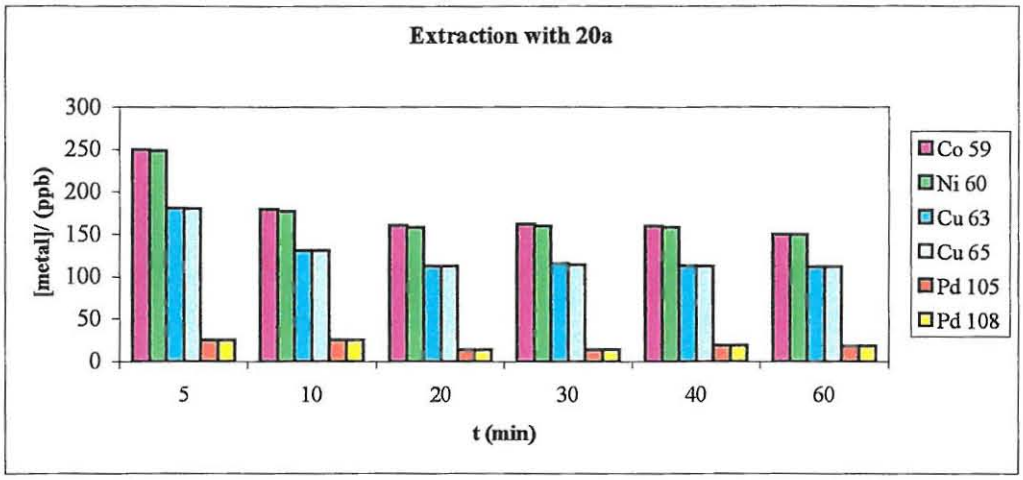


Compound **19e**

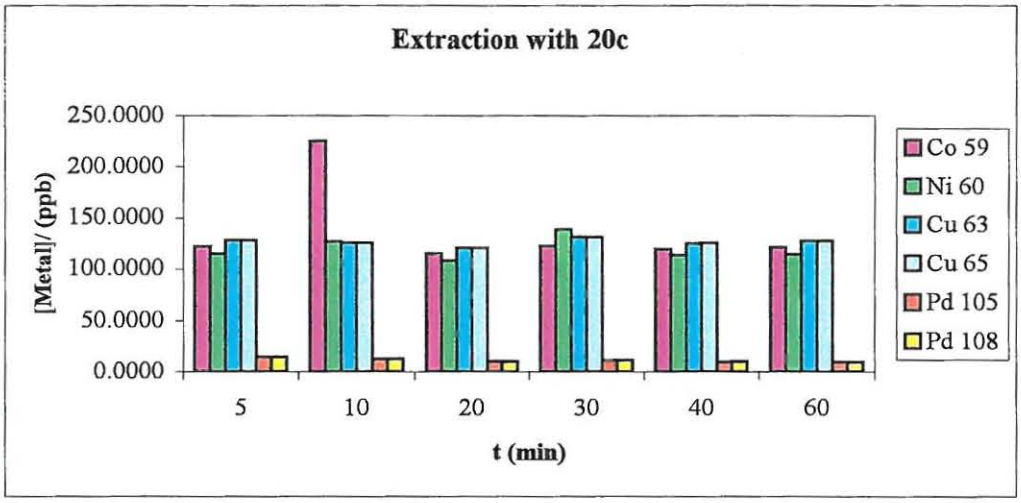


Compound 19f

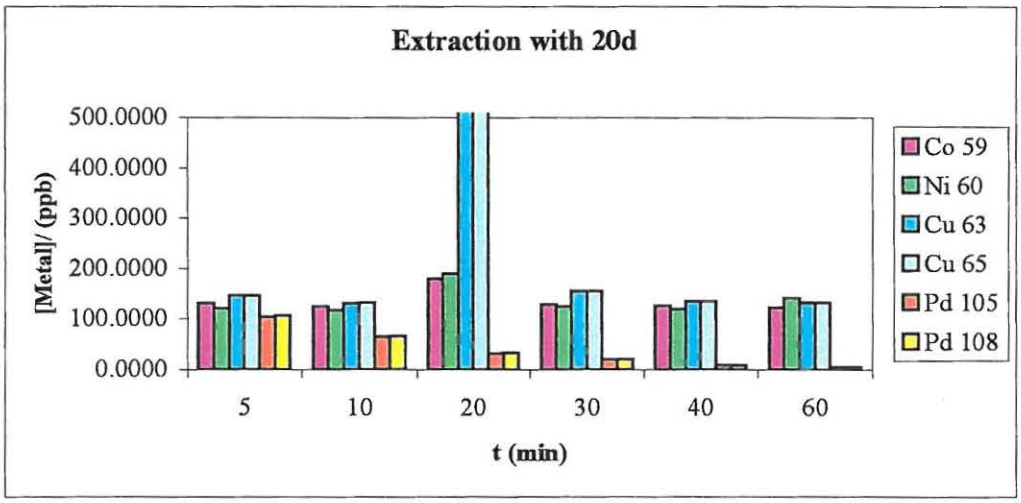
Figure 24: Residual metal concentration in the aqueous phase during competitive extraction with the 3,6-dithiaoctanediamide ligand **19d-f** in MIBK.



Compund **20a**



Compound **20c**



Compound **20d**

Figure 25: Residual metal concentration in the aqueous phase during competitive extraction with the 3,7-dithianonanediamide ligands **20a, c** and **d** in toluene.

2.5 Conclusions

The targeted sulfur-containing PGM-selective amide ligands **19a-f** and **20a-f** were successfully synthesized from a series of mercaptoacetanilide and ω-dibromoalkanes. Selected polymerisable 3,6- and 3,7-dithiadiamide ligands were also successfully prepared by incorporating an allyl group, either as an allyl ether in the mercaptoacetanilide moiety or as a 2-allyl-1,3-dihalide derived from diethyl malonate.

Complexation of the 3,6-dithiaoctanediamide ligands with platinum(II) and palladium(II) afforded solids which, unfortunately, were not suitable for characterization by single crystal X-ray analysis. Characterisation was achieved, however, using the elemental analysis and spectroscopic data. The ^{1}H and ^{13}C NMR spectra of these complexes indicate that they comprise mixtures of the *cis*- and *trans*-isomers – a conclusion based on the fact that both the NH and the thiomethylene signals are doubled in the ^{1}H NMR spectra and many of the ^{13}C NMR signals are doubled. The ^{1}H NMR spectra of these complexes also show four sets of methylene doublets, which is consistent with the formation of chelates.

Solvent extraction studies using, the 3,6-dithiaoctanediamide ligands **19a-f** and 3,7-dithianonanediamide ligands **20a, c** and **d,** revealed that the ligands are selective for palladium(II) in the presence of the base metals Co(II), Cu(II) and Ni(II), and that the 3,6-dithiaoctanediamide ligands **19** are much more efficient than the 3,7-dithianonanediamide ligands **20**. The study also revealed that extraction is much more efficient in MIBK than in toluene, and that equilibration is generally achieved within ten minutes.

Two MIP`s were prepared using platinum(II) complexes as the print species. Evaluation of the extraction capacity of the MIP`s in mixtures of the PGM`s, Pt(II) and Pd(II), and the base metals, Co(II), Cu(II) and Ni(II), showed that the MIP`s are, in fact, selective for palladium(II) at shaking times less than 4.5h, while after 4.5h, the MIP becomes increasingly selective for platinum(II) even though equilibration was not achieved during a shaking period of 17.5h. The reference polymer, on the other hand failed to show selectivity for the more kinetically inert palladium(II) or platinum(II) during this period.

The aims of the project have thus been realized, and future research is expected to include the following.

i) Optimization of the yields for the synthesis of the polymerisable ligands.

ii) Synthesis of structurally engineered dithiadiamide ligands that might afford crystalline complexes suitable for X-ray crystallographic analysis.

iii) Preparation and evaluation of additional and more efficient platinum(II)-selective MIP`s.

3. Experimental

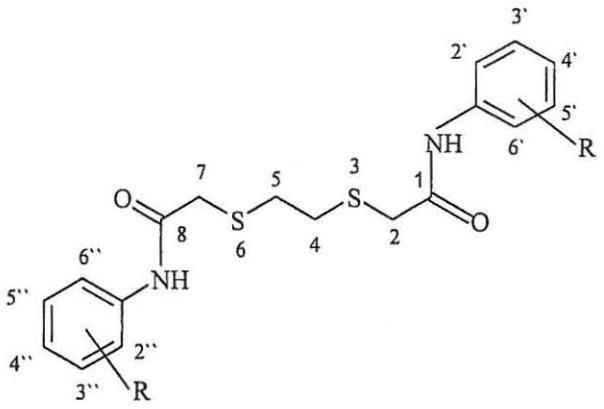
3.1. General

Reagents were used as supplied by the manufacturer. Solvents were re-distilled before use except for DMF, THF, diethyl ether and EtOH, which were dried by literature methods[83] and distilled before use. Plastic plates, pre-coated with silica gel 60 F_{254} (as supplied by Merck), were used for thin layer chromatography (TLC) and visualisation was effected by exposure to iodine vapour or by inspection under UV light. Silica gel 60 (particle size 0.040-0.063mm) was used as the stationary phase for flash chromatography.[84]

^{1}H (400MHz) and ^{13}C (100MHz) NMR spectra were recorded on a Bruker AVANCE 400MHz spectrometer. Chemical shifts are reported relative to the solvent peaks (δ_H: 7.25ppm for $CDCl_3$ and 2.50ppm for DMSO-d_6: δ_C 77.0ppm for $CDCl_3$ and 39.4ppm for DMSO-d_6). Infrared spectra were recorded on a Perkin-Elmer spectrum 2000 FT-IR spectrometer either as KBr discs or as thin films between NaCl windows (mid-infrared) and polyethylene windows (far-infrared). Melting points were determined using a Reichter hotstage apparatus and are uncorrected.

Low-resolution mass spectra were recorded on a Finnigan-MAT GCQ mass spectrometer, while high-resolution mass spectrometric data were obtained by Dr Phillip Boshoff (Cape Technikon Mass Spectrometry Unit) on a VG70-SEQ double-focusing magnetic sector instrument or by Dr Louis Fourie (Potchefstroom University). The Microanalysis (combustion analysis) data were obtained by Mr P. Benincasa at the University of Cape Town. Scanning electron micrographs were obtained on a JEOL JSM 840 SEM instrument, and the ICP-MS data were obtained by Dr Eric Hosten at the University of Port Elizabeth.

3.2. Ligand Synthesis



***N, N'*-Diphenyl-3,6-dithiaoctanediamide 19a**

A solution of 1,2-dibromoethane (0.44g, 2.3mmol) in MeOH (10ml) was added drop-wise to a stirred solution of 2-mercapto-*N*-phenylethanamide **21a** (0.77g, 4.6mmol) and KOH (0.26g, 4.6mmol) in MeOH (60 ml). The reaction mixture was stirred at room temperature for 24 h before adding H_2O (30 ml) and evaporating the MeOH *in vacuo*. The residual aqueous phase was extracted with EtOAc (3 x 30ml), and the combined extracts were dried with anhyd. $MgSO_4$. The solvent was evaporated *in vacuo* and the residue recrystallized from EtOH and washed with diethyl ether to afford, as cream crystals, *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** (0.36g, 43 %), mp.160-162°C (lit.[65] 150-152°C) (Found: M^+, 360.09669. Calc. for $C_{18}H_{20}N_2O_2S_2$, *M*: 360.09662); ν_{max} (KBr)/cm^{-1} 3305 (NH) and 1650 (C=O); δ_H (400MHz; $CDCl_3$) 2.87 (4H, s, 4- and 5-CH_2), 3.35 (4H, s, 2- and 7-CH_2), 7.13 (2H, t, *J* 7.4Hz, 4'- and 4''-H), 7.32 (4H, t, *J* 7.6Hz, 3'-, 3''-, 5'- and 5''-H), 7.55 (4H, d, *J* 7.6Hz, 2'-, 2''-, 6'- and 6''-H) and 8.52 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 32.0 (C-4 and C-5), 36.6 (C-2 and C-7), 119.8 (C-2', C-2'', C-6' and C-6''), 124.8 (C-4' and C-4''), 129.1 (C-3', C-3'', C-5' and C-5''), 139.4 (C-1' and C-1'') and 167.1 (2 x C=O).

