

Supramolecular Chemistry Using the Dithiocarbamate Ligand

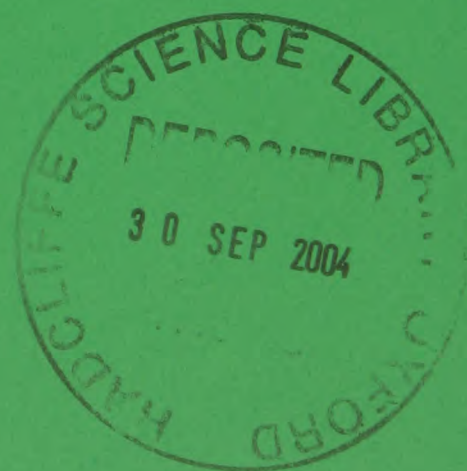
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A thesis submitted for the degree of Doctor of Philosophy

Inorganic Chemistry Laboratory
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**Abstract of thesis submitted for the degree of DPhil
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The aim of this thesis is to use the dithiocarbamate ligand in a range of supramolecular architectures. The ligand is exploited in the metal-directed self-assembly of transition metal-based complexes, the synthesis of interlocked structures, the stabilisation of gold and silver nanoparticles and the preparation of novel redox-active sensors.

Chapter One introduces the field of supramolecular chemistry. The underlying principles of molecular recognition are discussed and this is built upon with the development of self-assembly and nanotechnological applications.

Chapter Two describes the synthesis of transition metal macrocyclic dithiocarbamate-based complexes. These macrocyclic complexes are studied by a variety of spectroscopic and electrochemical techniques and X-ray crystallography. The synthesis of asymmetrical complexes is allowed due to the labile nature of the dithiocarbamate linkage.

Chapter Three details the preparation of nano-dimensional resorcinarene-based complexes. The syntheses of new multinuclear complexes are described as is the binding of suitable nano-dimensional guests.

Chapter Four illustrates the synthesis of cationic acyclic and macrocyclic gold(III) dithiocarbamate complexes. These structures may in addition be formed via a novel transmetallation reaction.

Chapter Five describes the generation of interpenetrating dithiocarbamate-based architectures. This is achieved by utilising the lability and favourable axial interactions of dithiocarbamate-based complexes

Chapter Six details the synthesis of gold and silver nanoparticles. These particles are prevented from agglomeration both by the use of stabilising thiol and dithiocarbamate ligands. A number of nanoparticles with a high degree of monodispersity are formed.

Chapter Seven described the preparation of the redox-active ruthenium(II) bis(2,2'-bipyridine) dithiocarbamate group. This has been demonstrated to act as novel a reporter group for anionic guests.

Chapter Eight reports the synthetic protocol used within the thesis.

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Glossary of Terms

A	Ampere, Adenine or hyperfine coupling constant (EPR)
Å	Angstrom
AIBN	2,2'-Azobib(2-methyl-propionitrile)
Aliquat	Methyltrioctylammonium chloride
aq	Aqueous
Ar	Aryl
Boc	<i>tert</i> -Butoxycarbonyl
br	Broad
bipy	2,2'-Bipyridine
Bu	<i>n</i> -Butyl
C	Cytosine
chex	Cyclohexyl
CPK	Corey-Pauling-Koltun
CTV	Cyclotrimeratrylene
d	Doublet
dd	Doublet of doublets
DMA	<i>N,N'</i> -Dimethyl acetamide
DMF	<i>N,N'</i> -Dimethyl formamide
DMSO	Dimethyl sulphoxide
DNA	Deoxyribonucleic acid
dt	Doublet of triplets
dtc	<i>N,N'</i> -Diethyldithiocarbamate

$E_{1/2}$	Half wave potential
E_{pa}	Anodic peak potential
E_{pc}	Cathodic peak potential
ϵ	Molar extinction coefficient
en	1,2-ethylenediamine
EDCI	3-Ethyl-1-[3(dimethylamino)propyl]carbodiimide
EIMS	Electron Impact Mass Spectrometry
ESMS	Electrospray Ionisation Mass Spectrometry
FAB	Fast Atom Bombardment
G	Guanine
g	Spectroscopic splitting factor
hex	<i>n</i> -Hexyl
HSAB	Hard and soft acids and bases theory
HS/LS	High spin/ low spin
HSQC	Heteronuclear single-quantum correlated spectroscopy
Hz	Hertz
J	Coupling constant (NMR)
K	Stability Constant
k	Boltzmann's constant ($1.38 \times 10^{-23} \text{ JK}^{-1}$)
L	Ligand
LC	Ligand centred
LFSE	Ligand field stabilisation energy
LMCT	Ligand to metal charge transfer
M	Molar (moles litre ⁻¹)
$[M]^+$	Molecular ion

m	Multiplet
MALDI-TOF	Matrix-assisted laser desorption ionisation-time of flight
MLCT	Metal to ligand charge transfer
mol	Moles
m/z	Mass-to-charge ratio
MRI	Magnetic Resonance Imaging
NBS	<i>N</i> -Bromosuccinimide
NMR	Nuclear Magnetic Resonance
q	Quartet
s	Singlet
sh	Shoulder
T	Thymine/ Tetrahedron/ Temperature (K)
TBA	Tetra- <i>n</i> -butylammonium
TEM	Transmission electron microscopy
TFA	Trifluoroacetic acid
TLC	Thin Layer Chromatography
TTF	Tetrathiafulvalene
UV-vis	Ultraviolet-visible

Chapter One

Introduction

Chapter One: Introduction

1.1 Supramolecular Chemistry

Supramolecular chemistry has been described as ‘the designed chemistry of the intermolecular bond’¹ whereby multicomponent molecular assemblies are held together by a variety of weak, reversible non-covalent interactions. This is in contrast to traditional organic synthesis where strong, irreversible covalent bonds are sequentially formed to build the desired target molecule.

The field of supramolecular chemistry is truly a multidisciplinary one. Syntheses are undertaken using traditional organic and inorganic chemical routes, interactions investigated with a variety of physical techniques and applications range from the areas of material science through to biology².

Supramolecular chemistry may be sub-divided into two categories: host-guest chemistry and self-assembly (Figure 1).

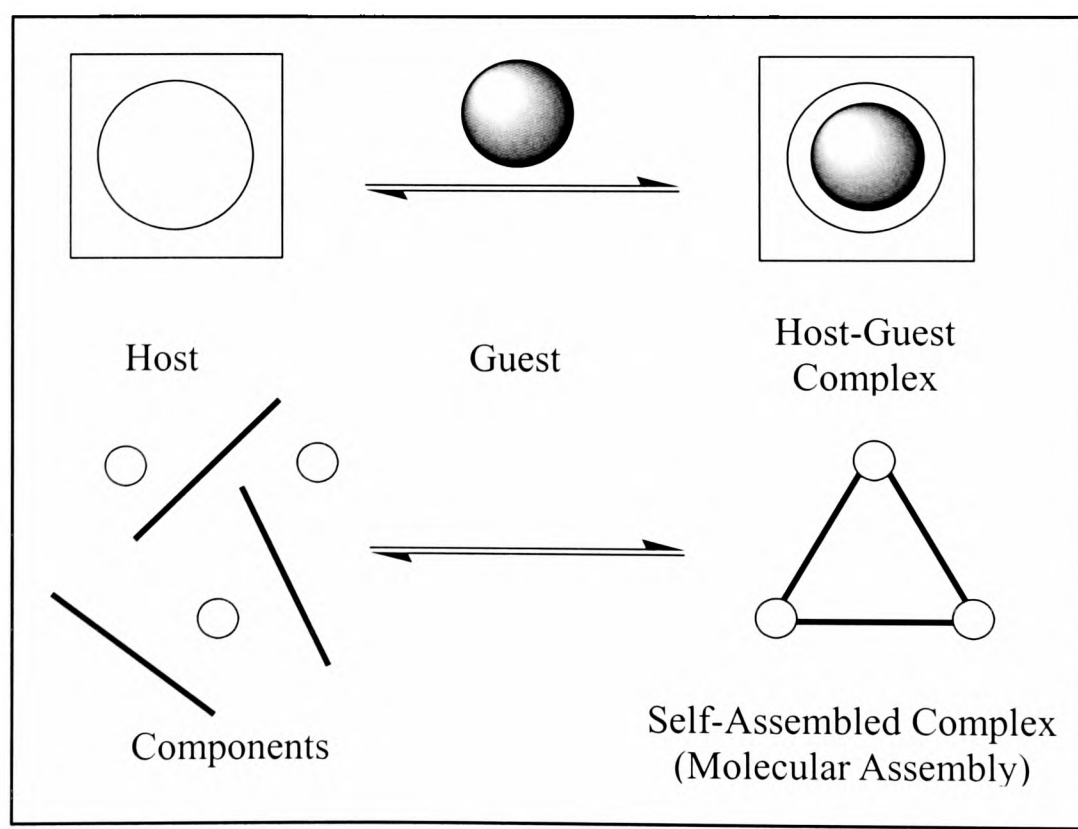


Figure 1 Host-guest chemistry and self-assembly

In host-guest systems, one molecule (a host) is bound by another molecule (the guest) to form a supermolecule. Self-assembled complexes are formed where specifically designed components spontaneously arrange themselves to form molecular assemblies with a well-defined geometry. Both approaches use non-covalent interactions that are individually weak but collectively provide significant stability and strength to the supermolecule or the assembly³.

It is perhaps somewhat surprising that supramolecular chemistry is a relatively recent area of research, considering its underlying principles were in place around the turn of the 20th century. Paul Ehrlich first introduced the idea of a biological receptor, after he realised that ‘molecules do not act if they do not bind’^{4,5}. Such recognition requires the various components of the complex to positively interact with each other, a concept proposed by Alfred Werner, in his theory of coordination^{6,7}. Finally, any interaction should be selective between the constituent parts, as illustrated in Emil Fischer’s “lock and key” principle for the recognition of substrates upon enzymes via geometric complementarity^{8,9}.

These three concepts lay the foundations of supramolecular chemistry, with the highly specific molecular recognition and architectures that occur in Nature its most elegant examples. Indeed, much of the activity within the area aims to mimic the processes of Nature¹⁰. One such example of biological molecular recognition, which highlights these principles, is the digestive metalloenzyme, carboxypeptidase A¹¹. This binds peptides containing aromatic side chains (those of phenylalanine, tyrosine and tryptophan) at the carboxy terminus, due to the complementary size and electronic fit of the aromatic residues with the active site of the enzyme¹² (Figure 2). The enzyme is then able to selectively hydrolyse these peptides using the adjacent Lewis acidic zinc(II) centre.

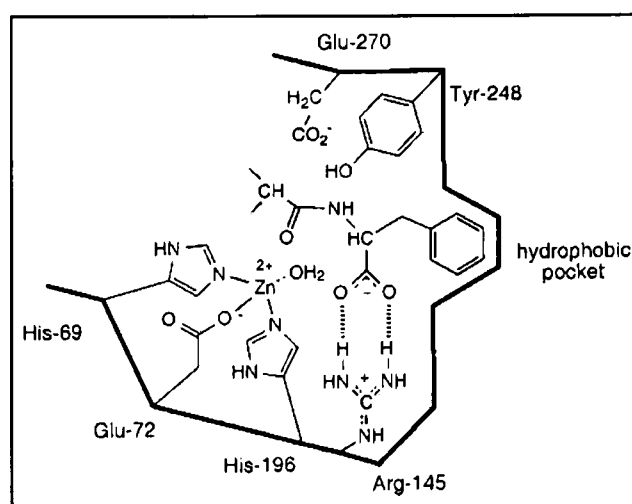


Figure 2 Schematic representation of the active site of carboxypeptidase A

The work presented in this thesis outlines the synthesis and binding properties of a variety of receptors that exploit non-covalent forces for both their construction and subsequent binding. A brief outline of the forces that may be manipulated by the supramolecular chemist is therefore discussed below.

1.2 Non-Covalent Interactions

A covalently bound molecule may be considered to be a group of atoms whose binding energy (typically 300kJmol^{-1}) is significantly greater than kT . At the other extreme, however, van der Waals' clusters are loose assemblies of atoms (such as noble gas complexes¹³) whose binding energy is of the order of kT and hence readily dissociate upon intermolecular collisions. As a result, these entities are usually only observable at low temperatures. Between these two categories lies the realm of supramolecular chemistry where weakly bound systems with definable structures and geometries are formed at room temperature.

The chemist has a variety of non-covalent interactions at his or her disposal to assemble supramolecular architectures. These include:

- Electrostatics¹⁴ (ion-ion, ion-dipole and dipole-dipole)
- Hydrogen bonding¹⁵
- π - π stacking¹⁶

- Charge-transfer interactions¹⁷
- Cation- π interactions¹⁸
- van der Waals' forces¹⁹ (dispersion and induction forces)
- Hydrophobic or solvatophobic effects²⁰
- Coordination chemistry

The strength of the various intermolecular forces varies with a range of factors, including the nature of the interaction, its directionality/orientation, the medium used as well as the steric and electronic complementarity of the constituent components.

Electrostatic forces are predominantly enthalpic in nature, and their strength tends to be reduced in more polar or aqueous solvent systems. Ion-ion interactions are amongst the strongest of non-covalent forces (up to 250 kJmol⁻¹) and are non-directional. Hydrogen bonding, on the other hand, is highly directional, with its strength proportional to its linearity. Similarly, π - π stacking interactions are maximised where there are favourable σ - π interactions¹⁶, and have been shown to play a vital role in stabilising DNA via vertical base-pair interactions.

Hydrophobic (or solvatophobic) interactions, describe the association of apolar binding partners in aqueous (or polar) solvent systems. Here, the binding process results in solvent being released into the bulk medium which is both entropically and enthalpically favoured.

Although coordination chemistry does not strictly involve non-covalent interactions, the use of coordinate bonds have proved useful in generating strong and directional architectures, and as such are frequently used.

Due to the relatively weak nature of the above forces, it is often necessary to use both a number of the same type of interaction in concert, as well as a range of different interactions, in order to create systems with the desired complexity and/or selectivity.

1.3 The Chelate and Macrocyclic Effects

Stable supermolecules may be generated using both summative and multiplicative non-covalent forces. Such combinations allow the creation of strong host-guest complexes. In many cases, however, it is observed that the interaction of the whole system is significantly greater than the sum of its parts. This increased stability has its basis in the phenomenon of the chelate effect.

The chelate effect is well known from coordination chemistry and refers to the observation that metal-ligand complexes that contain chelating ligands display significantly greater thermodynamic stabilities compared to those containing comparable unidentate ligands²¹.

This increased stability is highlighted in the equilibrium constants for the displacement of water molecules for both ammonia and the chelating 1,2-ethylenediamine (en) ligand (Figure 3). The chelate complex is ten orders of magnitude more stable than that of the unidentate ligand²².

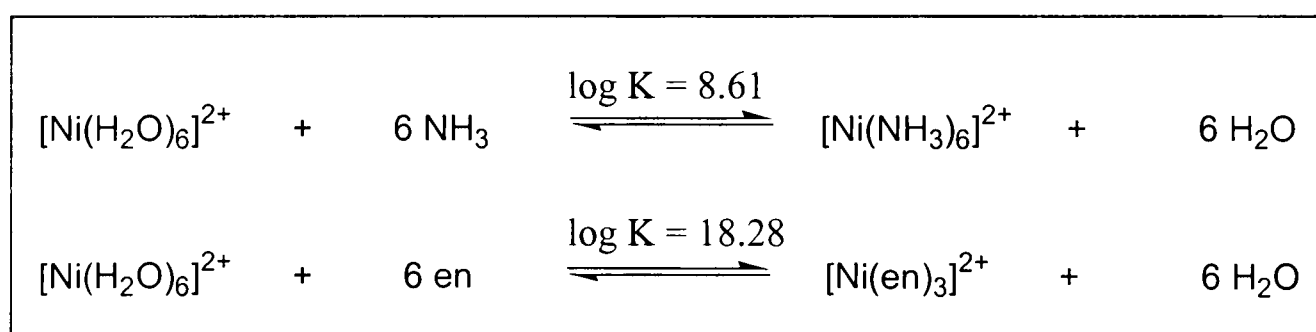


Figure 3 The chelate effect

The enhanced stability is largely due to an increase in the number of free species in solution, increasing the overall entropy of the system. There is also a significant enthalpic contribution to the increased stability, with mutual ligand repulsion decreased upon covalently bringing together the polar amino groups. The resulting alkylation of the donor atoms in the chelating ligand ($\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2$ verses NH_3) also has the effect of increasing the basicity, through inductive effects, leading to the formation of stronger complexes²³.

The macrocyclic effect is an extension of the chelate effect and concerns the increased

stability of complexes of macrocyclic hosts compared to their acyclic analogues. The formation of zinc(II) complexes with ligands **(1)** and **(2)** (Figure 4) has been demonstrated to be four orders of magnitude stronger for the macrocyclic complex **(1)**²⁴.

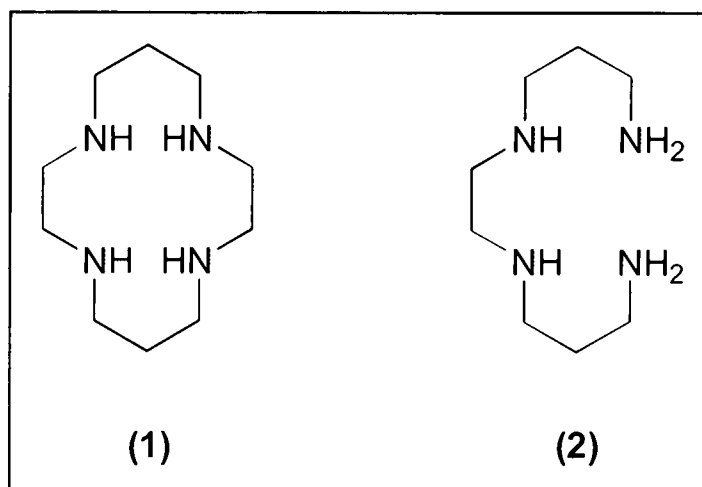


Figure 4 Macrocyclic **(1)** and acyclic **(2)** tetraaza ligands

This increased stability has both enthalpic and entropic contributions. Since macrocyclic hosts are less heavily solvated than their acyclic analogues, coordination of a guest requires less desolvation energy. The increased rigidity of macrocyclic ligands also leads to them losing fewer degrees of freedom upon binding, hence is entropically favoured. Additionally, complexation, and importantly, decomplexation rates tend to be significantly reduced for macrocyclic ligands²⁵.