***N,N'*-Bis(4-methoxyphenyl)-3,6-dithiaoctanediamide 19b**

The experimental procedure employed for the synthesis of *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (0.87g, 4.6mmol), 2-mercapto-*N*-(4-methoxyphenyl)ethanamide **21b** (1.83g, 9.3mmol) and KOH (0.52g,

9.3mmol). The crude diamide was recrystallized from EtOH to yield, as grey crystals, *N,N`*-bis(4-methoxyphenyl)-3,6-dithiaoctanediamide **19b** (0.95g, 48%), mp. 178-182°C (lit.[65] 163-165°C) (Found: M^+, 420.11780. Calc. for $C_{20}H_{24}N_2O_4S_2$, *M*: 420.11775); ν_{max} (KBr)/cm^{-1} 3292 (NH) and 1654 (C=O); δ_H (400 MHz; $CDCl_3$) 2.87 (4H, s, 4- and 5-CH_2), 3.33 (4H, s 2- and 7-CH_2), 3.77 (6H, s, OCH_3), 6.85 (4H, d, *J* 8.8Hz, 2'-, 2"-, 6'- and 6"-H), 7.47 (4H, d, *J* 8.8Hz, 3'-, 3"-, 5'- and 5"-H) and 8.44 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 32.0 (C-4 and C-5), 36.5 (C-2 and C-7), 55.5 (OCH_3), 114.2 (C-2', C-2", C-6' and C-6"), 121.7 (C-3', C-3", C-5' and C-5"), 130.5 (C-1' and C-1"), 156.7 (C-4' and C-4") and 166.9 (2 x C=O).

_N, N`_-Bis(2-methoxyphenyl)-3,6-dithiaoctanediamide 19c

The experimental procedure employed for the synthesis of *N,N`*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (0.44g, 2.3mmol), 2-mercapto-*N*-(2-methoxyphenyl)ethanamide **21c** (0.92g, 4.7mmol) and KOH (0.27g, 4.7mmol). The crude diamide was recrystallized from ethanol to yield, as a white powder, *N,N`*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide **19c** (0.59g, 60%), mp. 138-142°C (lit.[65] 137-140°C) (Found: M^+, 420.11832. Calc. for $C_{20}H_{24}N_2O_4S_2$, *M*: 420.11775); ν_{max} (KBr)/cm^{-1} 3293 (NH) and 1661 (C=O); δ_H (400MHz; $CDCl_3$) 2.89 (4H, s, 4- and 5-CH_2), 3.41 (4H, s, 2- and 7-CH_2), 3.83 (6H, s, OCH_3), 6.85 (2H, d, *J* 7.8Hz, 6`- and 6``-H), 6.95 (2H, t, *J* 7.8Hz, 5`- and 5``-H), 7.05 (2H, t, *J* 7.8Hz, 4`- and 4``-H), 8.30 (2H, d, *J* 7.8Hz, 3`- and 3``-H) and 9.05 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 32.5 (C-4 and C-5), 37.3 (C-2 and C-7), 55.7 (OCH_3), 110.1 (C-6' and C-6"), 119.8 (C-3' and C-3"), 121.0 (C-5' and C-5"), 124.2 (C-4' and C-4"), 127.1 (C-1' and C-1"), 148.4 (C-2' and C-2") and 166.3 (2 x C=O).

_N, N`_-Bis(3-chlorophenyl)-3, 6-dithiaoctanediamide 19d

The experimental procedure employed for the synthesis of *N,N`*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (1.31g, 6.96mmol), *N*-(3-chlorophenyl)-2-mercaptoethanamide **21d** (2.81g, 13.9mmol) and KOH (0.786g, 13.9mmol). The crude diamide was recrystallized from ethanol to yield, as pale yellow crystals, *N,N`*-bis(3-chlorophenyl)-3,6-dithiaoctanediamide **19d** (0.522g, 17.5%), mp. 120-122°C (lit.[65] 114-117°C) (Found: M^+, 428.01777. Calc. for

$C_{18}H_{18}N_2O_2S_2{}^{35}Cl_2$, *M*: 428.01868); ν_{max} (KBr)/cm^{-1} 3317 (NH) and 1658 (C=O); δ_H (400MHz; DMSO-d_6) 2.90 (4H, s, 4- and 5-CH_2), 3.35 (4H, s, 2- and 7-CH_2), 7.11 (2H, d, *J* 8.1Hz, 4'- and 4''-H), 7.32 (2H, t, *J* 8.1Hz, 5'- and 5''-H), 7.42 (2H, d, *J* 8.1Hz, 6'- and 6''-H), 7.79 (2H, s, 2'- and 2''-H) and 10.26 (2H, s, NH); δ_C (100MHz; DMSO-d_6) 31.4 (C-4 and C-5), 35.1 (C-2 and C-7), 117.4 (C-6' and C-6''), 118.5 (C-2' and C-2''), 123.0 (C-4' and C-4''), 130.3 (C-5' and C-5''), 133.0 (C-1' and C-1''), 140.2 (C-3' and C-3'') and 168.3 (2 x C=O).

N, N`-Bis(2-chlorophenyl)-3, 6-dithiaoctanediamide 19e

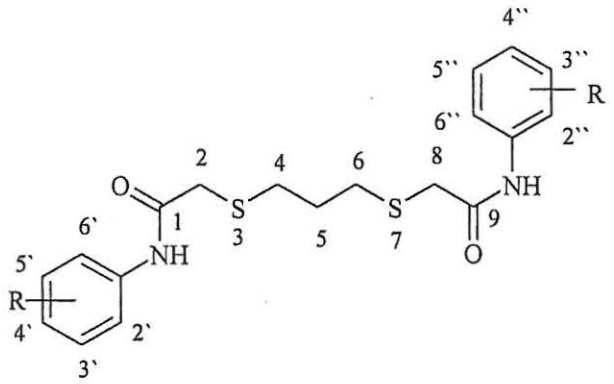
The experimental procedure employed for the synthesis of *N,N`*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (2.62g, 13.9mmol), *N*-(2-chlorophenyl)-2-mercaptoethanamide **21e** (5.62g, 27.8mmol) and KOH (1.56g, 27.8mmol). The crude diamide was recrystallized from EtOH-$CHCl_3$ (1:1) to afford, as white crystals, *N,N`*-bis(2-chlorophenyl)-3,6-dithiaoctanediamide **19e** (1.77g, 29.7%), mp. 176-178°C (lit.[65] 165-167°C) (Found: M^+, 428.01789. Calc. for $C_{18}H_{18}N_2O_2S_2{}^{35}Cl_2$, *M*: 428.01868); ν_{max} (KBr)/cm^{-1} 3273 (NH) and 1656 (C=O); δ_H (400MHz; $CDCl_3$) 2.92 (4H, s, 4- and 5-CH_2), 3.44 (4H, s, 2- and 7-CH_2), 7.05 (2H, t, *J* 7.3Hz, 4'- and 4''-H), 7.27 (2H, t, *J* 7.3Hz, 5'- and 5''-H), 7.35 (2H, d, *J* 7.3Hz, 3'- and 3''-H), 8.32 (2H, d, *J* 7.3Hz, 6'- and 6''-H) and 9.16 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 32.4 (C-4- and C-5), 37.3 (C-2 and C-7), 121.4 (C-6' and C-6''), 123.4 (C-1'- and C-1''), 125.1 (C-4' and C-4''), 127.7 (C-5' and C-5''), 129.1 (C-3' and C-3''), 134.1 (C-2' and C-2'') and 166.5 (2 x C=O).

N, N`-Bis(2-methylphenyl)-3, 6-dithiaoctanediamide 19f

The experimental procedure employed for the synthesis *N,N`*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (0.44g, 2.3mmol), 2-mercapto-*N*-(2-methylphenyl)ethanamide **21f** (0.84g, 4.6mmol) and KOH (0.26g, 4.6mmol). The crude diamide was recrystallized from ethanol to afford, as a white powder, *N,N`*-bis(2-methylphenyl)-3,6-dithiaoctanediamide **19f** (0.29g, 33%), mp. 178-184°C (lit.[65] 176-178°C) (Found: M^+, 388.12852. Calc. for $C_{20}H_{24}N_2O_2S_2$, *M*: 388.12792); ν_{max} (KBr)/cm^{-1} 3274 (NH) and 1651 (C=O); δ_H (400MHz; $CDCl_3$) 2.26

(6H, s, CH_3), 2.92 (4H, s, 4- and 5-CH_2), 3.41 (4H, s, 2- and 7-CH_2), 7.06- 7.19 (6H, series of multiplets, 3'-, 3''-, 4'-, 4''-, 5'- and 5''-H), 7.86 (2H, d, *J* 8.0Hz, 6'- and 6''-H) and 8.44 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 17.7 (2 x CH_3), 32.4 (C-4 and C-5), 36.9 (C-2 and C-7), 122.3 (C-6' and C-6''), 125.4 (C-5' and C-5''), 126.9 (C-4' and C-4''), 128.7 (C-1' and C-1''), 130.6 (C-3' and C-3''), 135.2 (C-2' and C-2'') and 166.5 (2 x C=O).

_N,N'_-Diphenyl-3,7-dithianonanediamide 20a



The experimental procedure employed for the synthesis of *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,3-dibromopropane (0.597g, 2.96mmol), 2-mercapto-*N*-phenylethanamide **21a** (0.994g, 5.94mmol) and KOH (0.333g, 5.93mmol). The mixture was stirred for 48h, and the crude product was recrystallized from H_2O-EtOH (2:1) and washed with diethyl ether to yield, as white crystals, *N,N'*-diphenyl-3,7-dithianonanediamide **20a** (0.811g, 73%), mp. 94-96°C (lit.[68] 109.5-111°C) (Found: M^+, 374.112663. Calc. for $C_{19}H_{22}N_2S_2O_2$, *M*: 374.112272); ν_{max} (KBr)/cm^{-1} 3250 (NH) and 1656 (C=O); δ_H (400MHz; $CDCl_3$) 1.95 (2H, quintet, *J* 7.0Hz, 5-CH_2), 2.71 (4H, t, *J* 7.0Hz, 4- and 6-CH_2), 3.34 (4H, s, 2- and 8-CH_2), 7.12 (2H, t, *J* 7.4Hz, 4'- and 4''-H), 7.32 (4H, t, *J* 8.0Hz, 3'-, 3''-, 5'- and 5''-H), 7.53 (4H, d, *J* 8.0Hz, 2'-, 2''-, 6'- and 6''-H) and 8.58 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 28.0 (C-5), 31.4 (C-4 and C-6), 36.8 (C-2 and C-8), 119.8 (C-2', C-2'', C-6' and C-6''), 124.7 (C-4' and C-4''), 129.0 (C-3', C-3'', C-5' and C-5''), 137.4 (C-1' and C-1'') and 166.9 (2 x C=O).

***N,N'*-Bis(4-methoxyphenyl)-3,7-dithianonanediamide 20b**

The experimental procedure employed for the synthesis of *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,3-dibromopropane (0.398g, 1.97mmol), 2-mercapto-*N*-(4-methoxyphenyl)ethanamide **21b** (0.779g, 3.95mmol) and KOH (0.23g, 4.1mmol). The mixture was stirred for 48h, and the crude oily product was purified by flash chromatography [on silica; elution with EtOAc/hexane (1:9)] and recrystallized from ethanol to afford, as cream powder, *N,N'*-bis(4-methoxyphenyl)-3,7-dithianonanediamide **20b** (0.028g, 3.2%), mp.130-134°C (lit.[69] 139°C) (Found: MH^+, 435.141876. Calc. for $C_{21}H_{27}N_2S_2O_4$, *M* +1: 435.141226); ν_{max} (KBr)/cm^{-1} 3297 (NH) and 1652 (C=O); δ_H (400MHz; $CDCl_3$) 1.96 (2H, quintet, *J* 7.0Hz, 5-CH_2), 2.71 (4H, t, *J* 7.0Hz, 4- and 6- CH_2), 3.33 (4H, s, 2- and 8- CH_2), 3.78 (6H, s, CH_3), 6.85 (4H, d, *J* 8.8Hz, 2'-, 2"-, 6'- and 6"-H), 7.43 (4H, d, *J* 8.8Hz, 3'-, 3"-, 5'- and 5"-H) and 8.44 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 28.0 (C-5), 31.5 (C-4 and C-6), 36.7 (C-2 and C-8), 55.5 (OCH_3), 114.2 (C-2', C-2", C-6' and C-6"), 121.7 (C-3', C-3", C-5' and C-5"), 130.4 (C-1' and C-1"), 156.7 (C-4' and C-4") and 166.6 (2 x C=O).

***N,N'*-Bis(2-methoxyphenyl)-3,7-dithianonanediamide 20c**

The experimental procedure employed for the synthesis of *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** was followed using, 1,3-dibromopropane (0.497g, 2.46mmol), 2-mercapto-*N*-(2-methoxyphenyl)ethanamide **21c** (0.970g, 4.92mmol) and KOH (0.280g, 4.99mmol). The crude oily product was purified by flash chromatography [on silica; elution with EtOAc/$CHCl_3$ (1:9)] to afford, as a golden viscous oil, N,N'-*bis(2-methoxyphenyl)-3,7-dithianonanediamide* **20c** (0.392g, 36.7%) (Found: MH^+, 435.141407. Calc. for $C_{21}H_{27}N_2O_4S_2$, *M* + 1: 434.141226); ν_{max} (nujol)/cm^{-1} 3326 (NH) and 1661 (C=O); δ_H (400MHz; $CDCl_3$) 1.88 (2H, quintet, *J* 7.0Hz, 5-CH_2), 2.66 (4H, t, *J* 7.0Hz, 4- and 6-CH_2), 3.29 (4H, s, 2- and 8-CH_2), 3.80 (6H, s, CH_3), 6.81 (2H, d, *J* 7.8Hz, 3'- and 3"-H), 6.89 (2H, t, *J* 7.8Hz, 5'- and 5"-H), 6.99 (2H, t, *J* 7.8Hz, 4'- and 4"-H), 8.28 (2H, d, *J* 7.8Hz, 6'- and 6"-H) and 9.16 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 27.9 (C-5), 31.2 (C-4 and C-6), 36.9 (C-2 and C-8), 55.4 (2 x OCH_3), 109.8 (C-6' and C-6"), 119.3 (C-3' and C-3"), 120.6 (C-5' and C-5"),

123.8 (C-4' and C-4"), 126.8 (C-1' and C-1"), 148.0 (C-2' and C-2") and 166.3 (2 x C=O).

_N,N'_-Bis(3-chlorophenyl)-3,7-dithianonanediamide 20d

The experimental procedure employed for the synthesis of _N,N'_-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,3-dibromopropane (0.419g, 2.08mmol), _N_-(3-chlorophenyl)-2-mercaptoethanamide **21f** (0.837g, 4.15mmol) and KOH (0.273g, 2.83mmol). The mixture was stirred for 3 days and the crude oily product was purified by flash chromatography [on silica; elution with EtOAc-$CHCl_3$ (1:9)] and recrystallized from ethanol to afford as, cream crystals, N,N'-*bis(3-chlorophenyl)-3,7-dithianonanediamide* **20d** (0.035g, 3.74%), mp. 96-98°C (Found: MH^+, 443.042896. Calc. for $C_{19}H_{21}N_2O_2S_2Cl_2$, _M_ +1: 443.042152); ν_{max} (nujol)/cm^{-1} 3338 (NH) and 1647 (C=O); δ_H (400MHz; $CDCl_3$) 1.95 (2H, quintet, _J_ 7.0Hz, 5-CH_2), 2.70 (4H, t, _J_ 7.0Hz, 4- and 6-CH_2), 3.36 (4H, s, 2- and 8-CH_2), 7.10 (2H, d, _J_ 7.8Hz, 4'- and 4"-H), 7.24 (2H, t, _J_ 7.8Hz, 5'- and 5"-H), 7.39 (2H, d, _J_ 7.8Hz, 6'- and 6"-H), 7.66 (2H, s, 2'- and 2"-H) and 8.57 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 27.9 (C-5), 31.4 (C-4 and C-6), 36.8 (C-2 and C-8), 117.7 (C-6' and C-6"), 119.8 (C-2' and C-2"), 124.8 (C-4' and C-4"), 130.1 (C-5' and C-5"), 134.8 (C-3' and C-3"), 138.4 (C-1' and C-1") and 166.9 (2 x C=O).

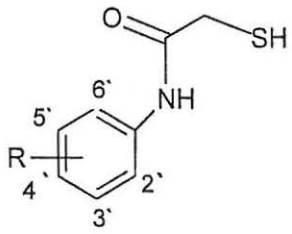
_N,N'_-Bis(2-chlorophenyl)-3,7-dithianonanediamide 20e

The experimental procedure employed for the synthesis of _N,N'_-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,3-dibromopropane (0.497g, 2.46mmol), _N_-(2-chlorophenyl)-2-mercaptoethanamide **21e** (0.995g, 4.93mmol) and KOH (0.281g, 5.01mmol). The mixture was stirred for 3 days and the crude product was re-crystallized from ethanol to afford as, white crystals, N,N'-*bis(2-chlorophenyl)-3,7-dithianonanediamide* **20e** (0.187g, 17.2%), mp. 126-128°C (Found: M^+, 442.034589. Calc. for $C_{19}H_{20}N_2S_2O_2Cl_2$, _M_: 442.034327); ν_{max} KBr/cm^{-1} 3296 (NH) and 1662 (C=O); δ_H (400MHz, $CDCl_3$) 1.97 (2H, quintet, _J_ 7.1Hz, 5-CH_2), 2.75 (4H, t, _J_ 7.1Hz, 4- and 6-CH_2), 3.40 (4H, s, 2- and 8-CH_2), 7.05 (2H, t, _J_ 8.1Hz, 4'- and 4"-H), 7.27 (2H, t, _J_ 8.1Hz, 5'- and 5"-H), 7.36 (2H, d _J_ 8.1Hz, 3'- and 3"-H), 8.35 (2H, d, _J_ 8.1Hz, 6'- and 6"-H) and 9.29 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 28.2 (C-5),

31.7 (C-4 and C-6), 37.4 (C-2 and C-8), 121.3 (C-6' and C-6"), 123.3 (C-1' and C-1"), 125.0 (C-4' and C-4"), 127.7 (C-5' and C-5"), 129.1 (C-3'- and C-3"), 134.2 (C-2'- and C-2") and 166.7 (2 x C=O).

_N,N'_-Bis(2-methylphenyl)-3,7-dithianonanediamide 20f

The experimental procedure employed for the synthesis of _N,N'_-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,3-dibromopropane (0.497g, 2.46mmol), 2-mercapto-_N_-(2-methylphenyl)ethanamide **21f** (0.893g, 4.93mmol) and KOH (0.280g, 4.99mmol). The mixture was stirred for 3 days and the crude diamide product was re-crystallized from ethanol to afford, as white crystals, N,N'-*bis(2-methylphenyl)-3,7-dithianonanediamide* **20f** (0.371g, 37.5%), mp. 116-118°C (Found: M^+, 402.143602. Calc. for $C_{21}H_{26}N_2O_2S_2$, _M_: 402.143572); ν_{max} KBr/cm^{-1} 3230 (NH) and 1656 (C=O); δ_H (400MHz; $CDCl_3$) 1.98 (2H, quintet, _J_ 7.1Hz, 5- CH_2), 2.27 (6H, s, CH_3), 2.74 (4H, t, _J_ 7.1Hz, 4- and 6-CH_2), 3.38 (4H, s, 2- and 8-CH_2), 7.05-7.22 (6H, series of multiplets, 3'-, 3"-, 4'-, 4"-, 5'- and 5"-H), 7.88 (2H, d, _J_ 7.6Hz, 6'- and 6"-H) and 8.59 (2H, s, NH); δ_H (100MHz; $CDCl_3$) 17.6 (2 x CH_3), 28.2 (C-5), 31.6 (C-4 and C-6), 36.9 (C-2 and C-8), 122.1 (C-6' and C-6"), 125.2 (C-5' and C-5"), 126.8 (C-4' and C-4"), 128.5 (C-1' and C-1"), 130.5 (C-3' and C-3"), 135.3 (C-2' and C-2") and 166.5 (2 x C=O).



2-Mercapto-_N_-phenylethanamide 21a [65]

A melt of aniline (5.01g, 53.8mmol) and 2-mercaptoacetic acid (4.90g, 53.2mmol) was stirred in a stream of nitrogen for 3 hours at 110-115°C. The melt was then cooled to room temperature, and the resulting solid was crushed into fine powder under water. The fine powder was filtered off, and washed sequentially with dilute

hydrochloric acid and water and then dried. The resulting material was recrystallized from ethanol and washed with cold diethyl ether to yield, as white crystals, 2-mercapto-*N*-phenylethanamide **21a** (3.73g, 42%), mp 110–114°C (lit.[65] 110-111°C); ν_{max} (KBr)/cm^{-1} 3300 (NH), 2573 (SH) and 1648 (C=O); δ_H (400MHz; $CDCl_3$) 2.01 (1H, t, *J* 9.2Hz, SH), 3.40 (2H, d, *J* 9.2Hz, CH_2), 7.14 (1H, t, *J* 7.4Hz, 4'-H), 7.34 (2H, t, *J* 8.0Hz, 3'- and 5'-H), 7.54 (2H, d, *J* 8.0Hz, 2'- and 6'-H) and 8.45 (1H, s, NH); δ_C (100MHz; $CDCl_3$) 29.0 (CH_2S), 120.0 (C-2' and C-6'), 124.7 (C-4'), 128.9 (C-3' and C-5'), 137.2 (C-1') and 167.6 (C=O).

2-Mercapto-*N*-(4-methoxyphenyl)ethanamide 21b

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *p*-methoxyaniline (5.01g, 40.7mmol) and 2-mercaptoacetic acid (3.79g, 41.1mmol). The crude product was recrystallized from aqueous ethanol to yield, as grey crystals, 2-mercapto-*N*-(4-methoxyphenyl)-ethanamide **21b** (4.56g, 56.8%), mp 116-120°C (lit.[65] 118.5-119.5°C); ν_{max} (KBr)/cm^{-1} 3283 (NH), 2575 (SH) and 1652 (C=O); δ_H (400MHz; $CDCl_3$) 2.00 (1H, t, *J* 9.2Hz, SH), 3.38 (2H, d, *J* 9.2Hz, CH_2S), 3.79 (3H, s, OCH_3), 6.87 (2H, d, *J* 9.8Hz, 2'- and 6'-H), 7.44 (2H, d, *J* 9.8Hz, 3'- and 5'-H) and 8.37 (1H, s, NH); δ_C (100MHz; $CDCl_3$) 29.0 (CH_2S), 55.5 (OCH_3), 114.2 (C-2' and C-6'), 121.7 (C-3' and C-5'), 130.4 (C-1'), 156.8 (C-4') and 166.9 (C=O).

2-Mercapto-*N*-(2-methoxyphenyl)ethanamide 21c

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *o*-methoxyaniline (3.71g, 30.1mmol) and 2-mercaptoacetic acid (2.78g, 30.2mmol). The crude product was recrystallized from aqueous ethanol to yield, as light grey plates, 2-mercapto-*N*-(2-methoxyphenyl)-ethanamide **21c** (3.23g, 54%), mp. 64-66°C (lit.[65] 64-66°C); ν_{max} (KBr)/cm^{-1} 3324 (NH), 2557 (SH) and 1669 (C=O); δ_H (400MHz; $CDCl_3$) 2.02 (1H, t, *J* 9.1Hz, SH), 3.38 (2H, d, *J* 9.1Hz, CH_2S), 3.88 (3H, s, CH_3), 6.87 (1H, d, *J* 8.2Hz, 6'-H), 6.95 (1H, t, *J* 7.8Hz, 5'-H), 7.05 (1H, t, *J* 7.8Hz, 4'-H), 8.32 (1H, d, *J* 8.0Hz, 3'-H) and 9.00 (1H,

s, NH); δ_C (100MHz; $CDCl_3$) 29.4 (CH_2S), 55.7 (OCH_3), 110.0 (C-6'), 119.6 (C-3'), 120.0 (C-5'), 124.1 (C-4'), 127.1 (C-1'), 148.2 (C-2') and 167.0 (C=O).

_N_-(3-Chlorophenyl)-2-mercaptoethanamide 21d

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *m*-chloroaniline (3.86g, 30.2mmol) and 2-mercaptoacetic acid (2.78g, 30.2mmol). The crude product was recrystallized from aqueous ethanol and washed with cold water to yield, as white crystals, *N*-(3-chlorophenyl)-2-mercaptoethanamide **21d** (3.02g, 49.7%), mp. 82-84°C (lit.[65] 70-73°C); ν_{max} (KBr)/cm^{-1} 3293 (NH), 2545 (SH) and 1655 (C=O); δ_H (400MHz; $CDCl_3$) 2.02 (1H, t, *J* 9.2Hz, SH), 3.39 (2H, d, *J* 9.2Hz, CH_2), 7.11 (1H, d, *J* 8.0Hz, 4'-H), 7.26 (1H, t, *J* 8.0Hz, 5'-H), 7.39 (1H, d, *J* 8.0Hz, 6'-H), 7.66 (1H, s, 2'-H) and 8.48 (1H, s, NH); δ_C (100MHz; $CDCl_3$) 29.1 (CH_2S), 117.7 (C-6'), 119.9 (C-2'), 124.9, (C-4') 130.1 (C-5'), 134.8 (C-1'), 138.4 (C-3') and 167.1 (C=O).