The remainder of this Introduction will expand on the principles illustrated above to highlight some of the important developments in the field of supramolecular chemistry, with relevance to the research undertaken within this thesis.

2 Cation Binding

Cations play a crucial role in biological chemistry, being involved in processes such as muscle contraction, the activity of many enzymes and the maintenance of specific tertiary structures within proteins²⁶. The naturally occurring macrocyclic antibiotic valinomycin (Figure 5) is

able to selectively transport potassium cations across mitochondrial membranes, even in the presence of a large excess of sodium cations²⁷. It is this selectivity and strength of binding that the supramolecular chemist aims to mimic.

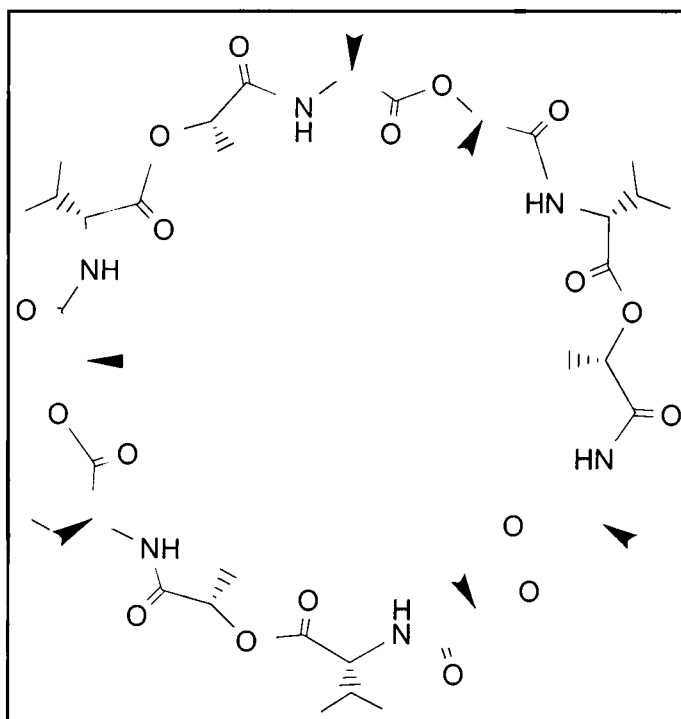


Figure 5 Structure of valinomycin

Complexes of paramagnetic lanthanide cations have been used as contrast agents in magnetic resonance imaging (MRI) of tissues²⁸. Cations also play a crucial role in industry, with receptors that are able to extract unwelcome metal ions from aqueous solution or remove toxic and polluting cations (such as Cs^+ and Pb^{2+}), being highly desirable²⁹.

2.1 Crown Ethers

Charles Pedersen catalysed the birth of supramolecular chemistry in the 1960s when he fortuitously synthesised the crown ether, dibenzo-18-crown-6 (**3**) (Figure 6)³⁰. Although cyclic polyethers had previously been synthesised³¹, Pedersen discovered their ability to solubilise alkali metal salts into organic solvents. This is a result of the alkali metal ion sitting within the centre of the macrocyclic cavity and forming six attractive ion-dipole interactions with the oxygen donors.

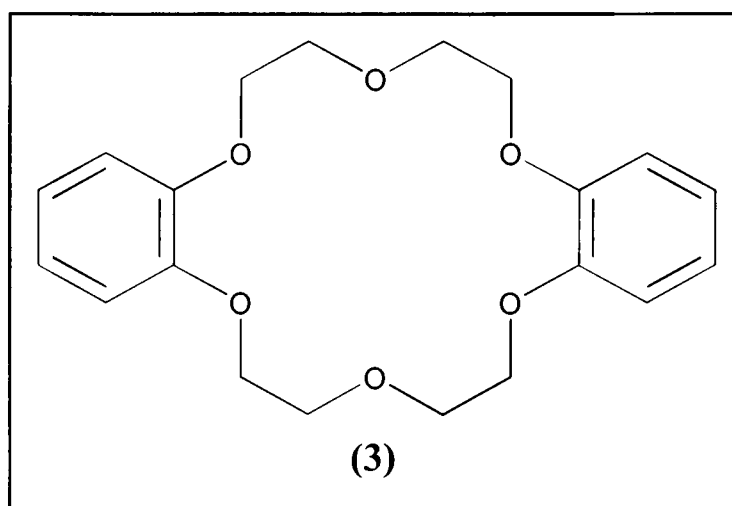


Figure 6 Dibenzo-18-crown-6 (3)

Pedersen went on to synthesise a range of different sized crown ethers and examined their binding with a variety of s-block, transition metal, lanthanide and organic based cations³². In general, it was found that the magnitude of the resulting stability constants are proportional to the goodness of fit between the size of the macrocyclic cavity and the cation³³ (Table 1).

	Na ⁺ (1.16Å)	K ⁺ (1.52 Å)	Ca ²⁺ (1.14 Å)	NH ₄ ⁺ (1.61 Å)
12-crown-4 (1.2-1.5 Å)	1.70	1.30	-	-
15-crown-5 (1.7-2.2 Å)	3.24	3.43	2.36	3.03
18-crown-6 (2.6-3.2 Å)	4.35	6.08	3.90	4.14
21-crown-7 (3.4-4.3 Å)	2.54	4.35	3.27	2.80

Table 1 Log *K* values for the stability of different sized crown ethers with a range of cationic guests (measured in MeOH) Ionic radii of cations³⁴ and estimated cavity dimensions of crown ethers³⁵ given in parentheses

The trend in stability constants is, however, further complicated by a variety of stoichiometries that the crown-cation complexes may adopt³⁶. Where there is a complementary fit (e.g. potassium with 18-crown-6) a 1:1 complex is formed. However,

where the cation is too large for the central cavity (e.g. potassium with 15-crown-5) it may form a 2:1 host:guest sandwich complex. Likewise, if the crown is too large, it is possible for the crown to encapsulate more than one ion (e.g. sodium with 24-crown-8 which forms a 1:2 host:guest complex).

The binding of ammonium-based cations is found to show preferential stability for receptors that exhibit a complementary geometry to the tetrahedral cation³⁷. As a result, these ions form stronger complexes with 18-crown-6 as this is able to form appropriate hydrogen bonding interactions (Figure 7).

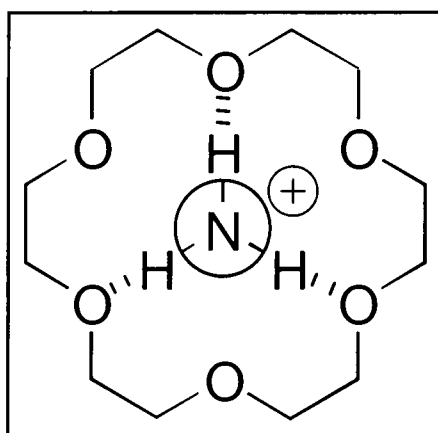


Figure 7 Complementary interactions between ammonium and 18-crown-6

It is also possible to replace one or more of the oxygen donors with other atoms generating a range of new crown ethers with different properties. For example, 1,10-dithio substituted 18-crown-6 analogue has been shown to have significantly different coordination properties to 18-crown-6, despite its similar size (Figure 8).

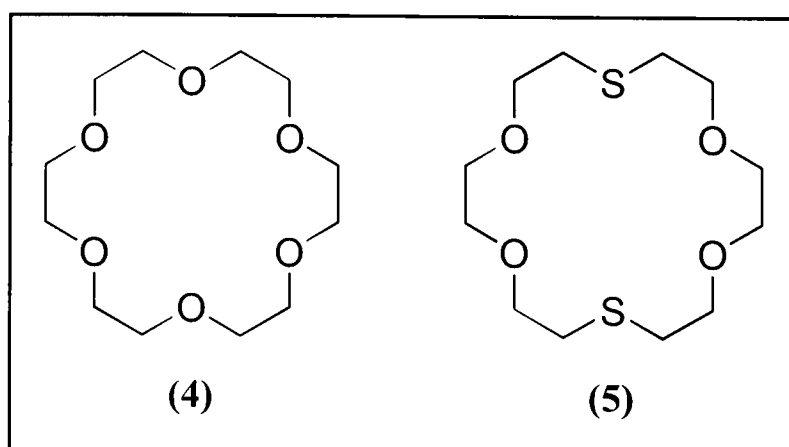


Figure 8 18-crown-6 (4) and 1,10-dithio derivative (5)

Replacement of the hard oxygen donors for softer sulphur ligands results in a change in the selectivity of the host for softer metals³⁸ (Table 2). This is a demonstration of the hard and soft acid-base principle where soft acids show a preference for soft bases, due to their greater polarising power^{39,40}.

	(4)	(5)
K ⁺	6.08 [†]	1.12 [†]
Ag ⁺	1.50	4.34
Hg ²⁺	2.42	19.5

Table 2 Stability constants (Log *K*) for the association of (4) and (5) with a range of cationic guests in H₂O
([†]Measured in MeOH)

2.2 Preorganised Hosts

Donald Cram stated that ‘the more highly hosts and guests are organised for binding, the more stable their complexes will be’⁴¹. This is primarily a result of more organised hosts not being required to rearrange themselves as much as more flexible analogues to undergo complexation. This molecular reorganisation is both an enthalpic and entropically unfavourable process. The fact that more organised hosts tend also to be less heavily solvated, also results in the binding process being more enthalpically favoured.

Consequently, the supramolecular chemist aims to design three-dimensional hosts that are preorganised to encapsulate a specific cationic guest (Figure 9).

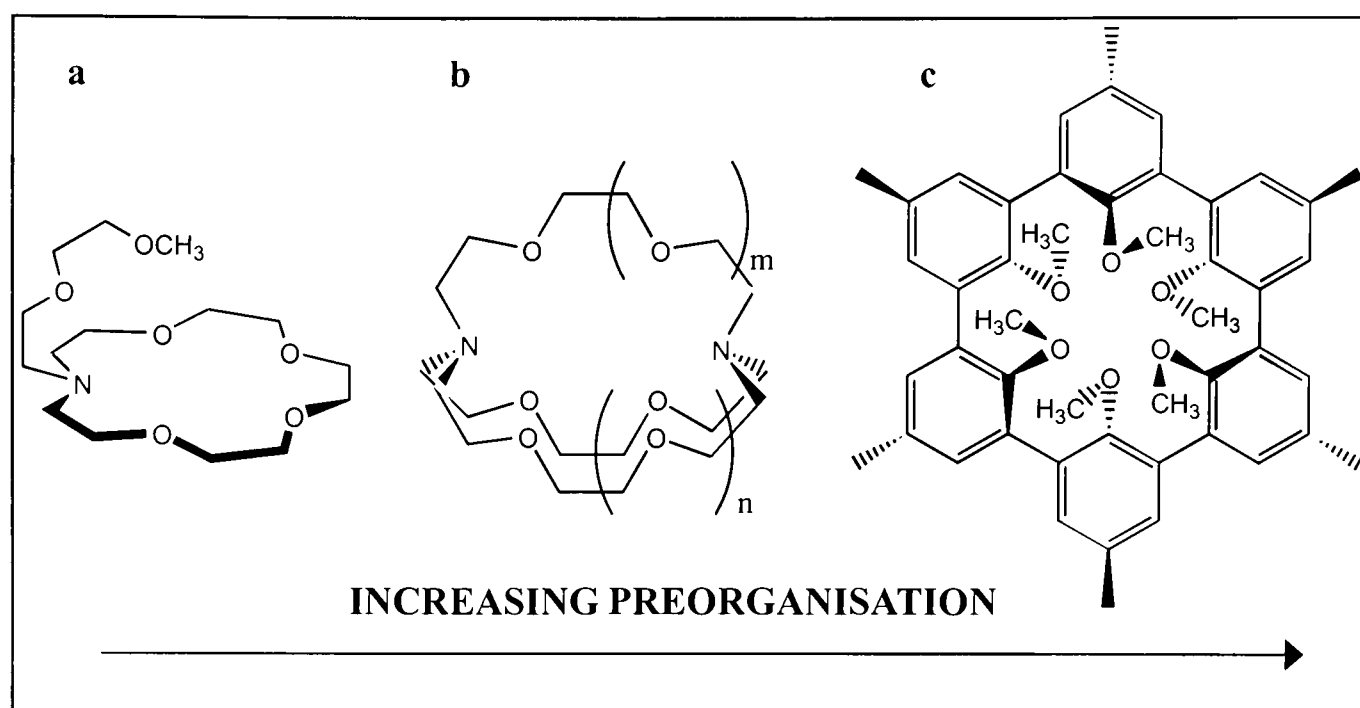


Figure 9 Preorganised cation binding hosts: a) lariat crown ether, b) cryptand ($n=0$ or 1 , $m=0$ or 1), c) spherand

Structures of increasing complexity, from lariat crown ethers⁴², through cryptands⁴³ onto spherands⁴⁴ have been synthesised and have formed very strong and highly selective complexes with suitably sized alkali metal cations. The spherand, displayed in Figure 9c, is able to bind lithium 600 times more strongly than sodium and twelve orders of magnitude more strongly than potassium⁴⁵. This remarkable selectivity is achieved by the enforced spherical cavity dimensions of the rigid host being ideal for the lithium cation.

2.3 Calixarene-Based Receptors

Calix[n]arenes are synthetically generated macrocycles consisting of cyclic arrays of n phenol groups linked by methylene bridges⁴⁶. The most common member of the family, calix[4]arene, is particularly interesting as a cation binding host when the molecule adopts its cone conformation (C_{4v}). In this conformation, the host is able to form four attractive π -cation interactions with the guest. Complexation within the cavity of the receptor is entropically favourable, due to the release of solvent into the bulk medium. For example, the caesium cation forms a 1:1 complex with *p*-*tert*-butylcalix[4]arene via such interactions and the axial coordination of a thiocyanate ligand⁴⁷.

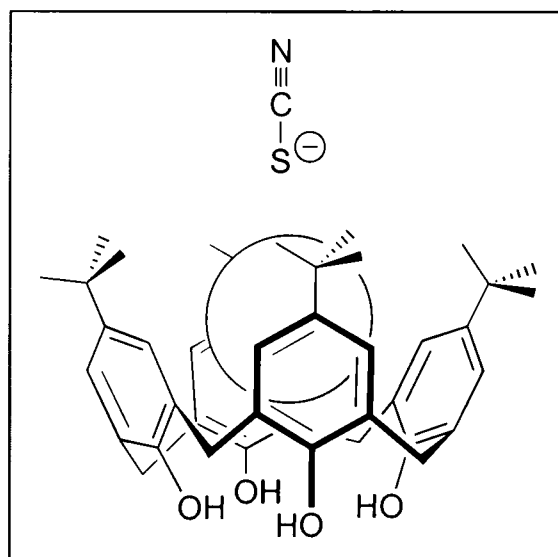


Figure 10 Schematic representation of p-tert-butylcalix[4]arene encapsulating a caesium ion

The phenolic groups on the lower rim of the calixarenes are easily functionalised with electron-rich ether and carbonyl moieties, providing a preorganised site for cation binding. Such architectures can associate with cations by a combination of ion-dipole and π -cation interactions^{48,49}.

The covalent linkage of two calix[4]arene moieties has lead to the formation of a calix[4]tube⁵⁰ which shows significant selectivity for the binding of potassium ions.

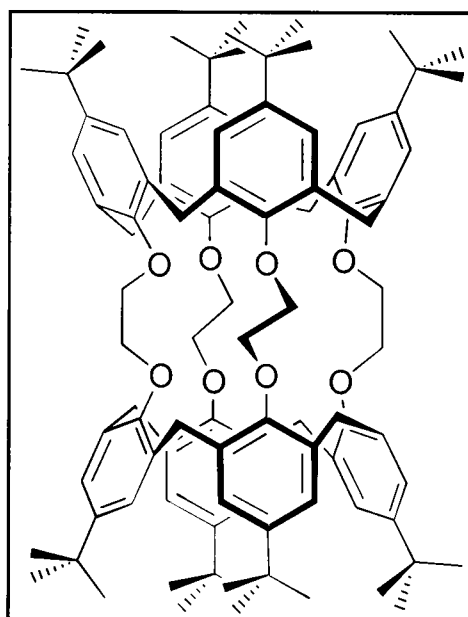


Figure 11 Calix[4]tube

Molecular mechanics calculations have suggested that such systems may, due to their structural similarity⁵¹, mimic potassium transport by gated ion channels across membranes.

3 Anion Binding

Unlike cation binding, the complexation of anions has until recently been an underdeveloped area of research. This is somewhat surprising considering the importance of anions in a variety of fields. Anions play pivotal roles in biological systems, with the majority of enzyme substrates and co-factors being anionic as is DNA, the carrier of genetic information. Medically, anions also have key functions, with cystic fibrosis a result of the misregulation of chloride channels⁵². Pollutant anions, such as nitrate and phosphates from arable farming⁵³ and pertechnetate, a by-product of the nuclear industry⁵⁴, are a matter of great environmental concern.

3.1 The Challenge of Binding Anions

The most distinguishing feature about anions in comparison to cationic guests is their opposite, negative electrostatic charge. However, there are several additional features that result in the coordination of anionic substrates being more challenging than their positively charged counterparts.