_N_-(2-Chlorophenyl)-2-mercaptoethanamide 21e

Method A

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *o*-chloroaniline (12.8g, 0.10mol) and 2-mercaptoacetic acid (9.2g, 0.10mol). After stirring for 4 hours, the melt was cooled to room temperature and conc. HCl was added drop-wise until all the oil solidified. The solid was crushed into a powder under water and then filtered off, washed with aqueous ethanol and dried *in vacuo* to afford, as white crystals, *N*-(2-chorophenyl)-2-mercaptoethanamide **21e** (5.46g, 27%), mp. 54-56°C (lit.[65] 56-59°C); ν_{max} (KBr)/cm^{-1} 3256 (NH), 2557 (SH) and 1659 (C=O); δ_H (400MHz; DMSO-d_6) 3.01 (1H, t, *J* 8.2Hz, SH), 3.41 (2H, d, *J* 8.2Hz, CH_2S), 7.19 (1H, t, *J* 7.9Hz, 4'-H), 7.34 (1H, t, *J* 7.6Hz, 5'-H), 7.50 (1H, d, *J* 7.6Hz, 3'-H), 7.79 (1H, d, *J* 7.9Hz, 6'-H) and 9.67 (1H, s, NH); δ_C (100MHz; DMSO-d_6) 27.8 (CH_2S), 123.5 (C-6'), 125.2 (C-1'), 126.1 (C-4'), 127.4 (C-5'), 129.4 (C-3'), 134.6 (C-2') and 168.9 (C=O).

Method B

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *o*-chloroaniline (5.03g, 39.4mmol) and 2-mercaptoacetic acid (5.03g, 54.6mmol). In this case, the melt did not solidify on cooling under water and, consequently, the mixture was acidified with conc. HCl and extracted with $CHCl_3$ (3 x 10ml). The extracts were washed with 10% aq. NaOH and the washings were acidified with conc. HCl and re-extracted, with $CHCl_3$ (3 x 10ml). The combined extracts were dried with anhydrous $MgSO_4$ and the excess solvent was evaporated *in vacuo* to give a pale-yellow, oily residue, which was purified by flash chromatography [on silica; elution with EtOAc/$CHCl_3$ (1:9)], to yield, as white crystals, *N*-(2-chorophenyl)-2-mercaptoethanamide **21e** (0.60g, 7.3%).

2-Mercapto -*N*-(2-methylphenyl)ethanamide 21f

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using *o*-toluidine (1.10g, 10.3mmol) and 2-mercaptoacetic acid (0.951g, 10.3mmol). The crude product was recrystalized from ethanol and washed with cold diethyl ether to yield, as pink crystals, 2-mercapto-*N*-(2-methylphenyl)ethanamide **21f** (0.86g, 46%), mp. 80-82°C (lit.[65] 88-90°C); ν_{max} (KBr)/cm^{-1} 3356 (NH), 2526 (SH) and 1651 (C=O); δ_H (400MHz; $CDCl_3$) 2.02 (1H, t, *J* 9.2Hz, SH), 2.31 (3H, s, CH_3), 3.44 (2H, d, *J* 9.2Hz, CH_2), 7.06-7.21 (3H, series of multiplets, 3'-, 4'-, 5'-H), 7.90 (1H, d, *J* 8.0Hz, 6`-H) and 8.51 (1H, s, NH), δ_C (100MHz; $CDCl_3$) 17.6 (CH_3), 29.1 (CH_2S), 121.2 (C-6'), 125.3 (C-5'), 126.8 (C-4'), 128.8 (C-1'), 130.4 (C-3'), 135.2 (C-2') and 167.1 (C=O).

Attempted synthesis of 2-Mercapto-*N*-(1-naphthyl)ethanamide 26

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using 1-aminonaphthalene (0.998g, 6.97mmol) and 2-mercaptoacetic acid (0.662g, 7.19mmol). The dark grey powder was recrystallized from aqueous ethanol and washed with cold diethyl ether to afford, as pale grey crystals, the disulfide **27** (0.184g); δ_H (400MHz; DMSO-d_6) 3.95 (4H, s, SCH_2), 7.52 (6H, series of multiplets, 2-, 2-, 3-, 3-, 4- and 4-H), 7.77 (4H, 2 x d, J

8.0Hz, 7-, 7-, 8-, and 8-H), 7.94 (2H, d, *J* 8.0Hz, 6- and 6-H), 8.12 (2H, d, *J* 8.0Hz, 9- and 9-H) and 10.17 (2H, s, NH).

N, N`-Bis(4-allyloxyphenyl)-3, 6-dithiaoctanediamide 28

The experimental procedure employed for the synthesis of *N,N`*-diphenyl-3,6-dithiaoctanediamide **19a** was followed, using 1,2-dibromoethane (0.131g, 0.696mmol), *N*-(4-allyoxyphenyl)-2-mercaptoethanamide **30** (0.298g, 1.33mmol) and KOH (0.0753g, 1.33mmol). The crude diamide was recrystallized from EtOH to yield, as yellow crystals, N,N`-*bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide* **28** (0.117g, 35.6%), mp. 120-124°C (Found: M^+, 472.149845. Calc. for $C_{24}H_{28}N_2S_2O_4$, *M*: 472.149051); ν_{max} (KBr)/cm^{-1} 3300 (NH) and 1654 (C=O); δ_H (400MHz, $CDCl_3$) 2.86 (4H, s, SCH_2CH_2S), 3.33 (4H, s, $COCH_2$), 4.50 (4H, d, *J* 4.8Hz, CH_2O), 5.33 (4H, 2 x d, *J* 17.2 and 10.4Hz, CH_2=CH), 6.02 (2H, m, CH_2=C*H*), 6.83 (4H, d, *J* 8.8Hz, 2'-, 2"- 6'- and 6"-H), 7.42 (4H, d, *J* 8.8Hz, 3'-, 3"-, 5'- and 5"-H) and 8.53 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 31.9 (C-4 and C-5), 36.4 (C-2 and C-7), 69.1 (2 x CH_2O), 115.0 (C-3'-, C-3"-, C-5'- and C-5"), 117.7 (2 x CH=CH_2), 121.8 (C-2', C-2", C-6' and C-6"), 130.7 (C-1' and C-1"), 133.2 (2 x *C*H=CH_2), 155.7 (C-4' and C-4") and 167.0 (2 x C=O).

***N*-(4-Allyloxyphenyl)-2-mercaptoethanamide 29**

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using 4-allyloxyaniline **31** (1.02g, 6.84mmol) and 2-mercaptoacetic acid (0.64g, 6.9mmol). The yellow powder was recrystallized from aqueous ethanol and washed with cold water to yield, as white crystals, N-*(4-allyloxyphenyl)-2-mercaptoethanamide* **29** (0.61g, 40%), mp. 102-104°C (Found: M^+, 223.0668. Calc. for $C_{11}H_{13}NO_2S$, *M*: 223.06670); ν_{max} (KBr)/cm^{-1} 3295 (NH), 2569 (SH) and 1657 (C=O); δ_H (400MHz; $CDCl_3$) 2.01 (1H, t, *J* 8.7Hz, SH), 3.36 (2H, d, *J* 8.2Hz, CH_2S), 4.50 (2H, d, *J* 5.1Hz, CH_2O), 5.33 (2H, 2xd, *J* 17.3 and 10.5Hz, CH_2=CH), 6.03 (1H, m, CH_2=C*H*), 6.87 (2H, d, *J* 8.8Hz, 2'- and 6'-H), 7.42 (2H, d, *J* 8.8Hz, 3'- and 5'-H) and 8.43 (1H, s, NH); δ_C (100MHz; $CDCl_3$) 29.0 (CH_2), 69.1

(OCH_2), 115.1 (C-2' and C-6'), 117.7 (CH_2=CH), 121.8 (C-3' and C-5'), 130.5 (C-1'), 133.2 (CH_2=CH), 155.8 (C-4') and 167.0 (C=O).

Attempted synthesis of *N*-[4-(1-buten-4-yloxy)phenyl]-2-mercaptoethanamide 30

The experimental procedure employed for the synthesis of 2-mercapto-*N*-phenylethanamide **21a** was followed, using 4-(1-buten-4-yloxy)aniline **32** (0.471g, 28.8mmol) and 2-mercaptoacetic acid (0.265g, 28.7mmol). The yellow powder was recrystallized from aqueous ethanol to afford, as greyish yellow powder, the disulfide **25g** (0.0547g); δ_H (400MHz; DMSO-d_6) 3.67 (4H, s, SCH_2), 6.69 (4H, d, *J* 8.8Hz, 2-, 2-, 6- and 6-H), 7.36 (4H, d, *J* 8.8Hz, 3-, 3-, 5- and 5-H), 8.41 (2H, s, NH) and 9.21 (2H, s, OH).

4-(Allyloxy)aniline 31

Method A

A solution of 4`-(allyloxy)acetanilide **37** (6.36g, 33.3mmol) in 20% aq. H_2SO_4 (170ml) was boiled under reflux for 1h. On cooling the solution to room temperature, fine crystals precipitated out and were filtered off and dried. The crystals (3.42g) were dissolved in hot water (200ml), and the solution was basified to pH 11 with 10% aq. NaOH. The amine was extracted into diethyl ether and the extracts were dried over solid KOH. The excess ether was evaporated *in vacuo* and the oily residue distilled under reduced pressure to yield, as a yellow oil, 4-(allyloxy)aniline **31** (1.02g, 49%), bp 110°C/0.05mmHg (lit.[70,71] 143°C/11mmHg); δ_H (400MHz; $CDCl_3$) 3.41 (2H, s, NH_2), 4.45 (2H, d, *J* 5.2Hz, CH_2O), 5.31 (2H, 2 x d, *J* 17.2 and 10.4Hz, CH_2=CH), 6.04 (1H, m, CH_2=CH), 6.62 (2H, d, *J* 8.8Hz, 2- and 6-H) and 6.76 (2H, d, *J* 8.8Hz, 3- and 5-H).

Method B

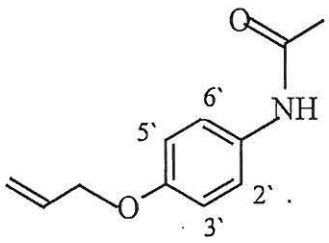
A solution of *p*-aminophenol (2.95g, 27.0mmol) and KOH (1.51g, 27.0mmol) in MeOH (50ml) was stirred for 2h at room temperature. Allyl bromide (3.27g, 27.0mmol) was added drop-wise and the mixture was stirred for a further 24 h. Water (50mL) was added to the mixture, and the EtOH was removed *in vacuo*. The aqueous

residue was extracted into EtOAc (7 x 40ml) and the EtOAc extracts were dried with anhyd. $MgSO_4$. The excess solvent was evaporated *in vacuo* to afford a black oily residue (3.50g), shown by ^1H NMR analysis to contain some of the expected product. Distillation under reduced pressure gave 4-(allyloxy)aniline **31** as yellow oil (0.60g, 15%).

4-(1-Buten-4-yloxy)aniline 32

The experimental procedure employed for the synthesis of 4-(allyloxy)aniline **31** was followed, using 4-(1-buten-4-yloxy)acetanilide **39** (1.72g, 8.38mmol) and 20% aq. H_2SO_4 (40ml). The resulting crystals (1.53g) were left to dry overnight, and then dissolved in hot water; the solution was basified to pH 11 with 5% aq. NaOH. Following extraction with diethyl ether and evaporation of the solvent, the dried oily residue was distilled under reduced pressure to yield, as a light purple oil, *4-(buten-4-yloxy)aniline* **32** (0.21g, 21.5%), bp. 120°C/0.1mmHg; δ_H (400MHz; $CDCl_3$) 2.50 (2H, quartert, *J* 6.7Hz, CH_2CH_2O), 3.31 (2H, s, NH_2), 3.94 (2H, t, *J* 6.7Hz, CH_2CH_2O), 5.14 (2H, 2 x d, *J* 17.2 and 10.2Hz, CH_2=CH), 5.90 (1H, m, CH_2=CH), 6.61 (2H, d, *J* 8.8Hz, 2- and 6-H) and 6.75 (2H, d, *J* 8.8Hz, 3- and 5-H); δ_C (100 MHz; $CDCl_3$) 33.7 (CH_2CH_2O), 67.9 (OCH_2), 115.6 (C-3 and C-5), 116.1 (C-2 and C-6), 116.6 (CH_2=CH), 134.6 (CH_2=CH), 139.9 (C-1) and 151.9 (C-4).