Anions are larger than their isoelectronic cations (Table 3), due to their reduced effective nuclear charge. Any potential synthetic host must subsequently be larger to accommodate the bigger anionic guest species. This increased relative size has the additional effect that the anions have a reduced charge density. Consequently, they show less electrostatic interactions with their environment, while their dispersion interactions (based on polarisability) are greatly enhanced. Furthermore, anions tend not to form as many multiple charged species as cations, with many elements combining with water in high negative oxidation states to form oxoanions, distributing their net charge over numerous atoms. Multiply charged anions tend to have their charges either well separated or extensively delocalised^{55,56}.

Cation	Radius (pm)	ΔH_{hyd} (kJmol ⁻¹)	Anion	Radius (pm)	ΔH_{hyd} (kJmol ⁻¹)
Na ⁺	102	-416	F ⁻	133	-510
K ⁺	138	-334	Cl ⁻	181	-367
Rb ⁺	148	-302	Br ⁻	196	-336
Cs ⁺	170	-283	I ⁻	220	-291

Table 3 Ionic radii and experimental enthalpies of hydration of selected isoelectronic anions and cations

Although anions possess a smaller charge density than their isoelectronic cations, they have significantly greater hydration energies (Table 3). This is a result of the efficient stabilisation that anions gain via the formation of hydrogen bonds with polar, protic solvents. This increased solvation creates competition between any potential receptor and the solvent for anion binding. The degree of aqueous solvation is highlighted in the Hofmeister series, which indicates the relative hydrophobicity of a given anion. In hydrophobic sites (where solvent cannot enter), it is found that less hydrated anions are bound most strongly and *vice versa*⁵⁷- an important feature in designing hosts for specific anions.

Anions also take the form of a variety of shapes, unlike cations, which are usually spherical (Figure 12). Care must therefore be taken to generate hosts that spatially complement the guest.

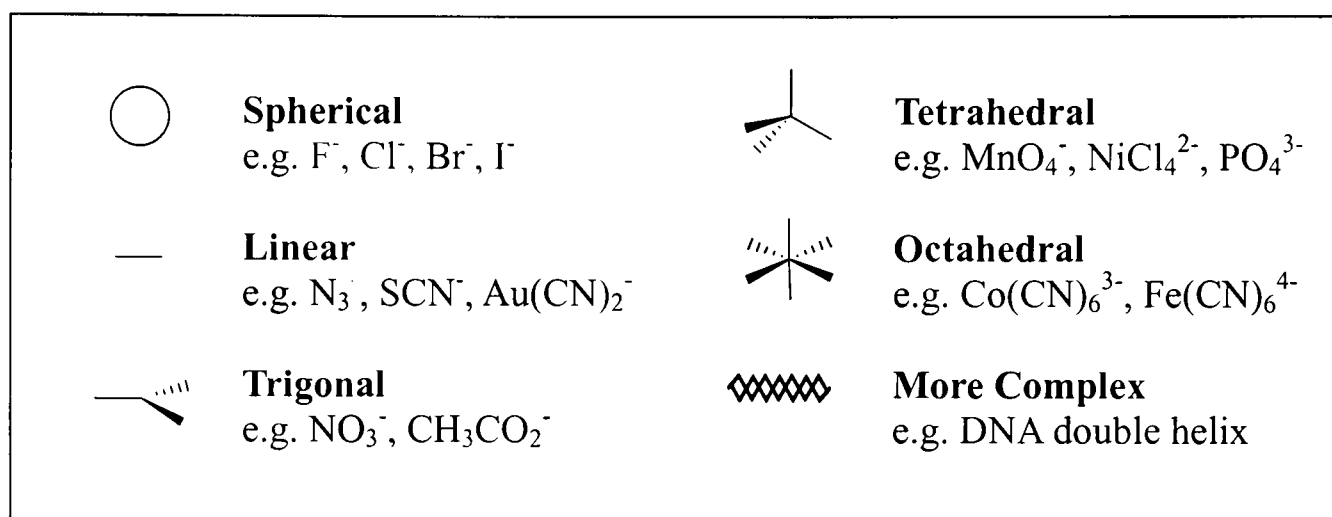


Figure 12 Geometries of anions

Finally, the pH dependence of anions must be taken into account, as many anions (such as carboxylates and sulphates) become protonated at low pH and hence lose their negative charge. This is further complicated if protonation is required by a host for complexation, restricting the host and guest species to a specific pH window.

Nature has evolved such that the above criteria are met by the use of selective proteins⁵⁸. This allows the recognition of anions of similar sizes and charges, such as phosphate and sulphate, via steric and electronic complementarity⁵⁹. The chemist must likewise address these properties of anions if similar selectivities are to be realised.

3.2 Positively Charged Anion Receptors

The first example of synthetic anion receptors were reported in 1968 by Park and Simmons⁶⁰ (Figure 13). They produced macrobicyclic ammonium cages, which were shown by NMR and X-ray crystallography to coordinate halide anions within the central cavity. This was achieved by a combination of electrostatic interactions and hydrogen bonding with the ammonium protons.

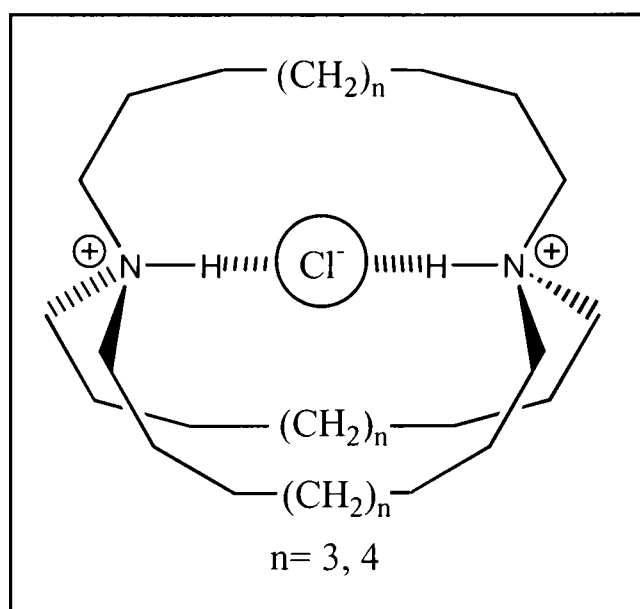


Figure 13 Park and Simmons' macrobicyclic anion receptors

Lehn and co-workers went on to develop this idea to generate a series of ammonium-based macrocyclic⁶¹ and cryptand⁶² structures, which were able to discriminate between anions on the basis of size^{63,64} and shape^{65,66}. Unfortunately, the restrictive pH window in which these studies must be undertaken, limit the usefulness of this class of receptor.

The guanidinium group is present in the side-chain of the amino acid arginine, and acts as a vital component of enzymatic catalytic domains that participate in the binding of anionic guests⁶⁷. Guanidinium-based receptors have therefore been developed for the binding of a range of anionic guests. They have the advantage of remaining protonated over wider pH ranges⁶⁸ ($pK_a = 13.5$ compared to secondary amines $pK_a \sim 10$)⁶⁹ due to delocalisation of the positive charge across three nitrogen atoms⁷⁰. This has the detrimental effect, however, that their derivatives suffer decreased binding affinities compared to polyammonium analogues. This can be overcome by building the receptor into a rigid system (Figure 14), which decreases the loss of entropy on binding an anion⁷¹. The bicyclic guanidinium receptor (**6**)⁷² has been shown to form strong complexes with bidentate oxoanions in organic solvents due to its complementary binding geometry and has been demonstrated to discriminate between enantiomers of carboxylate anions⁷³.

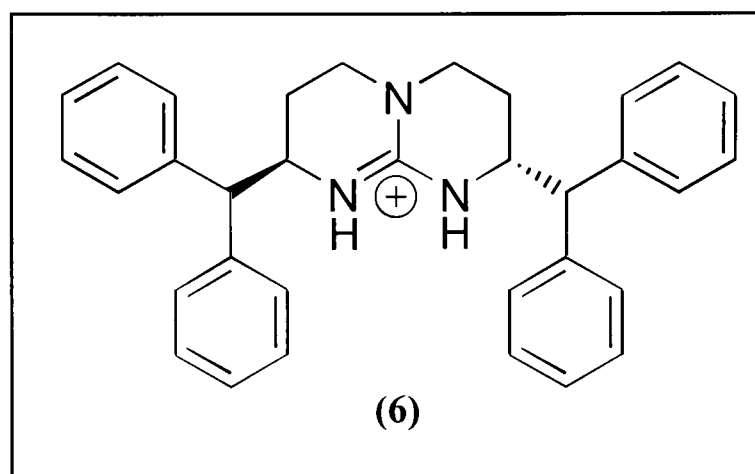


Figure 14 Bicyclic guanidinium receptor

The problem of pH dependence can be overcome by the synthesis of receptors that possess a permanent positive charge to electrostatically attract anions. Schmidtchen developed a range of quaternary ammonium macrotricyclic hosts, whose preorganisation reduces the problem of mutual electrostatic repulsions⁷⁴. These systems were shown, in water, to bind anions, which have a complementary size to the internal dimensions of the cavity⁷⁵ (Figure 15). Unfortunately, due to the absence of hydrogen bonding in these receptors, association constants are significantly lower than their analogous tertiary ammonium-based receptors.

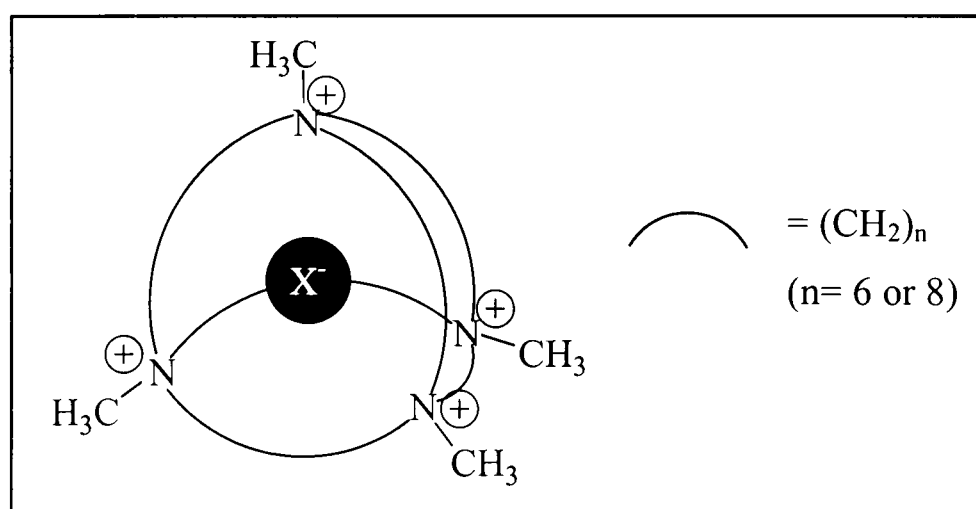


Figure 15 Schmidtchen's macrotricyclic anion receptor

A further method of generating positively charged anion receptors is by the incorporation of metal cations into the organic framework. One such example is a macrocycle synthesised by Martell and co-workers, which is able to bind two copper(II) ions⁷⁶. Anions, such as hydrogen phosphate, have been demonstrated to form a cascade complex with the ligand, through bridging between the two metal centres (Figure 16).

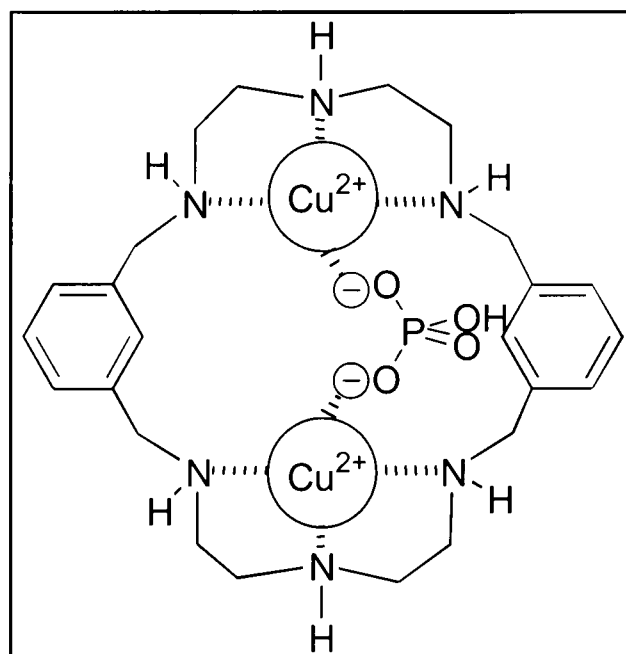


Figure 16 Anion recognition by the formation of cascade complexes

3.3 Lewis Acidic Anion Receptors

An alternative approach to using electrostatic interactions to attract anions is to use Lewis acidic complexes. Due to their electron-deficiency, such structures are able to bind anionic guests by means of orbital overlap causing a bonding interaction between the components. Such interactions are highly directional and, in addition to their sensitivity to hard/soft electronic factors, allow the possibility of generating highly selective hosts. The air and moisture sensitivity of many Lewis acid hosts can, however, limit their practicality⁷⁷.

There have been numerous receptors in which Lewis acidic centres have been incorporated into acyclic and macrocyclic structures, with hosts containing boron⁷⁸, silicon⁷⁹, tin⁸⁰, mercury⁸¹, germanium⁸² and uranyl derivatives being synthesised.

Reinhoudt *et. al.* have generated systems utilising the latter uranyl centre coordinated to a salophane ligand⁸³ (Figure 17). The electron-deficient metal centre has a high affinity for hard anions, such as dihydrogen phosphate and fluoride.

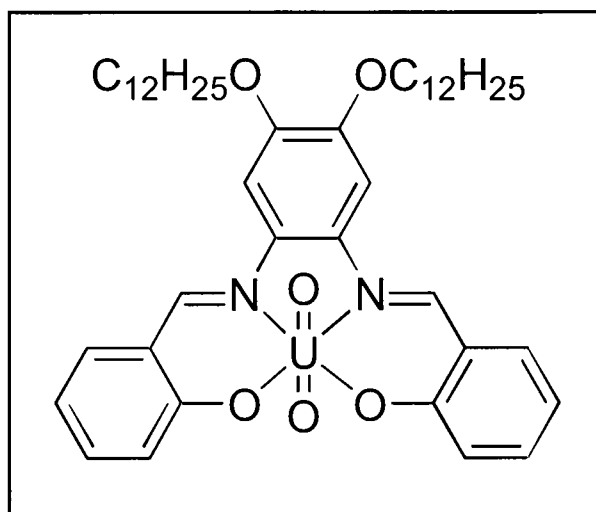


Figure 17 Uranylsalophane complex

3.4 Hydrogen Bonding Anion Receptors

As has already been seen, hydrogen bonds can be used in combination with other non-covalent interactions to generate anion binding hosts. It is also possible, however, to synthesise receptors that bind anions via the formation of hydrogen bonds alone. The high directionality of hydrogen bonds allows the construction of structures to bind anions that are able to differentiate between guests with different geometries and/or hydrogen bonding requirements⁸⁴. The use of neutral receptors also allows complexation studies to be performed in less-competitive non-polar solvent systems.

Pascal and co-workers synthesised the first receptor that bound anions by purely hydrogen bonding⁸⁵. Their organic structure (Figure 18) was found to bind fluoride ions in DMSO-d₆ via the formation of hydrogen bonds with the amide moieties.

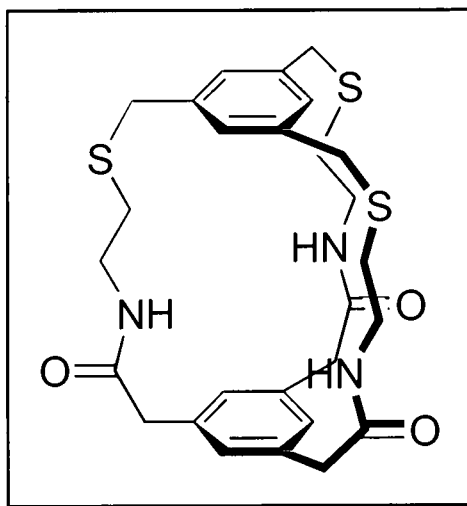


Figure 18 Pascal's amide-based anion receptor

Other hydrogen bond donors, such as urea, thiourea and sulphonamide groups, have been converted into three-dimensional arrays to selectively bind a range of complementary guest species⁸⁶. Davis and co-workers have taken advantage of the framework of the steroid cholic acid to construct a series of anion receptors via functionalisation with a variety of hydrogen bond donor groups (Figure 19)⁸⁷. This structure contains a cleft for anion recognition and has been demonstrated to extract chiral carboxylate anions into organic solvents with significant enantioselectivities⁸⁸.