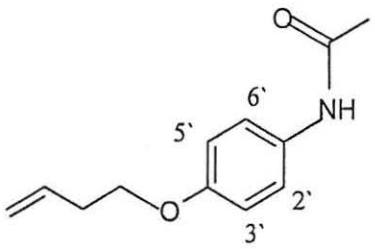
4`-(Allyloxy)acetanilide 38



Allyl bromide (4.50g, 37.2mmol) was added drop-wise to a stirred solution of *p*-acetamidophenol (5.11g, 33.8mmol) in ethanol (25ml), to which had been added a solution of KOH (2.37g, 42.2mmol) in water (2ml). The resulting mixture was boiled under reflux for 2h. Water was added to the mixture and the resulting solid was filtered off and recrystallized from dilute ethanol to afford, as fine white crystals, 4`-

(allyloxy)acetanilide **38** (5.59g, 85%), mp. 86-88°C (lit. [70,71] 88-89°C); ν_{max} KBr/cm^{-1} 3289 (NH) and 1661(C=O); δ_H (400MHz; DMSO-d_6) 2.00 (3H, s, CH_3), 4.50 (2H, d, CH_2O), 5.30 (2H, 2xd, *J* 17.2 and 10.4Hz, C*H*$_2$=CH), 6.02 (1H, m, CH_2=C*H*), 6.87 (2H, d, *J* 8.8Hz, 2'- and 6'-H), 7.46 (2H, d, *J* 8.8Hz, 3'- and 5'-H) and 9.76 (1H, s, NH); δ_C (100MHz; $CDCl_3$) 24.1 (CH_3), 69.0 (CH_2O), 114.9 (C-3' and C-5'), 117.6 (CH=*C*H$_2$), 121.9 (C-2' and C-6'), 131.2 (C-1'), 133.2 (*C*H=CH$_2$), 155.4 (C-4') and 168.5 (C=O).

4`-(1-Buten-4-yloxy)acetanilide 40



The experimental procedure employed for the synthesis of 4`-(allyloxy)acetanilide **38** was followed, using *p*-acetoamidophenol (5.02g, 33.2mmol), 4-bromobutene (4.92g, 36.4mmol) and KOH (2.33g, 41.5mmol). Recrystallization of the crude product from aqueous ethanol afforded, as white crystals, *4`-(1-buten-4-yloxy)acetanilide* **40** (3.39g, 49.7%), mp. 82-84°C (Found: M^+, 205.10947. Calc. for $C_{12}H_{15}NO_2$, *M*: 205.11208); ν_{max} (KBr)/cm^{-1} 3299 (NH) and 1661 (C=O); δ_H (400MHz; $CDCl_3$) 2.14 (3H, s, CH_3), 2.52 (2H, quartet, *J* 6.7Hz, C*H*$_2$CH$_2$O), 3.98 (2H, t, *J* 6.7Hz, CH_2O), 5.12 (2H, 2xd, *J* 17.2 and 10.2Hz, C*H*$_2$=CH), 5.92 (1H, m, CH_2=C*H*), 6.84 (2H, d, *J* 8.9Hz, 2'- and 6'-H), 7.09 (1H, s, NH) and 7.36 (2H, d, *J* 8.9Hz, 3'- and 5'-H); δ_C (100MHz; $CDCl_3$) 24.3 (CH_3), 33.6 (CH*C*H$_2$), 67.5 (CH_2O), 114.9 (C-3' and C-5'), 117.0 (*C*H$_2$=CH), 121.9 (C-2' and C-6'), 130.9 (C-1'), 134.4 (CH$_2$=*C*H), 155.8 (C-4') and 168.3 (C=O).

Diethyl allylmalonate 42[74]

Diethyl malonate (33.5g, 0.209mol) was added drop-wise to a solution of sodium ethoxide [prepared by adding Na metal (4.81g, 0.209mol) in portions to dry ethanol (133ml)] at 40°C, and the mixture was stirred for 1h. Allyl bromide (25.3g, 0.209mol)

was added drop-wise and the resulting mixture was boiled under reflux for a further 9h. Water was added and the mixture was extracted several times with diethyl ether. The extracts were then washed with brine and dried over $CaCl_2$. The solvent was evaporated *in vacuo* and the oily residue distilled *in vacuo* to yield, as a colourless oil, diethyl allylmalonate **42** (27.5g, 65.7%), bp. 122-124°C/20mmHg (lit.[74] 116-124°C/20mmHg); δ_H (400MHz; $CDCl_3$) 1.00 (6H, m, 2 x CH_3), 2.37 (2H, d, *J* 7.4Hz, CH_2), 3.17 (1H, d, *J* 7.5Hz, CH), 3.92 (4H, m, 2 x OCH_2), 4.82 (2H, 2xd, *J* 17.1 and 10.2Hz, CH=C*H*$_2$), 5.54 (1H, m, C*H*=CH_2); δ_C (100MHz; $CDCl_3$) 13.4 (CH_3), 32.2 (CH_2), 51.0 (CH), 60.6 (OCH_2), 116.7 (CH=C*H*$_2$), 133.7 (C*H*=CH_2) and 168.1 (C=O).

2-(Hydroxymethyl)-4-penten-1-ol 43[75]

A suspension of $LiAlH_4$ (3.69g, 0.0972mol) in dry diethyl ether (80ml), was boiled under reflux for 1h. A solution of diethyl allylmalonate **42** (9.35g 0.0468mol) in dry diethyl ether (30ml) was added drop-wise, and the mixture was boiled under reflux for 9h. The excess $LiAlH_4$ was destroyed by carefully adding water (4ml), 15% aq. NaOH (4ml) and water (8ml) to the mixture cooled in an ice-bath.[17,50] The ethereal solution was retained and the precipitated solid was filtered off and washed several times with diethyl ether. The ether layer and washings were dried with anhyd. $MgSO_4$ and evaporated *in vacuo*. The colourless oily residue was purified by flash chromatography [on silica; elution with; EtOAc-$CHCl_3$ (3:2)] to afford, as a pale-yellow oil, 2-(hydroxymethyl)-4-penten-1-ol **43** (3.01g, 55.6%) (Found: MH^+, 117.091428. calc. for $C_6H_{13}O_2$, *M* +1: 117.091555); δ_H (400MHz; $CDCl_3$) 1.83 (1H, m, 2-CH), 2.03 (2H, t, *J* 7.0Hz, 3-CH_2), 3.39 (2H, s, OH), 3.62 and 3.75 (2x2H, 2 x dd, *J* 4.0 and 10.8Hz, 2 x OCH_2), 5.03 (2H, overlapping doublets, 5-CH_2) and 5.77 (1H, m, 4-CH); δ_C (100MHz; $CDCl_3$) 32.4 (C-3), 41.7 (C-2), 64.9 (C-1), 116.5 (C-5) and 136.1 (C-4).

5-Chloro-4-(chloromethyl)-1-pentene 44a

$SOCl_2$ (3.07g, 25.8mmol) was added drop-wise to a mixture of 2-(hydroxymethyl)-4-penten-1-ol **43** (0.749g, 6.46mmol) and pyridine (0.510g, 6.46mmol), and the mixture was left to stand overnight. The mixture was then boiled under reflux for 3h,

following which water was added. This mixture was extracted several times with diethyl ether, the ethereal extracts were combined and washed with 15% aq. $NaHCO_3$, and the ether was evaporated *in vacuo* to yield a brown residue. The residue was distilled *in vacuo* to afford, as a colourless oil, 5-chloro-2-(chloromethyl)-1-pentene **44a** (0.190g, 19.4%), bp. 67-70°C/20mmHg (lit.[85] 62-64°C/16mmHg); δ_H (400MHz; $CDCl_3$) 2.13 (1H, m, CH), 2.22 (2H, t, *J* 7.0Hz, CH_2), 3.58 and 3.70 (4H, 2 x dd, *J* 4.4 and 6.1Hz, 2 x CH_2Cl), 5.13 (2H, 2 x d, *J* 4.6 and 12.0Hz, CH=CH_2), 5.72 (1H, m, C*H*=CH_2); δ_C (100MHz; $CDCl_3$) 33.9 (CH), 42.2 (CH_2), 45.0 (CH_2Cl), 118.2 (CH=*C*H_2) and 134.3 (*C*H=CH_2).

Attempted synthesis of 5-bromo-2-(bromomethyl)- 1-pentene 44b

Method A

Sulphuric acid (1.2ml) was added drop-wise to a stirred solution of 47% aq. hydrobromic acid (2.4ml) cooled in an ice-bath. To this mixture, 2-(hydroxymethyl)-4-penten-1-ol **43** (0.833g, 7.17mmol) was added drop-wise, and the mixture was boiled under reflux for 3h. Water was added, and the mixture was extracted with diethyl ether. The ether extracts were washed with sodium bicarbonate and dried with anhyd. $MgSO_4$. The ether was evaporated *in vacuo* and the brown residue was distilled *in vacuo* to afford, a colourless oil, (0.511g), bp. 50-52°C/0.5mmHg, the NMR of which did not correspond with the expected structure.

Method B

To a stirred solution of 2-(hydroxymethyl)-4-penten-1-ol **43** (1.07g, 9.23mmol) in dry benzene (2ml), dry pyridine (0.1ml) was added, and the mixture was cooled to 0°C. To this mixture, phosphorous tribromide (2.85g, 10.5mmol) in dry benzene (2ml) was added at a rate such that the temperature of the mixture did not exceed 10°C. The mixture was left at room temperature for 14.5h and then boiled under reflux for 8h. The excess phosphorous tribromide was cautiously destroyed by the drop-wise addition of water (2ml). The mixture was extracted several times with diethyl ether, and the ethereal solution was washed with sat. aq. $NaHCO_3$ and dried with anhyd. $MgSO_4$. The ether was removed *in vacuo* and the resulting oily residue was purified by distillation *in vacuo*. Two fractions were obtained, the first boiling at 56-

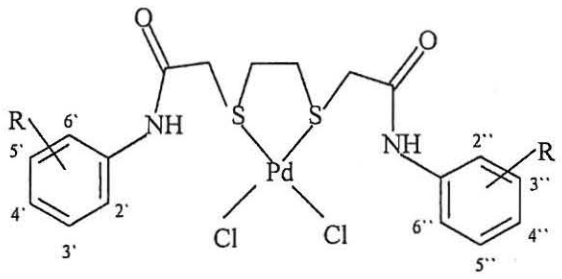
58°C/1mmHg (shown by ^{1}H NMR analysis not to contain the expected product) and the second, the residue, which was shown to contain the expected product. The residue was purified by PLC and HPLC but the impurities could not be removed.

5-Allyl-*N,N*`-bis(4-methoxyphenyl)-3,6-dithianonanediamide 45

A solution of 2-mercapto-*N*-(4-methoxyphenyl)ethanamide **21b** (0.18g, 0.92mmol) and KOH (0.050g, 0.92mmol) in methanol (5ml) was boiled under reflux for 5min under nitrogen. The solution was cooled to room temperature and 5-chloro-2-(chloromethyl)-1-pentene **44a** (0.070g, 0.46mmol) was added drop-wise and the mixture refluxed for another 3h. The reaction was then stirred overnight at room temperature and the resulting precipitate was filtered off. The methanol was evaporated *in vacuo* and the oily residue was purified by column chromatography [on silica; elution with EtOAc-$CHCl_3$ (1:9)] to afford, as a yellow oil *5-allyl*-N,N`-*bis(4-methoxyphenyl)-3,6-dithianonanediamide* **45** (0.022g, 2%); δ_H (400MHz; $CDCl_3$) 2.05 (1H, m, 5-H), 2.23 (2H, t, *J* 7.0Hz, $CH_2CH{=}CH_2$), 3.34 (4H, s, 2- and 8-CH_2), 3.61 and 3.72 (4H, 2xdd, *J* 4.3 and 5.1Hz, 4- and 6-H), 3.78 (6H, s, OCH_3), 5.10 (2H, m, $CH{=}CH_2$), 5.70 (1H, m, $CH{=}CH_2$), 6.87 (4H, d, *J* 9.0Hz, 2'-, 2"-, 6'- and 6"-H), 7.44 (4H, d, *J* 9.0Hz, 3'-, 3"-, 5'- and 5"-H) and 8.51 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 35.4 ($CH_2CH{=}CH_2$), 37.2 (C-4 and C-6), 39.4 (C-5), 46.5 (C-2 and C-8), 55.5 (OCH_3), 114.2 (C-2', C-2", C-6' and C-6"), 118.2 ($CH{=}CH_2$), 121.6 (C-3', C-3", C-5' and C-5"), 130.5 (C-1' and C-1"), 134.5 ($CH{=}CH_2$), 156.7 (C-4' and C-4") and 166.3 (2 x C=O).