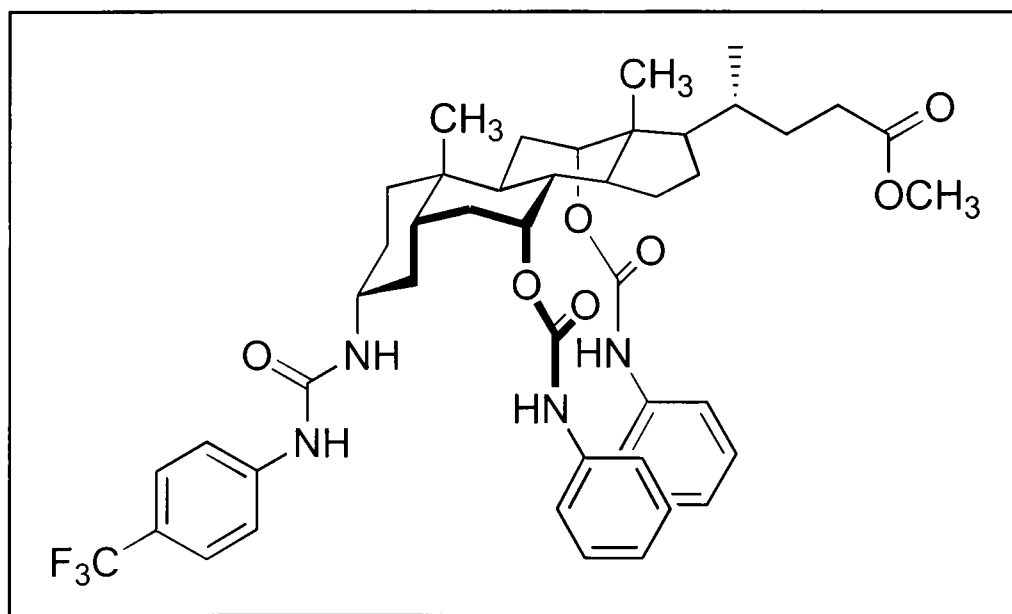


Figure 19 Hydrogen bond donating receptor based on cholic acid

Sessler and co-workers have developed a range of calix[n]pyrrole macrocycles, which have been shown to form strong complexes with halide ions by the formation of hydrogen bonds with the pyrrole NH groups⁸⁹. Recently, cryptand-based pyrrole systems have been developed

(Figure 20) which have been shown to encapsulate a variety of inorganic anions within their cavities⁹⁰.

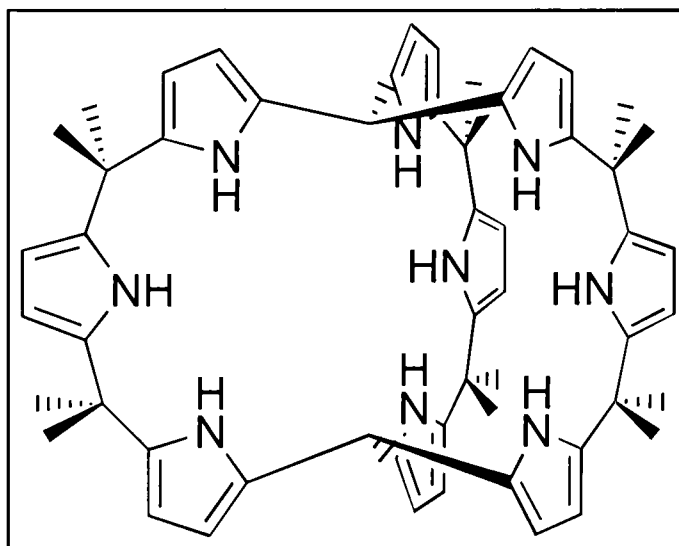


Figure 20 Calixpyrrole cryptand structure

4 Neutral Guest Binding

The binding of neutral guest species is one of the hardest challenges of supramolecular chemistry due to the absence of electrostatic interactions between host and guest and the huge variety of size and shape of potential targets. The most common method for binding neutral guests is through the combination of hydrogen bonding groups, the incorporation of hydrophobic interactions and π - π stacking.

4.1 Hydrogen Bonding

Perhaps the most important type of interaction for binding neutral guest species is hydrogen bonding, as this generates strong, directional and complementary bonds between the host and the guest.

Adrian and Wilcox prepared hosts which are preorganised for forming complementary hydrogen bonds with 2-aminopyrimidine⁹¹ (Figure 21). These ‘molecular tweezers’ were shown to have stability constants with the guest in the order of 10^4 in chloroform.

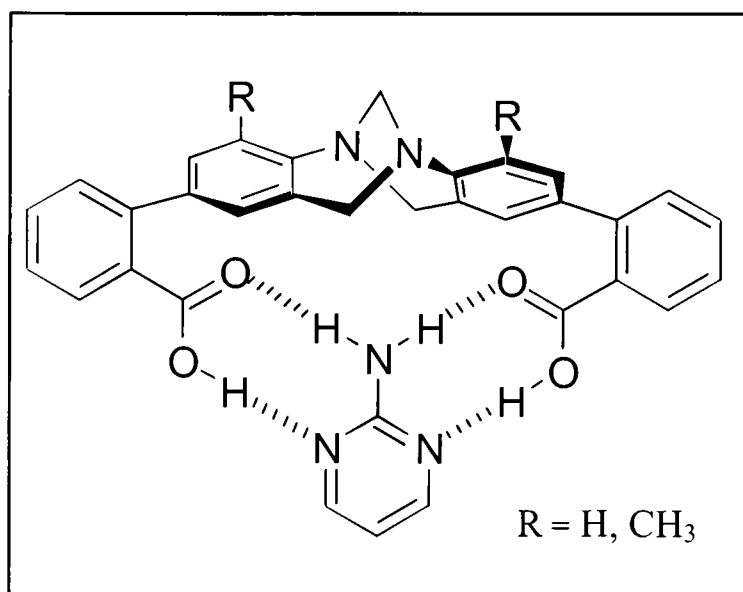


Figure 21 'Molecular tweezers' as a host for 2-aminopyrimidine

4.2 Hydrophobic Binding

One of the most effective methods of binding hydrophobic guests is to generate hosts with 'greasy' binding sites to encapsulate the suitable targets. Macrocyclic structures such as cyclophanes⁹², cyclodextrins⁹³ and calixarenes⁹⁴ have all been used to bind aromatic moieties within their central cavities. Such recognition is predominantly entropically driven, due to the displacement of solvent molecules into the bulk solution upon association of the given guest. Favourable π - π stacking interactions may also assist the association process.

Cyclotrimeratrylene (CTV) has proved to be a highly versatile host for a range of neutral molecules in both solution and the solid state (Figure 22). This is mainly due to its conformational preference for the three aryl rings to point in the same direction, providing a bowl-shaped cavity for guest inclusion. CTV has both a steric and electronic complementarity with fullerenes such as C₆₀. The radius of curvature of the wide CTV cavity is similar to that of the large fullerene sphere. In addition, the aromatic rings are very electron-rich because of the electron-donating effect of the methoxy substituents, complementing the electron-deficient nature of C₆₀⁹⁵.

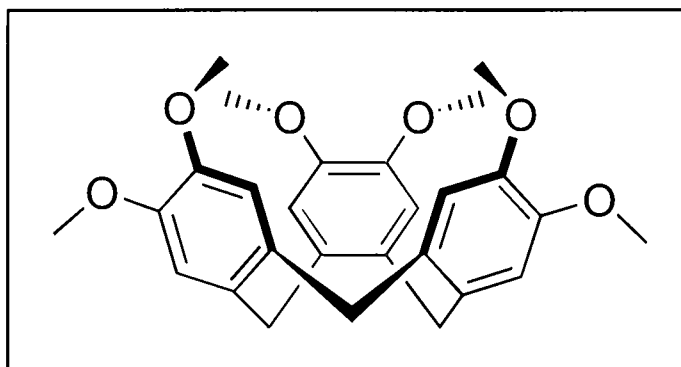


Figure 22 Cyclotrimeratrylene

5 Chemical Sensing

One of the most significant practical applications of supramolecular chemistry has been in the field of chemical sensing^{96,97}. A sensor may be defined as a device that reports the presence of a target molecule via a measurable physical response. Such an array usually consists of a known binding motif linked in close proximity to a reporter group. The reporter group is often a known optically-, luminescent- or redox-active centre, whose normal response will be perturbed upon the binding of the guest. Ideally, the device will be specific for one particular target, as well as reporting not only the presence of a guest but also its concentration in solution (Figure 23).

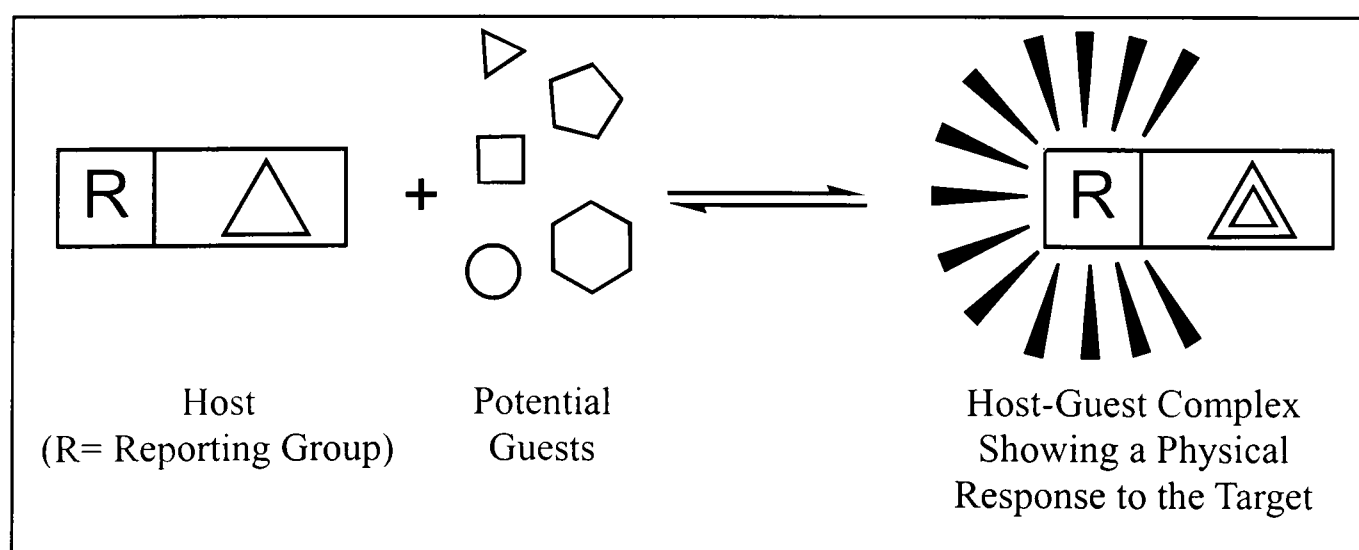


Figure 23 Schematic representation of a host sensing a specific target

5.1 Electrochemical Sensing

The complexation of a guest species by a redox-active host may result in a perturbation of the electrochemical properties of the host. The binding process may be coupled to the redox centre through one or a combination of these factors:

- i) Electrostatic communication either through bond or through space
- ii) Direct coordination between the redox centre and the coordinated guest
- iii) Conformational change of the host due to complexation by the guest

The redox-active quinone moiety has recently been incorporated into a bis-calix[4]arene framework^{98,99} (Figure 24). This ionophore has shown significant affinity for Group 1 cations, such as caesium, through direct coordination to the eight oxygen donors within the central cavity of the receptor. This binding may be monitored via electrochemical techniques, where new waves are evolved upon addition of cations that are significantly anodically shifted compared to the free ligand.

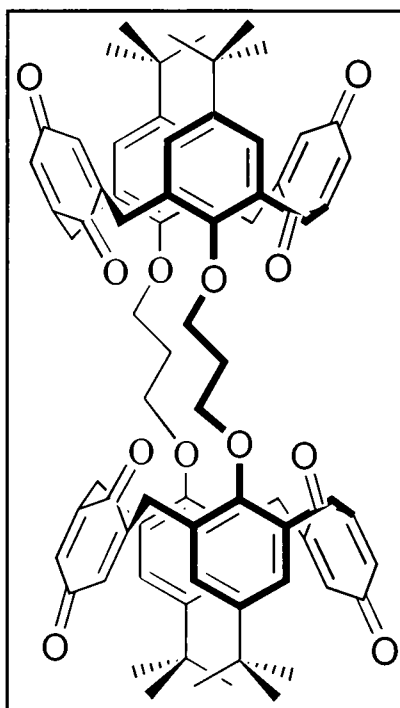


Figure 24 Bis-(calix[4]diquinone) redox-active cation receptor

Ferrocene derivatives have been frequently used as electrochemical sensors as their cyclopentadiene rings can be readily appended with recognition sites. Recently, Tucker and

co-workers have developed a ferrocene-based receptor that possesses urea moieties for anion recognition¹⁰⁰ (Figure 25). Addition of carboxylate anions results in a 70mV cathodic shift in the reversible ferrocene/ferrocenium oxidation wave, due to the electrostatic stabilisation of the higher oxidation state by the adjacently bound anion.

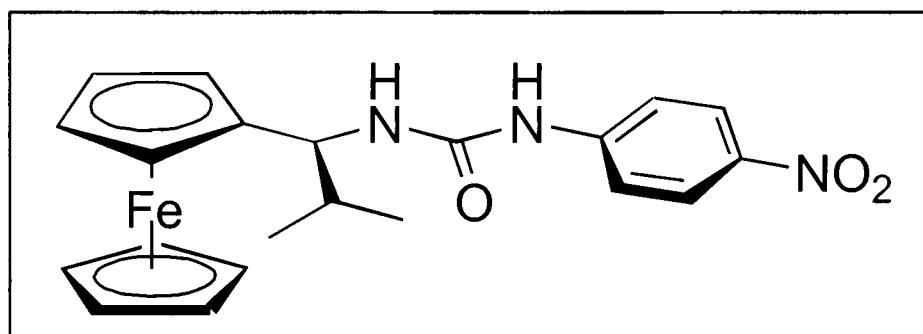


Figure 25 Ferrocene-based urea derivatised anion receptor

5.2 Luminescent Sensors

The combination of a molecular recognition site with a fluorophore has recently been used in the development of a range of chemosensors¹⁰¹. Where there is efficient coupling between the fluorescent unit and the binding site, the association of the target guest may be monitored by the fluorescent output of the host. This technique is particularly attractive as fluorescence measurements are usually very sensitive (single molecule detection is possible), low cost, easily performed and versatile¹⁰².

An early example of a luminescent chemosensor was reported by de Silva and de Silva (Figure 26)¹⁰³. Here, aza-18-crown-6 is covalently linked to a luminescent anthracene core. Addition of potassium ions, in methanolic solution, results in a fifty-fold increase in the fluorescence quantum yield of the sensor, due to the suppression of the intramolecular photoelectron transfer process that quenches the luminescence of the free receptor.

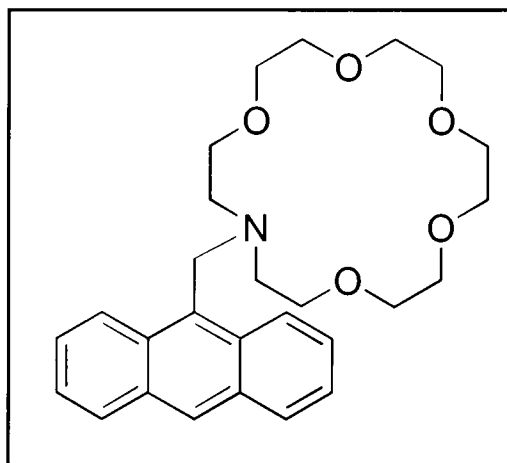


Figure 26 Luminescent potassium ion sensor

There have also been numerous examples of inorganic fluorophores being used as chemosensors^{104,105}. Parker has reported the use of cyclen-derivatised lanthanide complexes, which show significant increases in their fluorescence intensities upon the addition of anions. The europium complex (Figure 27) is found to sense the binding of bidentate oxoanions, such as citrate and malonate, via the displacement of the weakly bound water molecules at physiological pH¹⁰⁶.

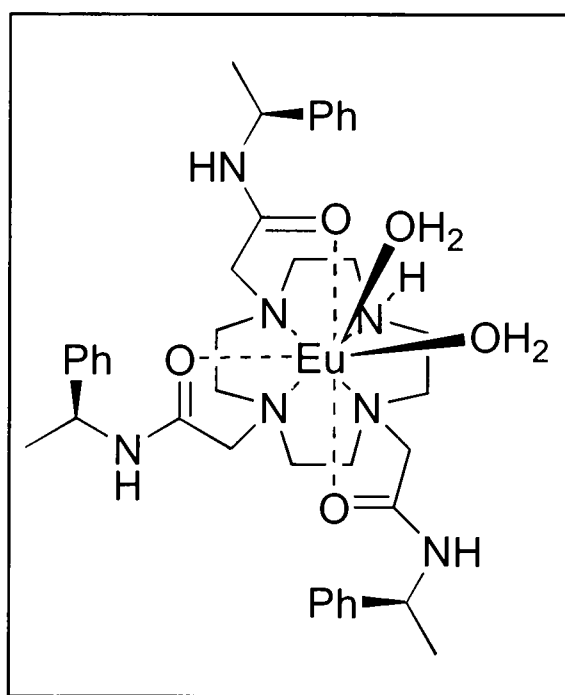


Figure 27 Luminescent europium complex for anion sensing

5.3 Colourimetric Sensors

The development of colourimetric sensors, species that allow the “naked-eye” detection of targets through their colour changes, without requiring expensive and bulky spectroscopic or electrochemical instrumentation, is currently a keen area of research^{107,108}. There have been numerous host molecules that undergo a colour change upon binding a guest^{109,110,111}. An alternative method that has been used in anion colourimetric sensing is to coordinate a weakly bound dye to a receptor and monitoring its release upon addition of an anionic guest. This displacement assay principle has been demonstrated by Gale *et. al.* who have found that calix[4]pyrrole forms a colourless complex with the 4-nitrophenolate anion (a yellow dye) in organic solvents. However, addition of the fluoride anion (which has a strong affinity for the macrocycle) results in the liberation of the dye, which colours the solution yellow (Figure 28). The intensity of the resultant colour is proportional to the quantity of fluoride added¹¹².

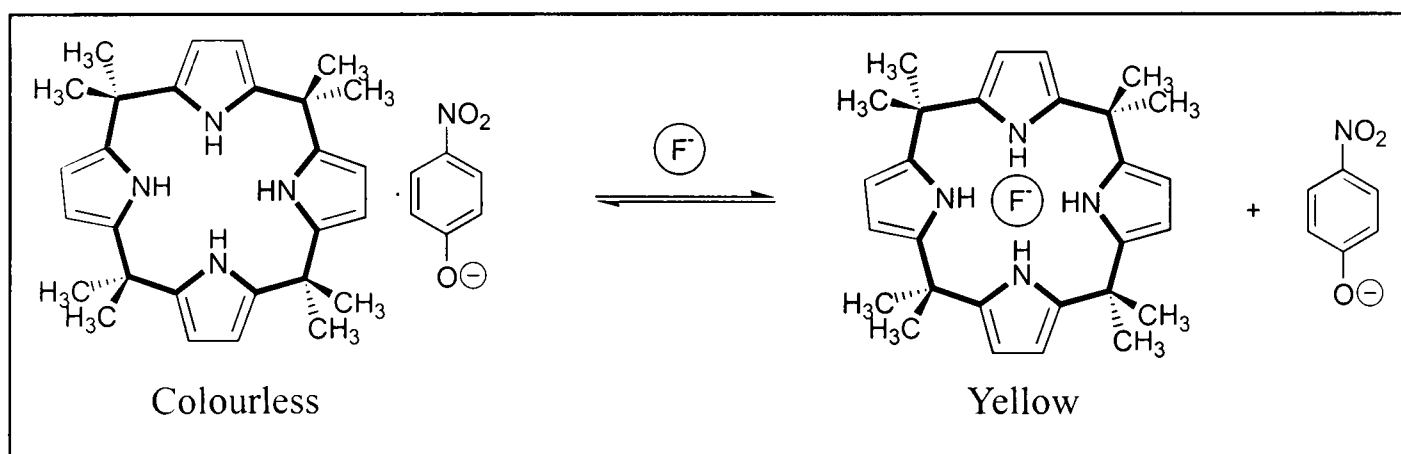


Figure 28 Colourimetric fluoride sensor

6 Self-Assembly

Self-assembly is the solution-phase formation of stable supermolecules via the non-covalent simultaneous and reversible assembly of multiple, specifically designed, complementary building blocks to form an array with a well-defined geometry¹¹³. The building block approach to these assemblies allows the synthesis of complex architectures which would not be accessible or whose synthesis would be non-viable via traditional stepwise, covalent

syntheses. The kinetic lability of these weak interactions also allows for error-recovery and structural change according to the environment of the structures.

There are many examples of self-assembly in Nature and one of the most elegant is that of the tobacco mosaic virus¹¹⁴. The virus consists of 2130 identical protein subunits that encase a central RNA strand to form a well-defined 300 nm-long rod (Figure 29). Remarkably, after the virus dissociates into its constituent parts it is found to spontaneously reassemble under physiological conditions to form the intact virus and regain its functionality. This demonstrates that mere non-covalent interactions, where suitably programmed, can generate complex and functional structures.

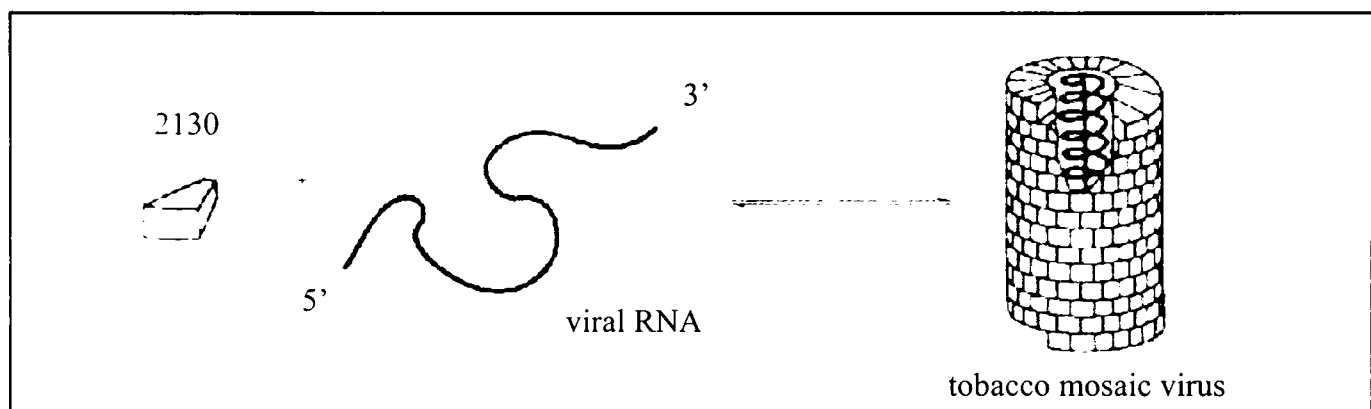


Figure 29 Self-assembly of the tobacco mosaic virus

The most important example of self-assembly is the formation of the DNA double helix from two complementary strands of deoxyribonucleic acid. The predominant driving force is hydrogen bond formation between complementary base pairs (Figure 30). The double helix is thermodynamically stable, and under the right conditions, the assembly is reversible, which is important in order that errors may be corrected.

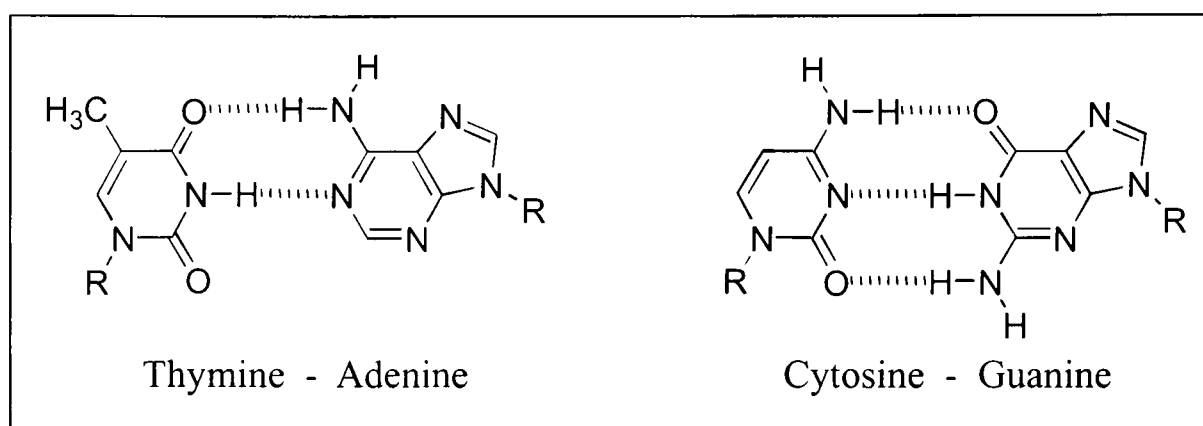


Figure 30 Complementary hydrogen bonding in nucleic acid base pairing

6.1 Hydrogen Bonding Assemblies

The directionality of the hydrogen bond makes it very attractive for the chemist to use for the assembly of complex supermolecules^{115,116}. Hydrogen bonds have been utilised to construct a variety of structures, such as rosettes^{117,118}, ribbons^{119,120}, zippers^{121,122}, capsules^{123,124} and helices^{125,126}.

The construction of such architectures requires the unambiguous pre-programming of the subunits by the incorporation of a suitable pattern of hydrogen bond donor/acceptor (D/A) sites. The hexameric macrocycle, synthesised by Lehn *et. al.* (Figure 31) possesses DDA/AAD hydrogen bonding faces, so may only create a fully connected hydrogen bonding array (the thermodynamic product) by forming the cyclic structure¹²⁷. The hydrogen bonding information of the subunit therefore determines the outcome of the self-assembly process.

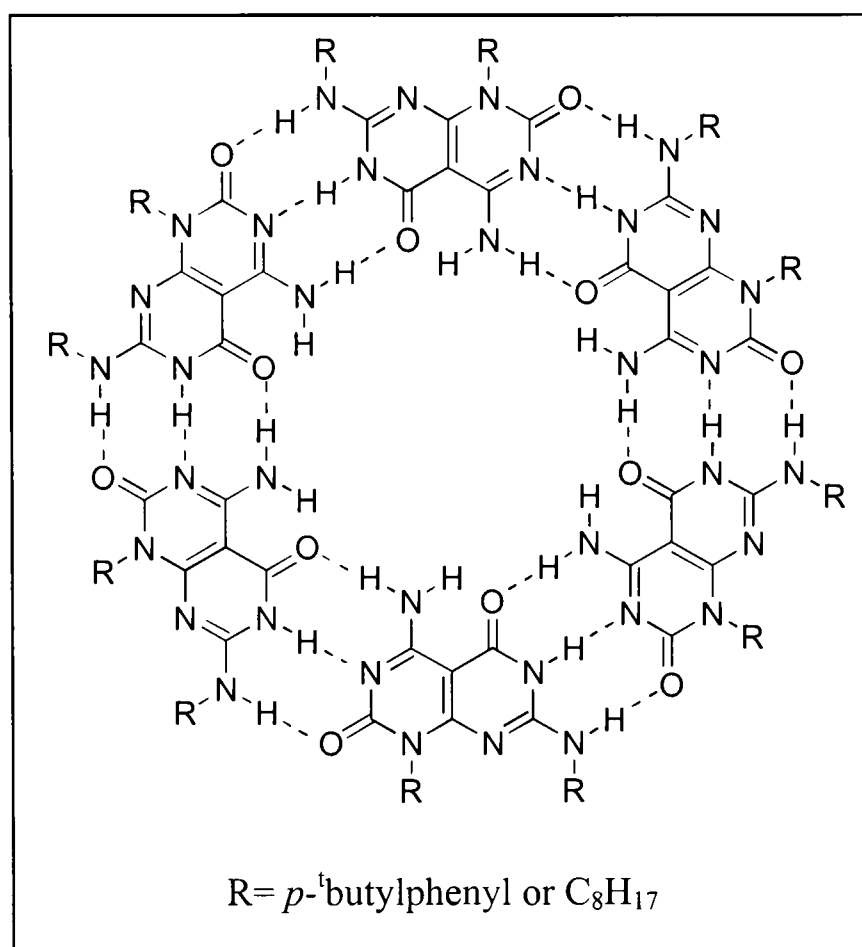


Figure 31 Self-assembled hydrogen-bonded macrocycle

The self-assembly of hydrogen bonding networks has been incorporated in the expanding field of crystal engineering¹²⁸. Three-dimensional hydrogen bond donating/accepting subunits (tectons) have been synthesised and used to generate networks (which are regarded as infinite supermolecules) whose geometry and dimensions are controlled by the nature of the building blocks. For example, the tetrahedral tecton (Figure 32) possesses one hydrogen bond donor and acceptor per pendant arm and hence forms a diamondoid polymeric framework¹²⁹. In this instance, large internal cavities are formed by the network, which are filled by the framework forming an interpenetrated structure with itself. Manipulation of the initial subunits has also allowed the formation of networks with large vacant internal cavities (a supramolecular zeolite) which have significant potential in the field of molecular storage¹³⁰.

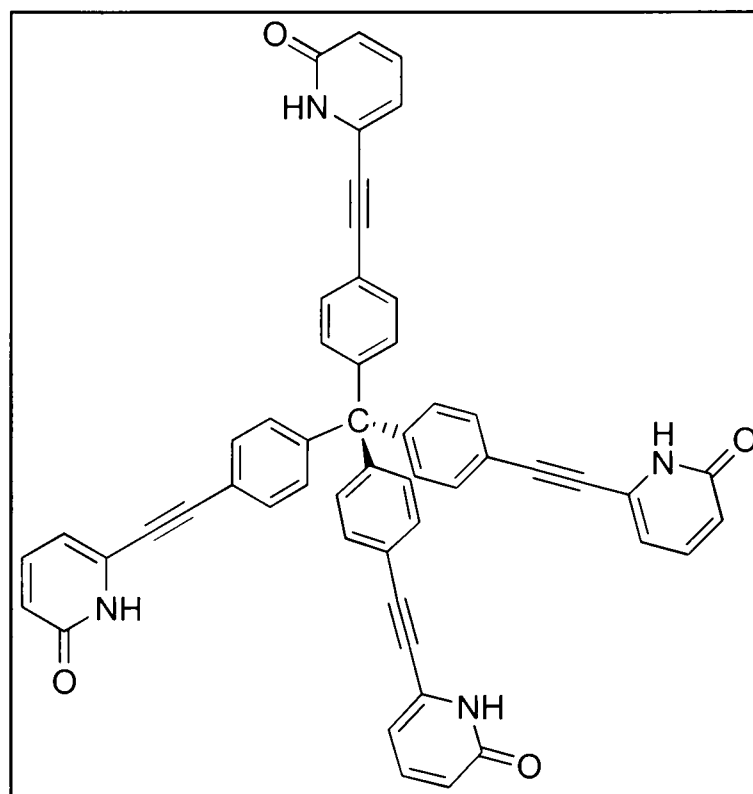


Figure 32 Tetrahedral hydrogen bond donating/accepting tecton

6.2 Interlocking Molecules

It has long been a desire of the chemist to be able to synthesise interlocked molecules¹³¹. This is not only for their aesthetic beauty, but also for their potential applications in molecular machines and devices¹³² and since such interpenetrating structures have been shown to occur naturally in mitochondrial DNA¹³³.

The two most common types of these structures are catenanes and rotaxanes. An [n]catenane consists of n interlinked ring structures that are not physically joined by covalent bonds. Similarly, an [n+m]rotaxane is composed of n macrocyclic components confined along m axles by bulky stopper groups. A pseudo-rotaxane lacks the bulky end stopper groups of a rotaxane, hence the central thread is free to dissociate (Figure 33).

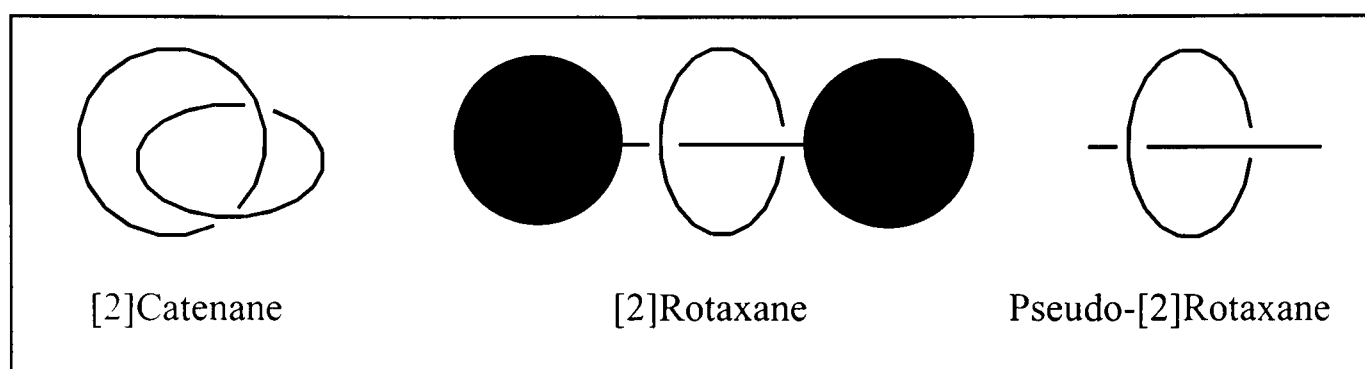


Figure 33 Interlocked molecules

The formation of such species may occur statistically in macrocyclic synthesis, but yields are generally pitiful for this method¹³⁴. As a result, their formation has generally relied on either templation or self-assembly methodologies¹³⁵.

Hydrogen-bonding motifs have recently proved a popular templating aid for the construction of interlocked molecules¹³⁶. Hunter demonstrated this principle in his serendipitous synthesis of a [2]catenane¹³⁷. During his stepwise preparation of a macrocyclic compound (Figure 34), it was found that the two precursors form intermolecular hydrogen bonds with each other, templating the formation of the interlocked structure upon cyclisation. This catenane structure was isolated in yields of up to 34%, and characterised by NMR and mass spectrometry.

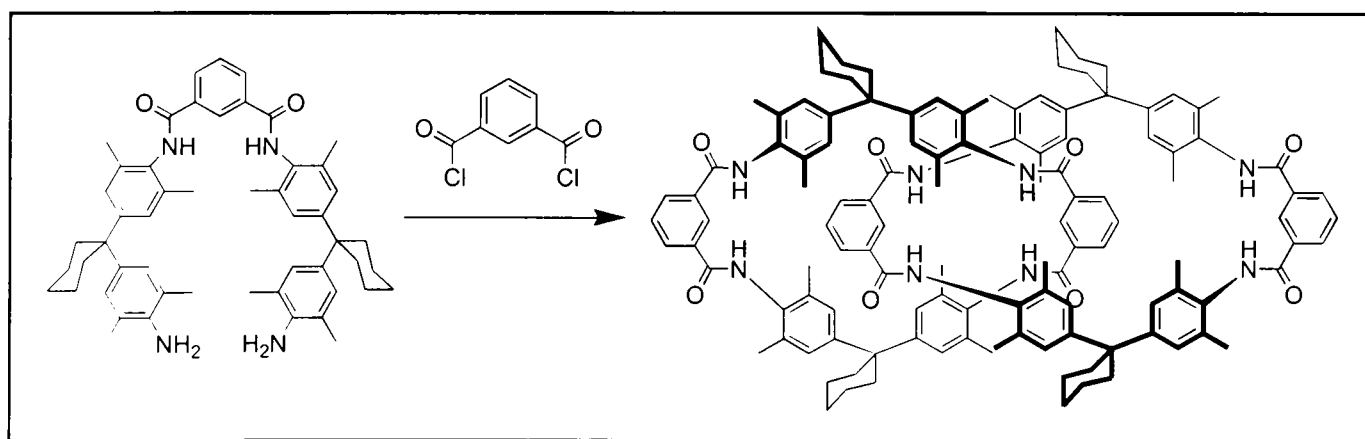


Figure 34 Hunter's [2]catenane formed via hydrogen bond directed assembly

Other hydrogen bonding templated syntheses have been undertaken, such as the utilisation of the high affinity of dialkylammonium cations for suitably sized crown ethers to form a pseudo-rotaxane precursor for the generation of numerous interlocked hosts¹³⁸.