3.3 Complexation Studies

3.3.1 Palladium complexes



***cis*-Dichloro-(*N,N'*-diphenyl-3,6-dithiaoctanediamide)-*S,S'*-palladium(II) 48a**

To a stirred 0.001M solution of $PdCl_2$ in 0.1000M aq.HCl (20ml), a solution of *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** (7.1mg, 0.020mmol) in MeOH (80ml) was added drop-wise. The mixture was stirred for 48h, and the resulting yellow solution was evaporated *in vacuo*. The residual solid was washed with methanol and dried under high vacuum to yield, as a yellow powder, *cis*-dichloro-(*N,N'*-diphenyl-3,6-dithiaoctanediamide)-*S,S'*-palladium(II) **48a** (9.6mg, 89.7%), mp. 230-236°C (decomp.) (Found: C, 40.6%; H, 3.4%; 5.2%; MH^+, 536.945207. Calc. for $C_{18}H_{21}N_2S_2O_2PdCl_2$, *M* +1: 536.945627; C, 40.3%; H, 3.7%; N, 5.2%); ν_{max} KBr/cm^{-1} 3299 (NH) and 1667 (C=O); ν_{max} polyethylene/cm^{-1} 336 and 326 (Pd—Cl); δ_H (400MHz; DMSO-d_6) 3.56¶ and 3.65 (4H, m, 4- and 5- CH_2), 4.08-4.15¶ and 4.38-4.48 (4H, 4 x d, *J* 15.6Hz, 2- and 7-CH_2), 7.10 (2H, t, *J* 7.4Hz, 4'- and 4"-H), 7.34 (4H, t, *J* 7.8Hz, 3'-, 3"-, 5'- and 5"-H), 7.60 (4H, d, *J* 7.2Hz, 2'-, 2"-, 6'- and 6"-H) and 10.52¶ and 10.58 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 31.5¶ and 35.1 (C-4 and C-5), 38.2¶ and 41.3 (C-2 and C-7), 119.1¶ and 119.4 (C-2', C-2", C-6' and C-6"), 123.3¶ and 123.9 (C-4' and C-4"), 128.6¶ and 128.7 (C-3', C-3", C-5' and C-5"), 138.2¶ and 138.9 (C-1' and C-1") and 163.8 (4 x C=O)

¶ Signal doubling due to presence of geometric isomers.

cis-Dichloro-[_N,N`_-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-S,S'-palladium(II) 48b

The experimental procedure employed for the synthesis of _cis_-dichloro-(_N,N'_-diphenyl-3,6-dithiaoctanediamide)-_S,S'_-palladium(II) **48a** was followed, using _N,N`_-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide **19c** (8.7mg, 0.020mmol) in MeOH (80ml) and a 0.001**M** solution of $PdCl_2$ in 0.1000**M** aq. HCl (20ml). The resulting solid was washed with methanol and dried under high vacuum to yield, as an orange powder, _cis_-dichloro-[_N,N`_-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-_S,S'_-palladium(II) **48b** (2.9mg, 26%), mp. 132-134°C (Found: M^+, 595.9876. Calc. for $C_{20}H_{24}N_2O_4S_2Cl_2{}^{106}Pd$, _M_: 595.9893); ν_{max} (KBr)/cm^{-1} 3270 NH) and 1661 (C=O); ν_{max} (polyethylene)/cm^{-1} 327 and 302 (Pd—Cl); δ_H (400MHz; DMSO-d_6) 3.45¶ and 3.63 (4H, 2 x d, _J_ 9.7Hz, 4- and 5-CH_2), 3.84 (6H, s, OCH_3), 4.23¶ and 4.44 (4H, 2 x d, _J_ 15.8Hz, 2- and 7-CH_2), 6.92 (2H, t, _J_ 7.3Hz, 4'- and 4"-H), 7.07 (2H, d, _J_ 7.3Hz, 6'- and 6"-H), 7.13 (2H, d, _J_ 7.3Hz, 3'- and 3"-H), 7.88 (2H, t, _J_ 7.3Hz, 5'- and 5"-H) and 9.82¶ and 9.86 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 38.2¶ and 38.5 (C-4 and C-5), 42.2¶ and 42.6 (C-2 and C-7), 55.6 (2 x OCH_3), 111.3 (C-6' and C-6"), 120.1 (C-3' and C-3"), 122.5¶ and 122.7 (C-5' and C-5"), 125.2¶ and 125.3 (C-4' and C-4"), 126.1¶ and 126.2 (C-1' and C-1"), 149.9¶ and 150.1 (C-2' and C-2") and 163.9¶ and 164.0 (2 x C=O).

cis-Dichloro-[_N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-_S,S'_-palladium(II) 48c

The experimental procedure employed for the synthesis of _cis_-dichloro-(_N,N'_-diphenyl-3,6-dithiaoctanediamide)-_S,S'_-palladium(II) **48a** was followed, using _N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide **19e** (8.8mg, 0.020mmol) in MeOH-acetone (1:1); (80ml) and a 0.001**M** solution of $PdCl_2$ in 0.1000**M** aq. HCl (20ml). The resulting solid was washed with methanol and dried under high vacuum to yield, as an orange powder, _cis_-dichloro-[_N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-_S,S'_-palladium(II) **48c** (10.9mg, 90.0%) (Found: C, 35.50%; H, 2.6%; N, 4.5%; MH^+, 604.868827. Calc. for $C_{18}H_{19}N_2S_2O_2PdCl_4$, _M_ +1: 604.867683; C, 35.8%; H, 3.0%, N, 4.6%); ν_{max} (KBr)/cm^{-1} 3264 (NH) and 1662 (C=O); ν_{max}

(polyethylene)/cm^{-1} 327 and 305 (Pd—Cl); δ_H (400MHz; DMSO-d_6) 3.48¶ and 3.65 (4H, series of multiplets, 4- and 5-CH_2), 4.21¶ and 4.45 (4H, 2 x overlapping doublets, 2- and 7- CH_2), 7.25 (2H, t, *J* 7.3Hz, 4'- and 4"-H), 7.36 (2H, t, *J* 7.3Hz, 5'- and 5"-H), 7.52 (2H, d, *J* 7.3Hz, 3'- and 3"-H), 7.70 (2H, d, *J* 7.3Hz, 6'- and 6"-H) and 10.15 and 10.21 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 38.2¶ and 38.6 (C-4 and C-5), 40.5¶ and 40.8 (C-2 and C-7), 126.4¶ and 126.5, 126.7 and 126.8, 127.0 and 127.1, 127.4, 129.5, 133.9 (Ar-C) and 164.4 (4 x C=O).

cis-Dichloro-[*N,N*`-bis(3-chlorophenyl)-3,6-dithiaoctanediamide]-*S,S*'-palladium(II) 48d

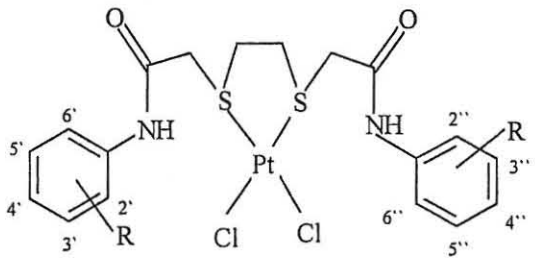
The experimental procedure employed for the synthesis of *cis*-dichloro-(*N,N*'-diphenyl-3,6-dithiaoctanediamide)-*S,S*'-palladium(II) **48a** was followed, using *N,N*`-bis(3-chlorophenyl)-3,6-dithiaoctanediamide **19d** (9.0mg, 0.020mmol) in MeOH (80mL) and a 0.001M solution of $PdCl_2$ in 0.1000M aq. HCl (20ml). The resulting solid was washed with methanol and dried *in vacuo* to yield, as an orange powder, *cis*-dichloro-[*N,N*`-bis(3-chlorophenyl)-3,6-dithiaoctanediamide]-*S,S*'-palladium(II) **48d** (4.7mg, 87%), (Found: C, 35.95%; H, 2.2%; N, 4.4%; MH^+, 605.875143. Calc. for $C_{18}H_{20}N_2S_2O_2PdCl_4$, *M* +1: 605.875508; C, 35.8%; H, 3.0%; N, 4.6%); ν_{max} (KBr)/cm^{-1} 3315 (NH), 1660 (C=O); ν_{max} (polyethylene)/cm^{-1} 329 and 314 (Pd—Cl); δ_H (400MHz; DMSO-d_6) 3.55-3.64 (4H, m, 4- and 5-CH_2), 4.09-4.40 (4H, series of multiplets, 2- and 7- CH_2), 7.17 (2H, d, *J* Hz, 4'- and 4"-H), 7.36-746 (4H, series of multiplets, 5'-, 5"-, 6'- and 6"-H), 7.79 (2H, s, 2'- and 2"-H) and 10.66¶ and 10.70 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 30.5¶ and 32.3 (C-3 and C-4), 38.2¶ and 38.7 (C-2 and C-7), 117.9 (C-6' and C-6"), 119.0 (C-2' and C-2"), 123.7 (C-4' and C-4"), 130.6 (C-5' and C-5"), 133.1¶ and 133.2 (C-1' and C-1"), 139.6 and 139.7 (C-3' and C-3") and 164.3¶ and 164.3 (2 x C=O).

cis-Dichloro-*N,N*`-bis(2-methylphenyl)-3,6-dithiaoctanediamide palladium(II) 48e

The experimental procedure employed for the synthesis of *cis*-dichloro-(*N,N*'-diphenyl-3,6-dithiaoctanediamide)-*S,S*'-palladium(II) **48a** was followed, using *N,N*`-

bis(2-methylphenyl)-3,6-dithiaoctanediamide **19f** (7.8mg, 0.020mmol) in acetone (80ml) and a 0.001M solution of $PdCl_2$ in 0.1000M aq. HCl (20ml). A fine precipitate was observed to form during addition of the ligand solution. The resulting solid was washed with methanol and dried *in vacuo* to yield, as yellow powder, *cis*-dichloro-[*N,N'*-bis(2-methylphenyl)-3,6-dithiaoctanediamide]-*S,S'*-palladium(II) **48e** (7.3mg, 66%), mp. 184-188°C (decomp.) (Found: MH^+, 564.976747. Calc. for $C_{20}H_{25}N_2O_2S_2PdCl_2$, *M*+1: 564.976927); ν_{max} (KBr)/cm^{-1} 3272 (NH) and 1654 (C=O); ν_{max} (polyethylene)/cm^{-1} 329 and 306 (Pd—Cl); δ_H (400MHz; DMSO-d_6) 2.23 (6H, s, CH_3), 3.32-3.64 (4H, series of multiplets, 4- and 5-CH_2), 4.11-4.41 (4H, series of multiplets, 2- and 7-CH_2), 7.10-7.24 (6H, series of multiplets, 3'-, 3''-, 4'-, 4''-, 5'- and 5''-H), 7.41 (2H, t, *J* 8.0Hz, 6'- and 6''-H) and 9.83¶ and 9.90 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 17.8 (2 x CH_3), 39.0¶ and 39.1 (C-3 and C-4), 39.6¶ and 40.0 (C-2 and C-7), 125.0¶ and 125.2, 125.7 and 125.8, 125.9, 130.3 and 130.4, 131.7 and 132.0 and 135.3 and 135.4 (Ar-C) and 164.1¶ and 164.2 (2 x C=O).