Stoddart and co-workers have used π -stacking for the formation of interlocked species¹³⁹. They have taken advantage of the strong charge transfer π - π stacking interactions that result

between electron-deficient compounds and electron rich aromatic moieties. Simple [2]rotaxanes, incorporating a hydroquinone thread through a bis-pyridinium macrocycle, were prepared via the initial formation of a pseudo-rotaxane and subsequent trapping by the attachment of bulky silyl stoppers¹⁴⁰ (Figure 35).

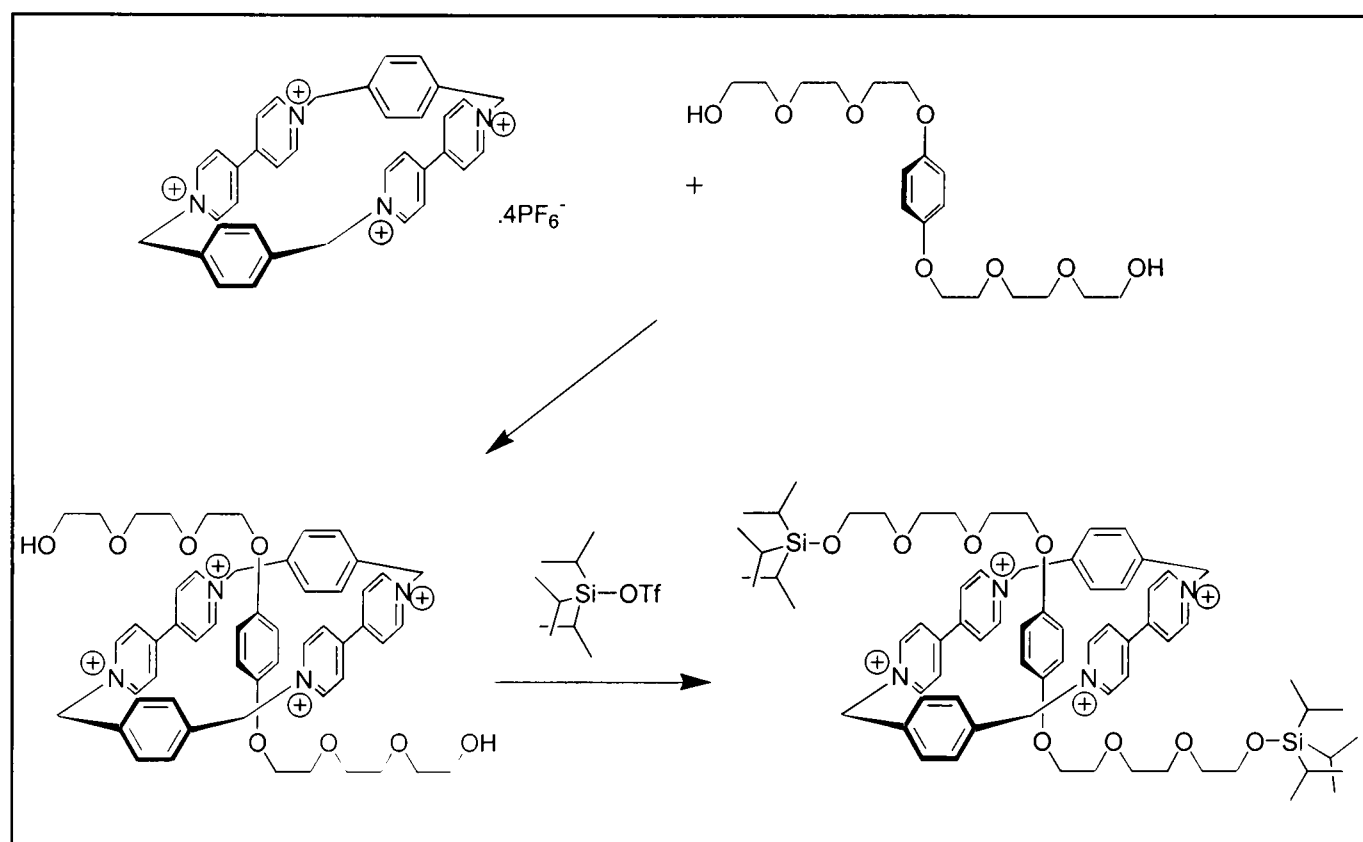


Figure 35 Formation of [2]rotaxane templated via π -stacking interactions

The formation of the same rotaxane product has also been possible via the techniques of clipping whereby the macrocycle is formed around the prestoppered thread. A further method of rotaxane formation (although not used in this case) is slippage¹⁴¹. Here, elevated temperatures are used to force the interlocking of the two preformed species.

Stoddart has exploited this simple idea to develop a vast range of architectures and devices based on these interactions, such as catenanes¹⁴², polycatenanes¹⁴³, the ‘olympiadane’ (a [5]catenane¹⁴⁴), catenanes confined on gold surfaces¹⁴⁵, molecular shuttles¹⁴⁶, sensors¹⁴⁷ and cables¹⁴⁸.

Cyclic organic bucket-shaped macrocycles, such as cyclodextrins and cucurbituril, have been shown to bind a vast range of rod-shaped guests, in aqueous solution, within their rigid, cylindrical, hydrophobic cavities. Such inclusion complexes have been used as a precursor for

the assembly of interlocked molecules¹⁴⁹. Anderson and co-workers have utilised this hydrophobic bonding to generate fluorescent rotaxanes through encapsulation of a diboronic acid core with cyclodextrins¹⁵⁰. Subsequent Suzuki coupling of this pseudo-rotaxane precursor added a bulky aromatic stopper to the system, generated the desired rotaxane (Figure 36). Shielding of the chromophore from the external environment was found to increase its fluorescence efficiency due to the reduction of the non-radiative decay processes of the host. This approach is now being used to fabricate insulated molecular wires,¹⁵¹ an area of interest for the opto-electronics industry.

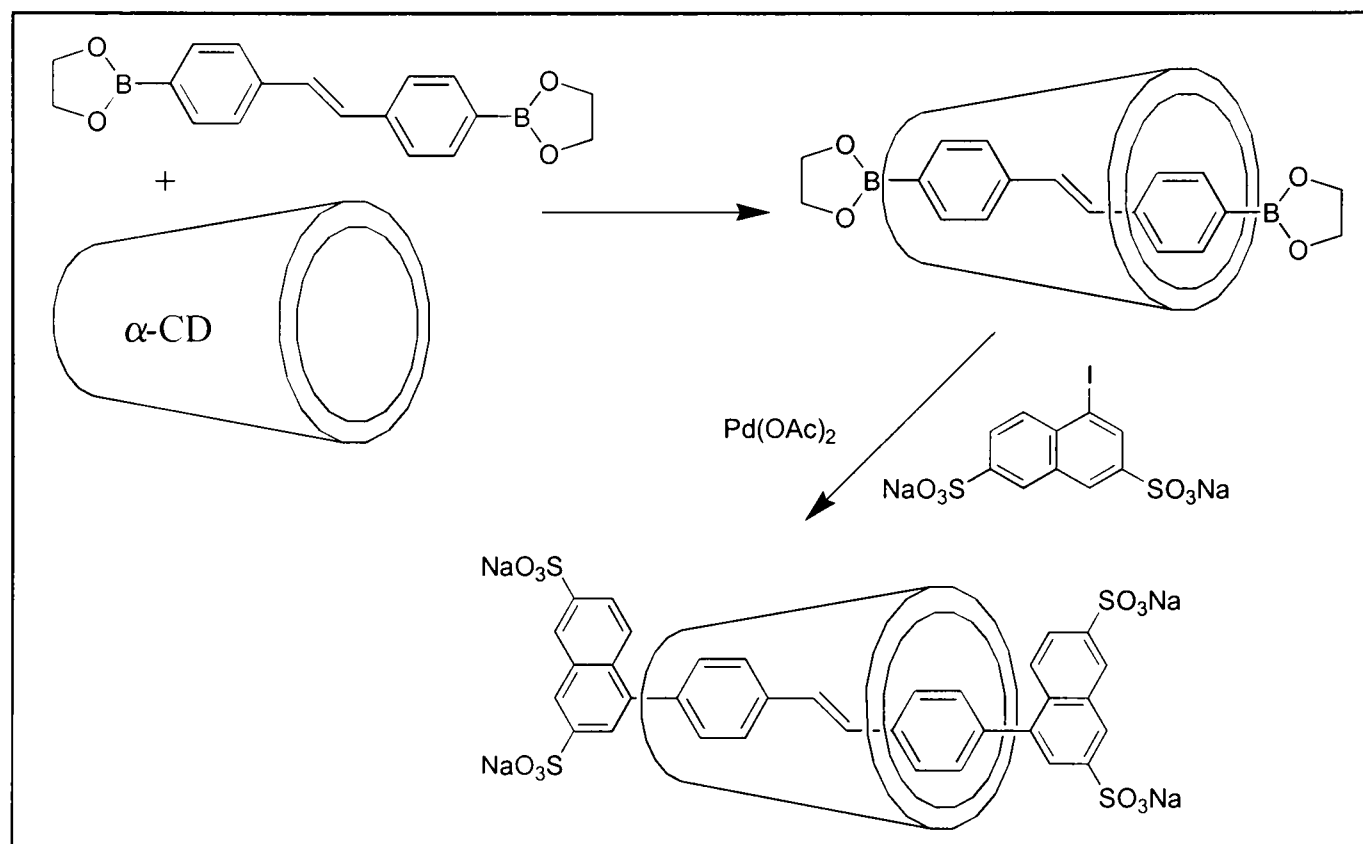


Figure 36 Fluorescent cyclodextrin sheathed rotaxane

7 Metal-Directed Self-Assembly

The metal-directed self-assembly of various host architectures is a well-established phenomenon in the literature^{152,153,154}. Metal-directed self-assembly has three major advantages over conventional self-assembly. Firstly, the metal-ligand dative coordinate bonds are thermodynamically strong. Consequently, many assemblies are robust, exhibiting less

solvent and pH dependence than hydrogen-bonded structures. Secondly, the product, stability and binding properties of metal-directed self-assembly may be controlled by the choice of metal ion and further altered by varying the metal's oxidation state. Finally, the incorporation of transition metal centres into structures confers potential new properties to the host such as charge, magnetism, colour and chemical and redox activity.

7.1 Macrocycles

One of the earliest examples of metal-directed self-assembled arrays was reported in 1973 by Pryde *et. al.*¹⁵⁵. Flexible phosphorous-based ligands were found to coordinate to rhodium(I) complexes to form a dinuclear macrocycle (Figure 37).

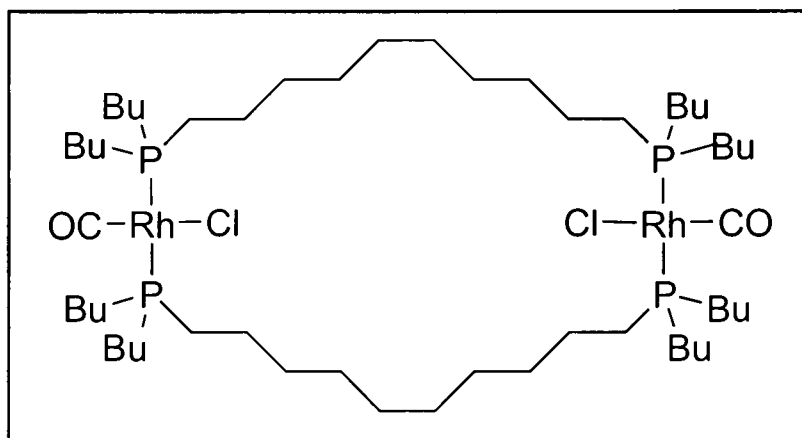


Figure 37 Dinuclear rhodium(I) macrocyclic complex

When using metals to construct a supramolecular architecture it is often difficult to control the number and direction of the coordinating ligands. To this end, protected metal ions (e.g. *cis*-ethylenediamine protected palladium(II) and platinum(II) building blocks) have been exploited to limit the coordination sites and control the number and direction of the ligand connectivities.

Hupp and co-workers used *cis*-phosphine-protected palladium(II) and rhenium centres to construct a molecular square with the planar 4,4'-bipyridine ligand (Figure 38)¹⁵⁶. This bimetallic complex was shown to luminesce and its intensity increased upon the addition of perchlorate in acetone, presumably due to its inclusion within the molecular cavity. This

demonstrates the possibility of utilising metallomacrocycles in developing molecular sensing devices.

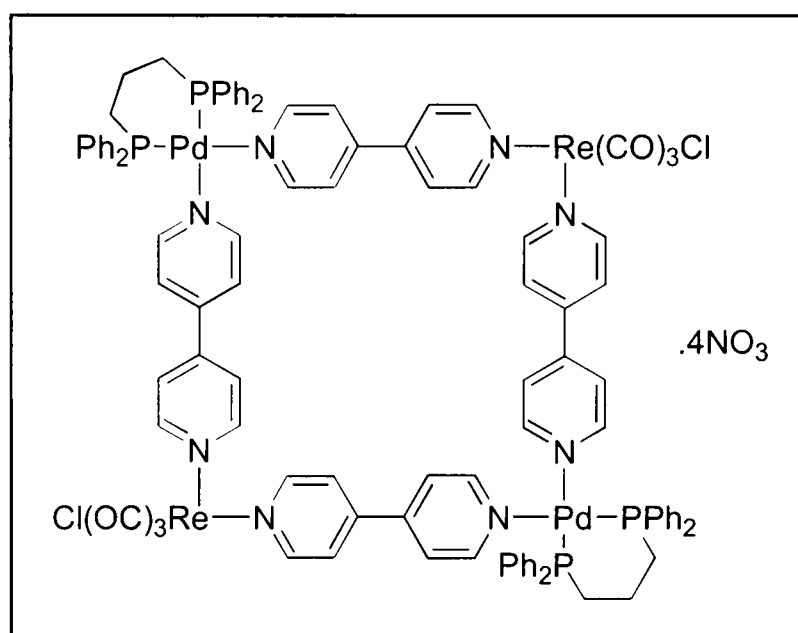


Figure 38 Self-assembled molecular square

The use of rigid ligands, such as 4,4'-bipyridine, result in the formation of predefined structures. However, the use of more flexible ligands allows the creation of a greater range of structures. The addition of *cis*-ethylenediamine-protected palladium nitrate with *trans*-1,2-bis(4-pyridyl)ethylene results in a mixture of a molecular square and a molecular triangle (Figure 39)¹⁵⁷. The equilibrium between these two structures is concentration dependent, with high concentrations resulting in the formation of the enthalpically favoured product - the tetranuclear square. Lower concentrations, on the other hand, result in the entropically less-disfavoured trinuclear triangle being formed. A number of guests can also induce reorganisation: addition of a small guest, such as *p*-dimethoxybenzene, resulted in increased trimer formation whereas addition of a larger guest, e.g. 18-crown-6 or 1,3-adamantanedicarboxylic acid disodium salt, promoted the formation of the tetramer.

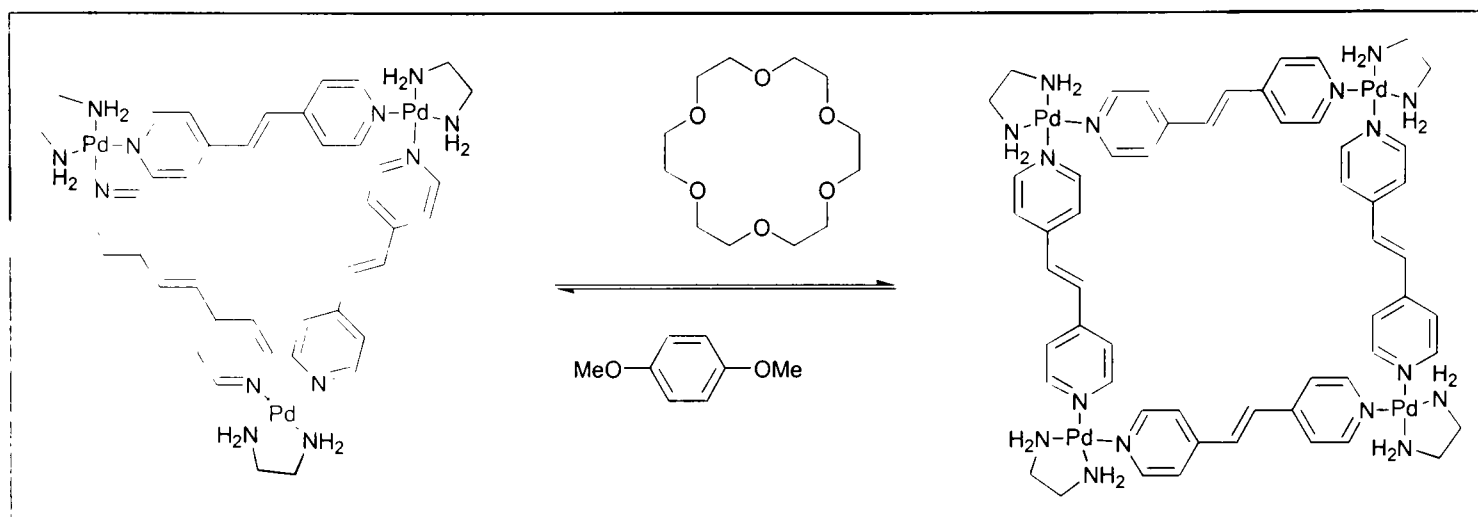


Figure 39 Guest-induced molecular reorganistaion

Hunter has developed a range of metalloporphyrins appended with pyridine side arms¹⁵⁸. These ligands coordinate to the vacant axial sites of the central metal ion to generate a range of multinuclear structures. In the case of the cobalt-based porphyrin, (Figure 40) a 30° inclination is formed by the variation in the two different side arms, resulting in the formation of a cyclic dodecamer in solution¹⁵⁹.

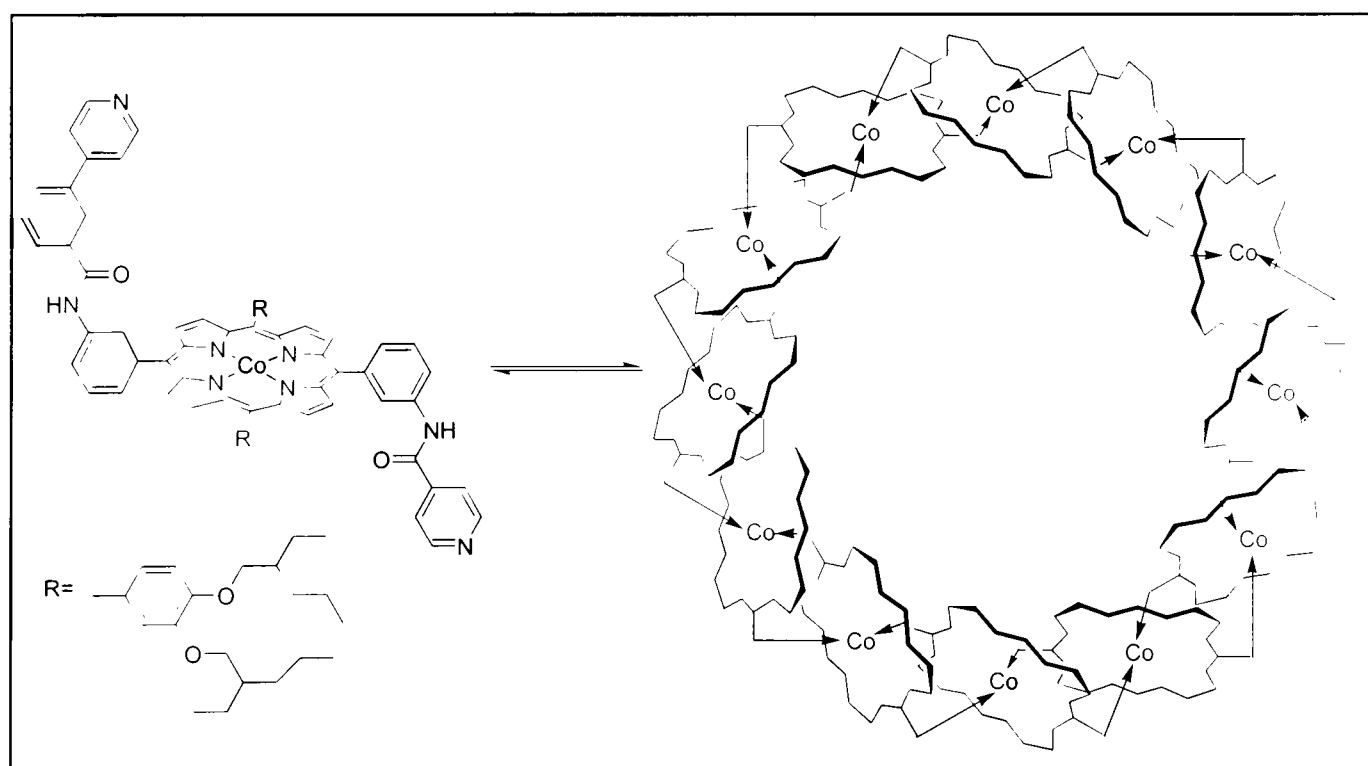


Figure 40 Self-assembled cobalt-porphyrin macrocycle

7.2 Cages

Manipulation of the various ligand components allows the construction of increasingly complex three-dimensional architectures. It is expected that such systems will exhibit interesting inclusion chemistry of large molecules as well as catalysis of chemical transformations within their resultant cavities¹⁶⁰.

Fujita has developed a range of ligands, which when coordinated to a *cis*-protected palladium centre generates a three-dimensional complex¹⁶¹. One such example is where the tripodal pyridyl-based ligand yields a trinuclear cage complex (Figure 41)¹⁶². Interestingly, the oligomeric product only forms in the presence of a suitably large template. When the bulky, 1-adamantanecarboxylic acid is used as a template, yields are greater than 90%, due to the induced fit that this provides.

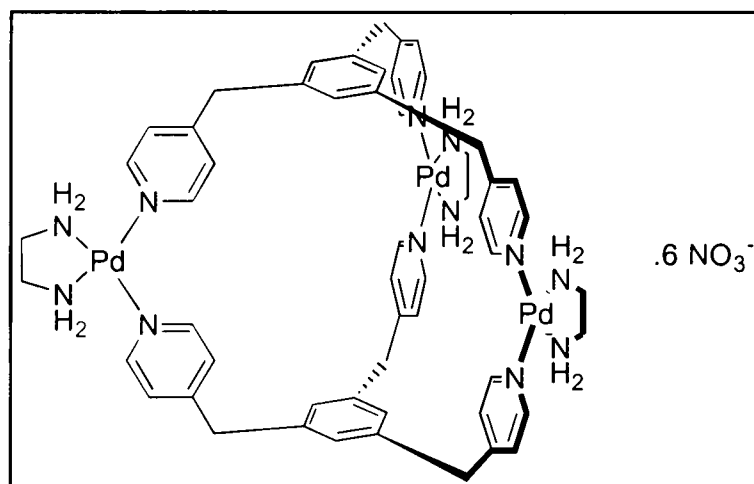


Figure 41 Fujita's three-dimensional cage complex

Through careful manipulation of the ligands and taking advantage of the numerous coordination geometries and numbers of metal ions, it is possible to generate a range of complicated architectures. For example, Thomas and co-workers designed components to synthesise a 'supramolecular cube'¹⁶³. This consisted of the divergent 4,4'-bipyridine ligand to act as the twelve linear edges and a *facially*-protected ruthenium(II) ion to act as the convergent site of the eight corners of the cube (Figure 42). Despite slow kinetics, and the product being a result of the (statistically unlikely) simultaneous assembly of twenty components in one-pot, the desired cube synthesis is achieved.

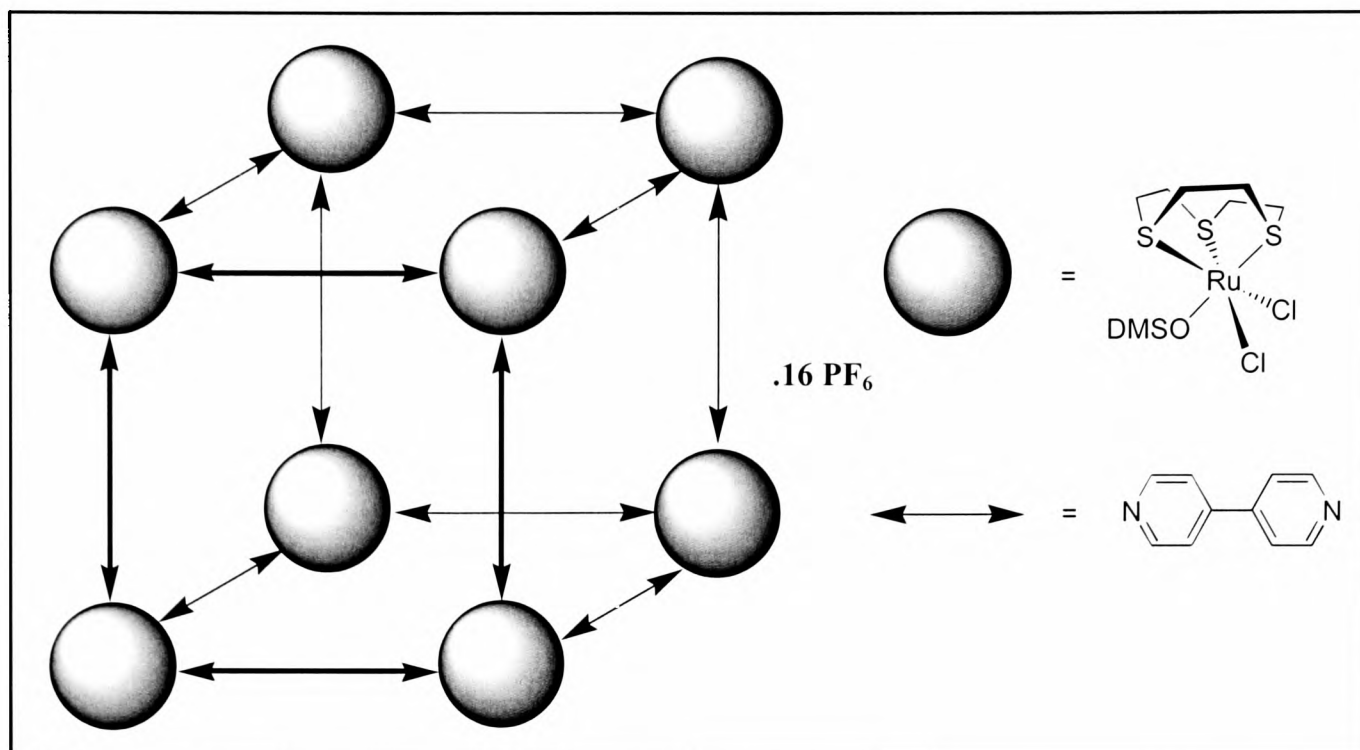


Figure 42 Schematic representation of Thomas' supramolecular cube

7.3 Interlocked Molecules

Metal-directed self-assembly has proved a valuable tool in the synthesis of interlocked molecules, with many examples of structures utilising the strength, directionality and potential lability of the metal-ligand bond.

Fujita has synthesised a range of *cis*-ethylenediamine protected palladium(II) metallomacrocycles which, by their previously observed ability to undergo guest-induced reorganisation, have been shown to possess labile palladium-pyridyl bonds. Where suitable cavity sizes exist, it is possible to force the formation of interlocked structures by increasing the concentration of the macrocyclic solution (Figure 43)¹⁶⁴. The resulting [2]catenanes are stabilised by a combination of hydrophobic and π - π stacking interactions. In the case of the analogous platinum(II)-based macrocycles, no such equilibration is observed at room temperature due to the greater inertness of the platinum-pyridyl bonds (*i.e.* the box is locked). However, heating the macrocycle at 100°C in 5 M sodium hydroxide labilises the bond (unlocks the box) and results in catenane formation¹⁶⁵. Cooling the reaction mixture and

removal of the salt results in the isolation of the kinetically stable [2]catenane (locked catenane).

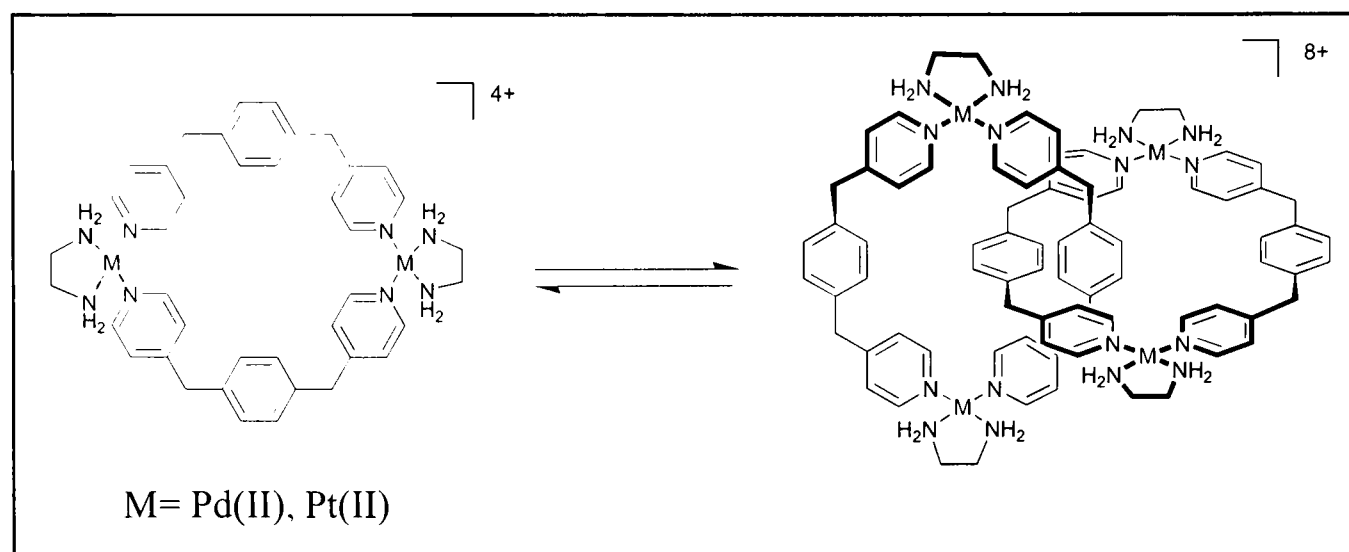


Figure 43 Equilibrium between metallomacrocycle and [2]catenane

Organometallic catenanes have proved difficult to isolate due to their instability¹⁶⁶. Recently, Puddephatt and co-workers found they were able to utilise intermolecular aurophilic interactions to template the interlinking of gold(I) based metallomacrocycles (Figure 44)¹⁶⁷.

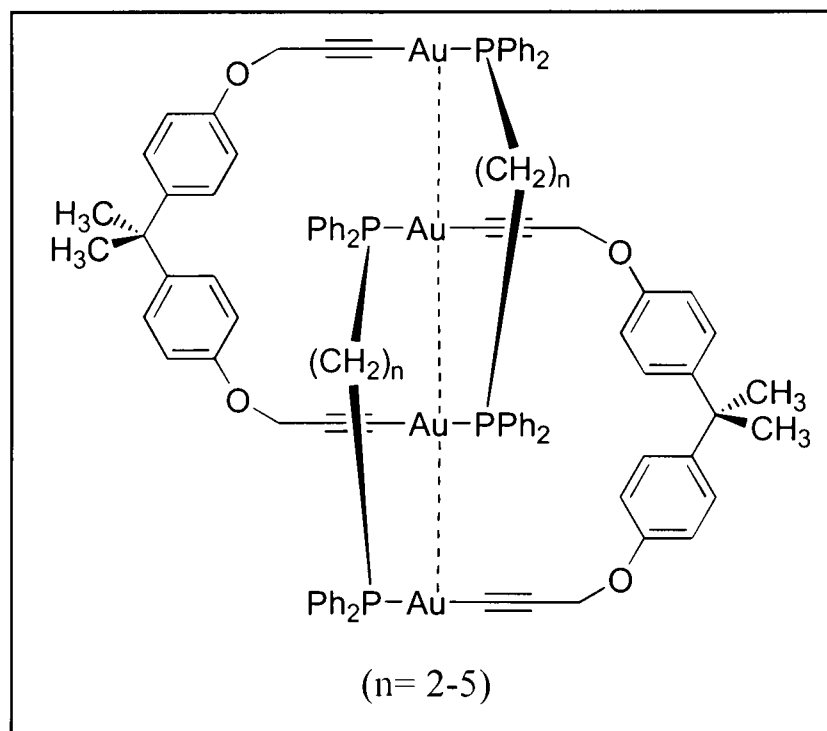


Figure 44 [2]Catenane stabilised by aurophilic interactions

Numerous researchers have utilised the tetrahedral geometry of copper(I), silver(I) and zinc(II) 2,2'-bipyridine derived systems to template a range of supramolecular architectures, such as rotaxanes¹⁶⁸, catenanes¹⁶⁹, helices¹⁷⁰, ladders¹⁷¹ and knots¹⁷². One of the most elegant

examples of this approach is the trefoil knot synthesised by Sauvage (Figure 45)¹⁷³. The trefoil knot consists of one molecule, which intertwines itself at three crossing points such that it cannot be unwound. Initially a double helical structure is self-assembled around two copper(I) ions. The termini of the ligands are then linked via a cyclisation reaction and the metal ions removed to leave the interpenetrating structure - one continuous ring that crosses over itself in three places.