3.3.2 Platinum (II) complexes



***cis*-Dichloro-(*N,N'*-diphenyl-3,6-dithiaoctanediamide)-*S,S'*-platinum(II) 49a**

To a stirred 10mL solution of K_2PtCl_4 (50mg, 0.12mmol) in water, *N,N'*-diphenyl-3,6-dithiaoctanediamide **19a** (43mg, 0.12mmol) in MeOH (25ml) was added drop-wise. The mixture was stirred for 48h and a white precipitate was formed, which turned yellow with time. The precipitate was washed with cold MeOH and dried under high vacuum to yield, as a yellow powder, *cis*-dichloro-(*N,N'*-diphenyl-3,6-dithiaoctanediamide)-*S,S'*-platinum(II) **49a** (45.1mg, 60%), mp. 256-258°C; ν_{max}

(KBr)/cm^{-1} 3298 (NH), 1665 (C=O); ν_{max} (polyethylene)/cm^{-1} 328 and 309 (Pt—Cl); δ_H (400MHz; DMSO-d_6) 3.21¶ and 3.49 (4H, 2 x d, *J* 9.4Hz, 4- and 5-CH_2), 3.93-4.27¶ and 4.16-4.40 (4H, 2 x d, *J* 15.5Hz 2- and 7-CH_2), 7.09 (2H, t, *J* 7.4Hz, 4`- and 4``-H), 7.32 (4H, t, *J* 7.8Hz, 3'-, 3"-, 5'- and 5"-H), 7.57 (4H, d, *J* 7.2Hz, 2'-, 2"-, 6'- and 6"-H) and 10.46¶ and 10.50 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 31.6¶ and 34.8 (C-3 and C-4), 38.4¶ and 38.5 (C-2 and C-7), 127.5¶ and 127.6 (C-2', C-2", C-6" and C-6'), 128.2 (C-4' and C-4"), 129.7¶ and 129.9 (C-3', C-3", C-5" and C-5'), 134.0¶ and 134.1 (C-1' and C-1") and 164.5 (4 x C=O).

cis-Dichloro-[*N, N`*-Bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-*S,S'*-platinum(II) 49b

A stock solution was made by dissolving *N,N`*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide **19c** (0.068g, 0.162mmol) and *N,N*-dimethyaniline (0.375g, 2.51mmol) in MeOH-acetone (4:1; 40ml). To a stirred 0.001**M** solution of K_2PtCl_4 in 0.0974**M** aq. HCl (2ml), 12.8ml of the stock solution was added drop-wise, and the resulting solution was stirred for 24h. The fine precipitate was filtered off, washed with MeOH and dried *in vacuo* to afford, as a fine cream powder, *cis*-dichloro-[*N, N`*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-*S,S'*-platinum(II) **49b** (28.4mg, 85%), mp. 180-184°C (Found: C, 34.5%; H, 3.2%; N, 3.9%; MH^+, 686.029142. Calc. for $C_{20}H_{24}N_2O_4S_2PtCl_2$, *M* +1: C, 35.0%; 3.5%, 4.1%; 686.028067); ν_{max} (KBr)/cm^{-1} 3410 (NH) and 1685 (C=O); ν_{max} (polyethylene)/cm^{-1} 326 and 316 (Pt—Cl); δ_H (400MHz; DMSO-d_6) 3.18¶ and 3.47 (4H, 2 x d, *J* 9.5Hz, 4- and 5-CH_2), 3.84 (6H, s, OCH_3), 4.09¶, 4.30 and 4.46 (4H, 3 x d, *J* 15.5Hz, 2- and 7-CH_2), 6.92 (2H, t, *J* 7.8Hz, 4`- and 4``-H), 7.07 (2H, d, *J* 7.8Hz, 6'- and 6"-H), 7.12 (2H, d, *J* 7.8Hz, 3'- and 3"-H), 7.87 (2H, t, *J* 7.8Hz, 5'- and 5"-H), 9.81¶ and 9.86 (2H, 2 x s, NH); δ_C (100MHz; $CDCl_3$) 38.0¶ and 38.2 (C-4 and C5), 40.0¶ and 40.8 (C-2 and C-7), 55.2 (2 x OCH_3), 110.9 (C-6' and C-6"), 119.7 (C-4' and C-4"), 122.0¶ and 122.2 (C-5' and C-5"), 124.8¶ and 124.9 (C-3' and C-3"), 125.7 (C-1" and C-1"), 149.5¶ and 149.6 (C-2" and C-2") and 163.9¶ and 164.0 (2 x C=O).

cis-Dichloro-[_N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-_S,S'_-platinum(II) 49c

The experimental procedure employed for the synthesis of _cis_-dichloro-(_N,N`_-diphenyl-3,6-dithiaoctanediamide)-_S,S'_-platinum(II) **49a** was followed, using $K_2PtCl_4$ (50.6mg, 0.12mmol) and _N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide **19e** (52.5mg, 0.12mmol). The resulting solid was washed with MeOH and dried in vacuo to yield, as lemon-yellow powder, _cis_-dichloro-[_N,N`_-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-_S,S'_-platinum(II) **49c** (49.9mg, 59%), mp. 250-254°C (Found: C, 31.0%; H, 2.2%; N, 4.0%; MH^+, 693.929435. Calc. for $C_{18}H_{18}N_2O_2S_2PtCl_4$, _M_ +1: C, 31.2%; H, 2.6%, N, 4.0%; 693.928993); ν_{max} (KBr)/cm^{-1} 3267 (NH) and 1660 (C=O); ν_{max} (polyethylene)/cm^{-1} 328 and 309 (Pt—Cl); δ_H (400MHz, DMSO-d_6) 3.20¶ and 3.52 (2H, d _J_ 9.0 Hz, 4- and 5- CH_2), 4.05-4.26¶ and 4.36-3.58 (4H, 2 x d, _J_ 15.2Hz, 2- and 7- CH_2), 7.23 - 7.37 (4H, series of multiplets, 3'-, 3"-, 4'- and 4"-H), 7.52 (2H, d, J 7.6Hz, 6'-and 6"-H), 7.70 (2H, t, _J_ 7.6Hz, 5'- and 5"-H) and 10.19¶ and 10.28 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 38.5¶ and 38.6 (C-4 and C-5), 39.1¶ and 39.9 (C-2 and C-7), 126.5¶ and 126.5 (C-6' and C-6"), 126.7¶ and 126.8 (C-1' and C-1"), 127.0¶ and 127.1 (C-4' and C-4"), 127.4¶ and 127.4 (C-5' and C-5"), 129.4¶ and 129.5 (C-3' and C-3"), 133.9¶ and 133.9 (C-2' and C-2") and 164.6¶ and 164.7 (2 x C=O).

***N, N`*-Bis(4-allyloxyphenyl)-*cis*-dichloro-3,6-dithiaoctanediamide-*S,S'*-platinum(II) 49f**

The experimental procedure employed for the synthesis of _cis_-dichloro-(_N,N`_-diphenyl-3,6-dithiaoctanediamide)-_S,S'_-platinum(II) **49a** was followed, using _N,N`_-bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide **32** (24.7mg, 0.0523mmol) and K_2PtCl_4 (22mg, 0.053mmol). The resulting solid was washed with MeOH and dried _in vacuo_ to yield, as a yellow powder, N,N`-_bis(4-allyloxyphenyl)_-cis-_dichloro-3,6-dithiaoctanediamide_-S,S'-_platinum_(II) **49f** (0.0231g, 59.2%), (Found: C, 36.9%; H, 3.4%; N, 3.5%; MH^+, 738.059844. Calc. for $C_{24}H_{28}N_2O_4S_2PtCl_2$, _M_ +1: C, 39.1%; H, 3.8%; N, 3.8%; 738.059367); ν_{max} (KBr)/cm^{-1} 3301 (NH) and 1658 (C=O); ν_{max} (polyethylene)/cm^{-1} 329 and 310 (Pt—Cl); δ_H (400MHz; DMSO-d_6) 3.23¶ and 3.49 (4H, 2 x d, _J_ 9.6Hz, 4- and 5-CH_2), 3.87-4.24¶ and 4.11-4.35 (4H, 2 x d, _J_ 15.2Hz 2-

and 7-CH_2), 4.52 (4H, d, *J* 4.4Hz, OCH_2), 5.25¶ and 5.38 (4H, 2 x d, *J* 10.4 and 17.2Hz, CH=CH_2), 6.03 (2H, m, C*H*=CH_2), 6.93 (4H, d, *J* 8.8Hz, 2'-, 2"-, 6'- and 6"-H), 7.48 (4H, d, *J* 8.8Hz, 3'-, 3"-, 5'- and 5"-H) and 10.38¶ and 10.34 (2H, 2 x s, NH); δ_C (100MHz; DMSO-d_6) 38.6¶ and 39.3 (C-4 and C-5), 40.1¶ and 41.2 (C-2 and C-7), 68.2 (4 x OCH_2), 114.6¶ and 114.7 (C-3', C-3", C-5' and C-5"), 117.3 (4 x CH=*C*H_2), 120.9¶ and 121.0 (C-2', C-2", C-6' and C-6"), 131.3¶ and 131.4 (C-1' and C-1"), 133.6¶ and 133.7 (2 x *C*H=CH_2), 154.6¶ and 154.6 (C-4' and C-4") and 163.6¶ and 136.6 (2 x C=O).

4-Allyloxyphenyl-2-mercaptoethanamide platinum(II) 50

The experimental procedure employed for the synthesis of *cis*-dichloro-[*N, N'*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-*S,S'*-platinum(II) 49b was followed, using 4-(allyloxyphenyl)-2-mercaptoethanamide **29** (0.033g, 0.148mmol), *N,N*-dimethyaniline (0.375g, 2.51mmol) in MeOH-acetone (4:1; 40ml). The resulting fine precipitate was filtered off, washed with MeOH and dried *in vacuo* to afford, as orange powder, **50** (10.3mg); ν_{max} (KBr)/cm^{-1} 3285(NH) and 1656 (C=O); ν_{max} (polyethylene)/cm^{-1} 326 and 303 (Pt—Cl); The ^{1}H NMR showed broad signals.

3.4. Preparation and Evaluation of the Molecularly Imprinted Polymers (MIP`s)

3.4.1. Preparation of the MIP`s

MIP 1

To a solution of the Pt(II) complex **50** (0.040g, 0.082mmol) in DMF (3ml) in a boiling tube a large excess (100eq.) of EGDMA (0.315g, 1.64mmol) was added under nitrogen. To this mixture, a very small quantity (0.1eq) of AIBN (1.3mg, 0.0082mm0l) was added and the mixture was heated at 65°C for 4h. A greenish yellow solid was produced and the mixture left to stand at room temperature overnight. The solid was removed from the tube, washed with methanol and dried *in vacuo* to afford a greenish yellow polymer (*ca* 0.7g). The polymer was ground into fine particles and washed several times with conc. HCl and then kept in conc. HCl overnight. Repeated washing with conc. HCl and then with MeOH, followed by drying *in vacuo* for 2 days afforded pale-yellow particles of **MIP 1**.

MIP 2

To a solution of K_2PtCl_4 (0.0442g, 0.106mmol) in water (1ml), a solution of *N,N`*-bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide **28** (0.0507g, 0.107mmol) in MeOH (3ml) was added drop-wise, and the mixture stirred overnight at room temperature. A fine precipitate formed, and the methanol-water supernatant mixture was removed by a Pasteur pipette. The residual solid was re-dissolved in DMF (3ml) and the experimental procedure used for the synthesis of **MIP 1** was followed, using EGDMA (0.420g, 2.19mmol) and AIBN (0.0018g, 0.011mmol). The resulting yellow solid was washed sequentially with $CHCl_3$ and MeOH and then dried *in vacuo* to afford the crude yellow polymer (*ca* 0.8g). After washing with conc. HCl and then MeOH, drying *in vacuo* for 2 days, cream particles of **MIP 2** were obtained.

Blank synthesis

The experimental procedure employed for the synthesis of **MIP 1** was followed, using the ligands (in absence of the metal) *N*-(4-allyloxyphenyl)-2-mercaptoethanamide **29** for the preparation of **Blank 1.**

3.4.2. Evaluation of the MIP`s

The metal ion solution was prepared by dissolving the appropriate amount of the salts, $PdCl_2$, $CoCl_2.H_2O$, $NiCl_2.6H_2O$ and $CuCl_2.2H_2O$ in 2% aq. HCl such that the concentration of each of the metals was 400ppm.

Method A

The finely ground polymer particles (100mg and 50mg for the MIP and blank respectively) were mechanically shaken with the metal solution (5ml and 2.5ml, MIP and blank respectively) for 17.5h. Equilibration was monitored over this period by analysing the solutions after shaking for 5min, 30min, 1.5h, 4.5h and 17.5h. The residual metal concentrations in the supernatant solutions corresponding to the shaking periods were then diluted to make 1ppm solutions and analysed by ICP-MS. The results are detailed in **Tables 11-13.**

Method B

The polymer particles (100mg) were loaded into a Pasteur pipette, as in column chromatography, and the metal ion solution (5ml) was passed through the column. The eluents were then analysed by ICP-MS and the results are detailed in **Table 14.**

Table 11: ICP-MS results (μg/L) for the equilibration experiments using reference polymer **Blank 1**

	5min	30min	1.5h	4.5h	17.5
Co 59	925.236	1013.677	988.393	1088.906	1069.655
Ni 60	913.298	1002.971	1101.61	1006.881	1056.459
Cu 63	901.075	997.922	975.408	993.146	1039.346
Cu 65	901.197	994.723	975.669	994.137	1040.69
Pd 105	890.91	935.471	821.496	731.776	526.659
Pd 108	895.07	938.196	823.961	738.074	525.97
Pt 194	911.113	987.717	952.308	886.726	509.349
Pt 195	910.985	984.654	951.302	882.871	507.561

Table 12: ICP-MS results (μg/L) for the equilibration experiments using **MIP 1**

	5min	30min	1.5h	4.5h	17.5h
Co 59	1021.693	1035.523	1014.324	993.673	976.118
Ni 60	991.675	1022.958	1002.593	1105.263	960.321
Cu 63	991.181	1005.624	988.182	968.632	943.852
Cu 65	987.002	1002.863	995.079	967.584	941.772
Pd 105	830.182	813.803	746.88	716.923	691.421
Pd 108	835.801	807.087	748.438	719.768	695.648
Pt 194	974.641	969.385	912.565	817.621	500.984
Pt 195	970.819	965.51	910.301	815.362	499.51

Table 13: ICP-MS results (μg/L) for the equilibration experiments using **MIP 2**

	5min	30min	1.5h	4.5h	17.5h
Co 59	966.823	1001.114	944.568	965.743	998.858
Ni 60	959.307	994.176	939.407	955.113	989.494
Cu 63	949.305	980.761	929.753	949.846	972.167
Cu 65	943.881	982.712	928.528	951.229	974.887
Pd 105	905.012	936.339	876.543	876.921	907.76
Pd 108	907.187	940.445	876.098	882.027	902.481
Pt 194	933.109	962.654	900.509	878.04	804.418
Pt 195	934.7582	963.395	903.523	878.746	804.747

Table 14: ICP-MS results from (μg/L) evaluation of the polymers as column chromatography stationary phases.

Metal ion	Blank 1	MIP 1	MIP 2
Co 59	1009.587	1128.749	1109.529
Ni 60	1002.343	1491.564	1142.226
Cu 63	1001.053	1122.166	1087.536
Cu 65	1000.453	1118.885	1086.991
Pd 105	980.858	-2.911	420.548
Pd 108	992.742	-2.972	419.951
Pt 194	998.678	500.574	692.351
Pt 195	994.567	499.983	692.538

3.5. Solvent Extraction Procedure and Data

3.5.1. General Method

The metal solution was prepared by dissolving the appropriate amount of the salts $PdCl_2$, $CoCl_2.H_2O$, $NiCl_2.6H_2O$ and $CuCl_2.2H_2O$ in 1**M** aq. HCl such that the concentration of each of the metals was 1 x 10^{-3}**M**. The ligand solutions were prepared by dissolving the appropriate amount of each of the 3,6-dithiaoctanediamide ligands **19a-f** or 3,7-dithianonanediamide ligands **20a**, **c** and **d** in either toluene or MIBK, such that the concentration of the ligand was 1.1 x 10^{-3}**M**. Equal volumes (50ml for toluene extractions and 20ml for MIBK extractions) of each phase were stirred vigorously in a jacketed beaker (150 ml) and the temperature was maintained at 30°C by a digital thermostat. Aliquots (2ml) of each phase were removed after 5, 10, 20, 30, 40 and 60 minutes. The aqueous phase aliquots were evaporated to dryness on a steam bath to remove residual organic solvents and then diluted to afford 10ml solutions. The residual metal was determined by ICP-MS analysis and the results are detailed in **Tables 15-29**.

Table 15: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19a** in toluene.

	5	10	20	30	40	60
Co 59	59.3839	59.1799	58.8355	59.9530	57.5403	88.6623
Ni 60	48.2774	100.3409*	47.0912	49.3847	46.8042	69.7278
Cu 63	71.2629	68.7885	65.6171	69.0158	77.4772	108.6576
Cu 65	71.7025	69.2623	66.0410	69.2206	77.9322	109.3555
Pd 105	13.8282	13.2248	4.6495	4.4411	5.1243	6.5040
Pd 108	13.8682	13.2812	4.6814	4.4461	5.1428	6.3642

* Measurement probably erroneous.

Table 16: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19b** in toluene.

	5	10	20	30	40	60
Co 59	86.8417	57.6333	60.7355	46.9675	58.0903	65.3339
Ni 60	108.0948	58.3217	89.0423	55.8229	149.4231	190.1007
Cu 63	99.7475	70.6105	74.3513	55.2932	79.8818	95.1271
Cu 65	100.8503	70.8983	74.5908	55.6515	80.2549	95.6368
Pd 105	5.2537	3.2957	4.7265	6.7983	7.3250	2.4274
Pd 108	5.2985	3.3717	4.7811	6.8044	7.4161	2.7444

Table 17: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19c** in toluene.

	5	10	20	30	40	60
Co 59	48.6257	48.7896	41.3600	50.8151	48.5874	47.4574
Ni 60	48.0618	88.4702	41.7951	49.9998	47.5319	46.0811
Cu 63	56.9926	60.7260	48.8690	56.0510	55.3624	52.8160
Cu 65	57.2106	60.8013	48.9960	56.4051	55.5378	52.9719
Pd 105	22.8482	4.6207	4.4677	5.0536	5.0816	3.7461
Pd 108	22.7635	4.6768	4.4489	4.9676	5.0997	3.8314

Table 18: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19d** in toluene.

	5	10	20	30	40	60
Co 59	120.0034	130.6510	130.9503	119.2861	123.3979	129.8093
Ni 60	115.7850	131.1142	130.0758	114.7984	117.9558	125.5824
Cu 63	165.1599	145.6277	143.5809	130.3673	131.2374	143.8531
Cu 65	165.3548	145.6788	143.4717	130.5428	131.1313	144.4740
Pd 105	168.0021	166.3179	145.9662	112.3590	98.8855	67.2083
Pd 108	167.8718	166.9513	146.2202	112.5774	100.0082	67.7544

Table 19: ICP-MS results (µg/L) for competitive liquid-liquid extraction experiment with ligand **19e** in toluene.

	5	10	20	30	40	60
Co 59	67.1147	60.3458	57.2742	57.5433	56.6015	55.9255
Ni 60	159.7883	61.1129	55.3269	83.7044	55.3376	55.8923
Cu 63	161.2367	74.7216	63.9000	76.3630	68.6295	65.7656
Cu 65	161.6761	75.1089	63.9577	76.6338	69.0060	65.9074
Pd 105	5.7584	3.5962	4.8286	3.1740	4.1924	4.1898
Pd 108	5.8212	3.5281	4.7040	3.1184	4.2472	4.1836

Table 20: ICP-MS results (µg/L) for competitive liquid-liquid extraction experiment with ligand **19f** in toluene.

	5	10	20	30	40	60
Co 59	118.5045	119.5226	114.0174	132.7096	125.7818	125.3785
Ni 60	113.0018	113.5021	107.7256	127.4681	119.7454	121.0792
Cu 63	126.8465	131.6960	128.5998	145.1441	131.2419	134.8559
Cu 65	127.3212	132.0947	128.9969	146.5280	131.3282	134.9535
Pd 105	8.9059	5.8852	6.2103	4.0363	7.1625	7.1936
Pd 108	8.9614	5.9006	6.2736	4.0916	6.8754	7.1631

Table 21: ICP-MS results (µg/L) for competitive liquid-liquid extraction experiment with ligand **19a** in MIBK.

	5	10	20	30	40	60
Co 59	118.4344	116.9276	115.2549	108.6803	107.2173	103.5652
Ni 60	120.9492	117.7489	111.2760	105.7089	102.2649	100.9533
Cu 63	159.4441	132.7509	120.7066	116.0957	111.6734	112.8287
Cu 65	160.1009	133.1197	120.8158	116.3626	111.5978	113.1447
Pd 105	113.7276	25.7282	7.1262	3.2291	3.6547	2.2273
Pd 108	113.7936	26.0116	7.2070	3.2446	3.8068	2.2489

Table 22: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19b** in MIBK.

	5	10	20	30	40	60
Co 59	76.3171	71.9822	109.7383	100.1111	103.7353	100.5943
Ni 60	77.2328	69.4969	102.8873	112.0675	97.5552	98.8140
Cu 63	413.1893	75.5955	116.1834	137.0805	147.5213	240.0343
Cu 65	412.8225	75.9156	115.8498	136.9115	147.6497	240.6091
Pd 105	19.7892	3.9989	3.0369	2.7079	1.8947	1.2073
Pd 108	19.7806	4.0429	2.9968	2.6130	1.8603	1.1831

Table 23: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19c** in MIBK.

	5	10	20	30	40	60
Co 59	108.5175	99.4296	101.6851	110.2002	108.9092	102.4010
Ni 60	102.5407	95.6904	95.3356	104.1329	103.0535	98.5811
Cu 63	117.0299	97.1473	106.8351	117.3143	116.7422	107.5031
Cu 65	116.4567	96.7924	106.2704	116.7463	116.2297	107.0213
Pd 105	78.3801	45.8743	18.0467	8.0897	4.0918	2.5799
Pd 108	78.9499	46.3953	18.1922	8.1461	4.1483	2.5532

Table 24: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19d** in MIBK.

	5	10	20	30	40	60
Co 59	118.5933	112.4788	111.6245	117.4971	115.4196	115.3033
Ni 60	111.6273	105.6087	105.5160	110.5477	108.7115	108.3071
Cu 63	124.1251	118.0478	287.1709	120.1209	117.2498	117.5122
Cu 65	123.6128	117.8600	286.0879	120.1362	117.3591	117.4645
Pd 105	146.7184	114.2645	76.6544	47.4733	28.9124	2.7777
Pd 108	146.7280	113.9754	77.3062	47.8361	29.1727	2.8651

Table 25: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **19e** in MIBK.

	5	10	20	30	40	60
Co 59	111.1433	108.4996	152.4695	105.5811	110.8754	108.4063
Ni 60	103.6754	101.2191	109.7947	98.7335	103.6279	104.5261
Cu 63	115.9814	114.8082	116.5271	109.9992	114.6331	115.8211
Cu 65	116.1810	115.1022	116.8139	110.3863	114.9811	116.0283
Pd 105	95.4767	74.0564	20.6557	7.5017	4.4087	3.0096
Pd 108	95.9678	74.4731	20.8317	7.5732	4.3782	3.0226

Table 26: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **21f** in MIBK.

	5	10	20	30	40	60
Co 59	116.8341	116.4854	119.9468	117.4670	112.6714	125.1168
Ni 60	218.3367	123.7077	116.0731	157.7937	105.7087	161.6604
Cu 63	122.5264	139.5328	127.0703	121.3869	117.4686	131.2295
Cu 65	122.7367	139.3614	126.7678	121.6888	117.2906	131.0536
Pd 105	27.0511	7.2170	3.7541	4.1671	3.3651	3.2948
Pd 108	27.2819	7.3291	3.8237	4.2627	3.4587	3.3963

Table 27: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **20a** in toluene.

	5	10	20	30	40	60
Co 59	250.025	179.086	160.441	161.663	159.862	149.998
Ni 60	248.738	177.056	158.091	159.658	158.133	150.074
Cu 63	181.107	130.67	112.792	115.099	112.856	111.74
Cu 65	180.223	130.278	112.78	114.144	112.711	111.341
Pd 105	25.115	25.589	13.886	14.034	19.523	18.387
Pd 108	25.043	25.717	13.887	14.163	19.474	18.431

Table 28: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **20c** in toluene.

	5	10	20	30	40	60
Co 59	121.6270	225.3335	114.6068	122.5616	119.2204	121.3814
Ni 60	114.7121	126.5671	107.9910	138.6287	113.6490	114.0967
Cu 63	127.7061	125.5612	120.6486	130.8547	125.0396	127.4286
Cu 65	127.7048	125.2804	120.3980	130.8975	125.3479	127.3447
Pd 105	14.4396	12.6086	10.1780	11.6304	9.8004	9.2578
Pd 108	14.5564	12.4555	10.2396	11.6359	9.8675	9.3346

Table 29: ICP-MS results (μg/L) for competitive liquid-liquid extraction experiment with ligand **20d** in toluene.

	5	10	20	30	40	60
Co 59	131.2739	124.8244	179.2546	128.6467	125.5695	121.7116
Ni 60	120.3230	117.3677	189.7477	124.0779	118.9900	141.5879
Cu 63	146.2936	131.2077	6118.7432	155.7169	135.3141	132.4980
Cu 65	146.4669	132.2654	6163.3712	155.5593	135.2556	132.3599
Pd 105	104.6090	64.7360	32.1093	19.6915	8.5457	5.2483
Pd 108	106.1856	65.7654	32.2925	20.2142	8.7272	5.3717

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