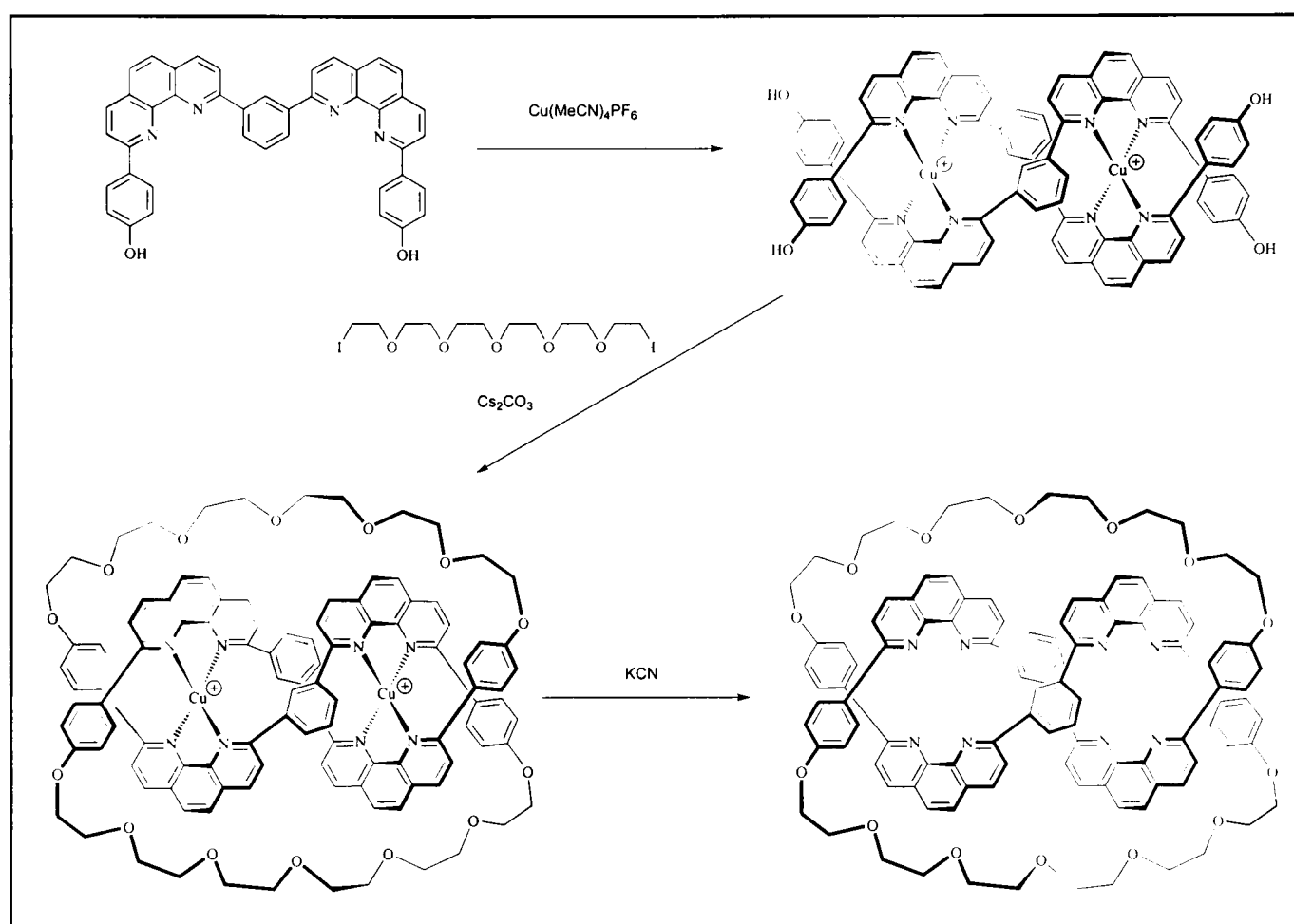


Figure 45 Sauvage's trefoil knot synthesis

7.4 Nanotechnology

In his foresightful address, 'There's Plenty of Room at the Bottom,' to the American Physical Society in 1959, Richard Feynman discussed the notion of artificial molecular machines¹⁷⁴. He envisaged a world in which atoms/molecules could be used to store "bits" of information, a feat that would enable the entire Encyclopedia Britannica to be stored on the head of a pin. This was particularly forward thinking considering computing was in its infancy and the

‘computing machines’ of the day took up an entire room. In recent years, Feynman’s dream has approached a reality with research in artificial nano-dimensional molecular structures and machines growing rapidly. This is mainly due to the advances in surface techniques (such as scanning tunnelling microscopy and atomic force microscopy) enabling greater visualisation and understanding of these sub-microscopic objects. The development of functional nano-sized architectures has wide-ranging applications such as advanced drug delivery systems and the generation of new materials and computational devices¹⁷⁵.

Currently, lithographic techniques are used to make silicon chips for computers, but this ‘top-down’ approach for generating smaller and faster molecular devices is rapidly approaching its limits on the grounds of both practicality and expense¹⁷⁶. The use of self-assembly has been shown to create a range of nano-dimensional architectures. It is predicted that these frameworks will enable the chemist to construct artificial molecular electronic devices from this ‘bottom up’ approach¹⁷⁷. There has therefore been a motivated effort to synthesise molecules that display switching behaviour, to act as hardware components such as information storage and logic circuitry in future molecular computers using binary systems¹⁷⁸. Among the different types of superstructures that may be created, entities in which metal ions are arranged in a grid-type fashion are of special interest¹⁷⁹, in view of their eventual incorporation into information storage devices. Lehn, Gülich and co-workers have synthesised a [2x2] square grid consisting of four pseudo-octahedral Fe(II) ions held together by pyridyl-based ligands (Figure 46)^{180,181}. The four iron centres in the array can be converted between their high- (HS) and low-spin (LS) states via the application of external perturbations including light, pressure and temperature. The conversion between three distinct magnetic levels (3HS/1LS, 2HS/2LS and 1HS/3LS) results in this simple system being a multiswitchable multilevel device.

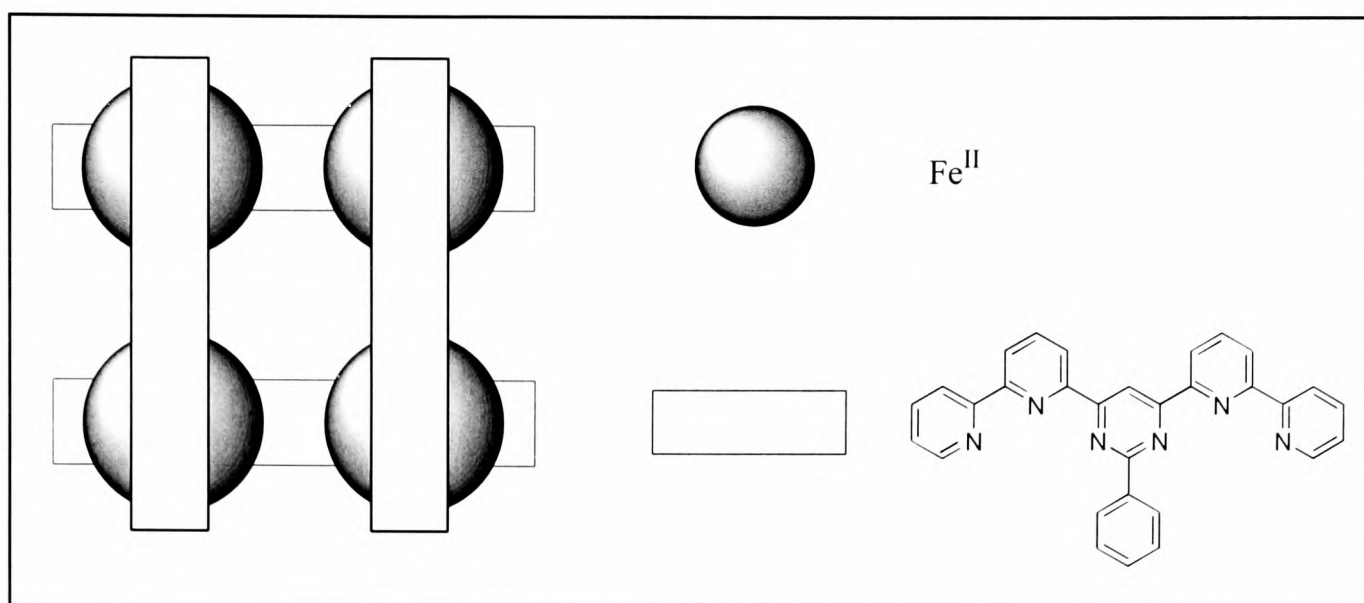


Figure 46 $\text{Fe}_4(\text{II})$ [2x2] supramolecular grid

Another keen area of nanotechnological research is the development of molecular-level machines: assemblies of discrete molecular components that undergo mechanical movements (output) as a consequence of appropriate external stimuli (input)¹⁸². Sauvage and co-workers have developed a series of molecular shuttles, based on interlocked molecules, which are controlled by the oxidation state of the metal ions (Figure 47). This is a result of the different geometric requirements of the copper(I) and copper(II) oxidation states. Copper(I) complexes preferentially adopt a pseudo-tetrahedral geometry. However, oxidation of this ion, via electrochemical or photochemical methods, demands higher coordination numbers. Design of [2]rotaxanes with two different covalently linked coordinating sites for transition metal ions allows the construction of devices whereby physical perturbations induce changes within the molecule so as to afford a coordination situation favourable to the corresponding metal oxidation state¹⁸³.

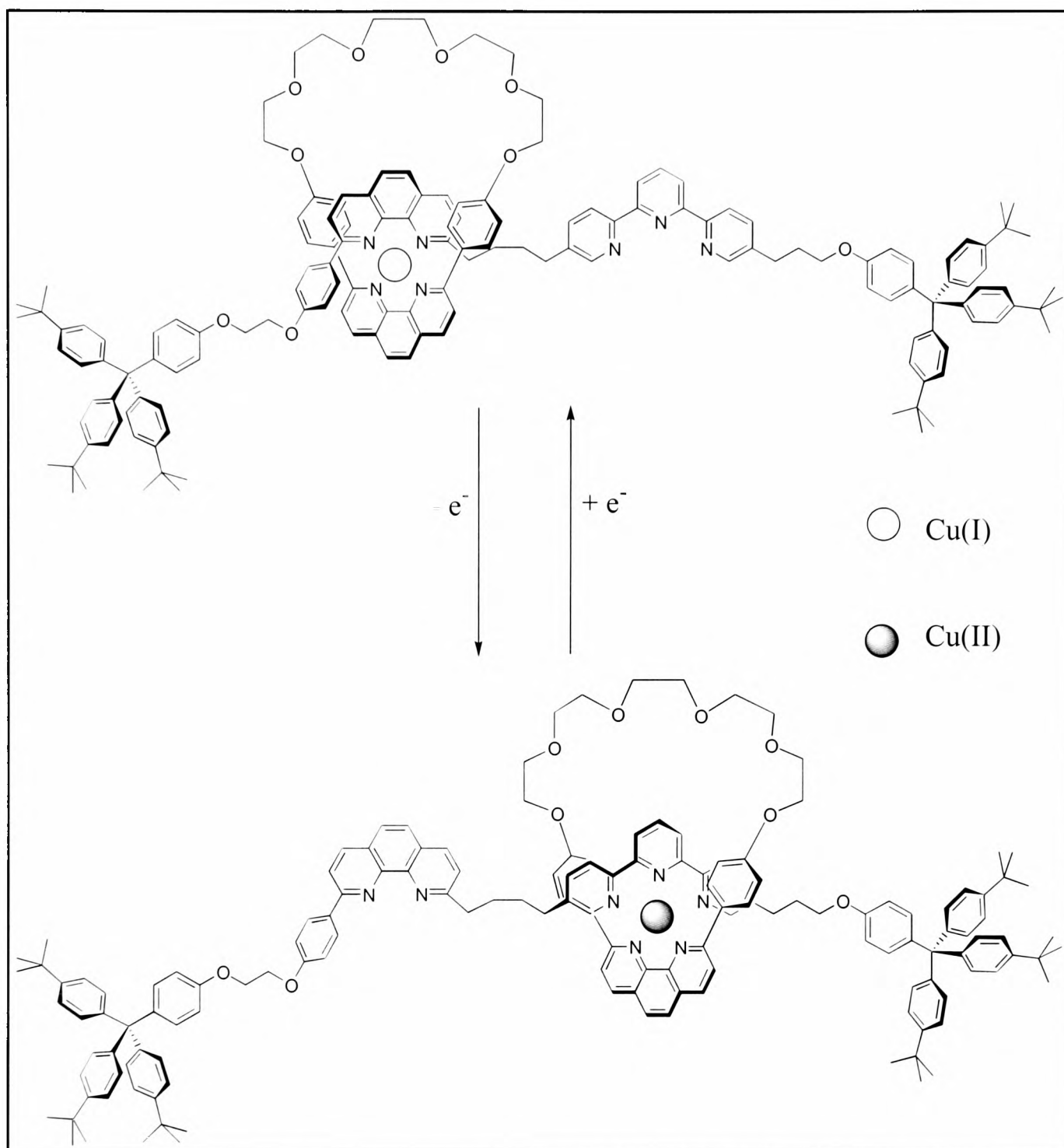


Figure 47 Sauvage's electrochemically and photochemically induced molecular shuttle

Gold nanoparticles are nano-dimensional particles of gold metal, typically less than 10nm in diameter, which possess unique properties due to their intermediate size¹⁸⁴. As a result of this, they have been at the forefront of the development of nanotechnological devices and architectures.

Mirkin and co-workers have recently used gold nanoparticles functionalised with oligonucleotide side chains to detect specific DNA sequences in solution^{185,186} (Figure 48). Upon addition of the complementary strand of DNA, a short duplex is formed between the structures and the nanoparticles become closer together in space. This results in a change in

the optical properties of the nanoparticles with an observable red to blue shift. Since the nanoparticles only assemble in the presence of the complementary DNA strand, the change in material properties induced by nanoparticle assembly can be used as an indicator of whether a particular sequence is present in a sample or not. This method offers a practical method for the detection of targets, which may prove useful in the diagnosis of genetic and pathogenic diseases, down to femtomolar concentrations.

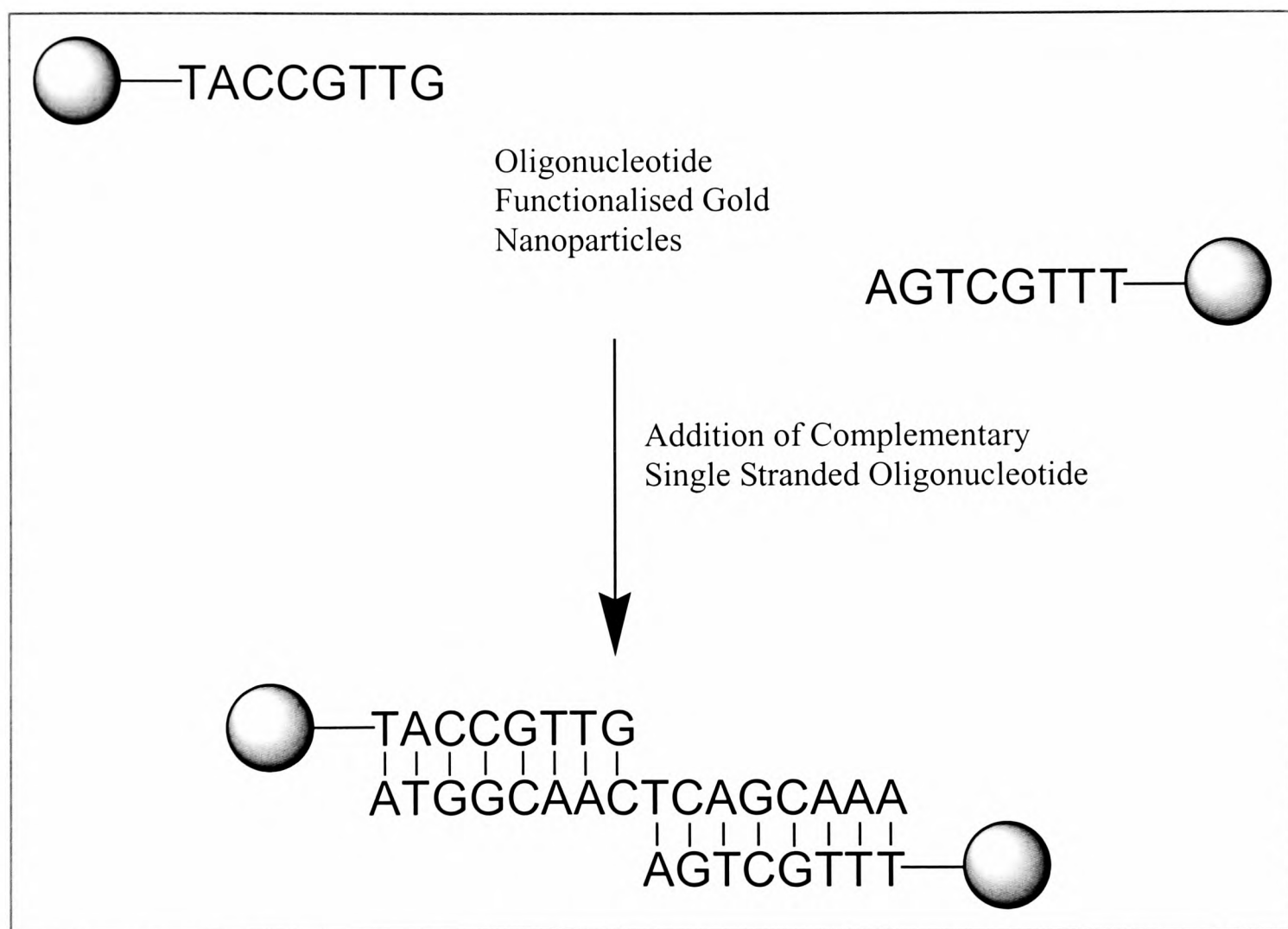
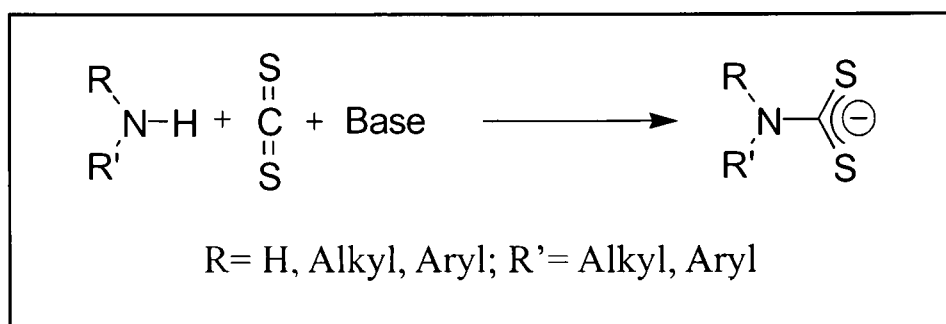


Figure 48 Optical detection of polynucleotides via the functionalisation of gold nanoparticles

8 The Dithiocarbamate Ligand

The dithiocarbamate ligand was first identified during the early days of organosulphur chemistry, by the nucleophilic attack of primary or secondary amines with carbon disulphide in basic solution (Figure 49)¹⁸⁷. Free dithiocarbamic acids (R_2NCS_2H) are highly unstable and so the ligands are usually isolated as their alkali metal salts.

Figure 49 Preparation of *N*-substituted dithiocarbamate ligands

The dithiocarbamate anion has been shown to form strong chelate complexes with a range of transition metal and main group elements, with their coordination chemistry having been extensively studied¹⁸⁸. Such complexes have had numerous industrial uses, for example, they have acted as lubricants, antioxidants, fungicides and accelerators for rubber vulcanisation¹⁸⁹.

The most studied of the dithiocarbamates are those derived from secondary amines as these are stable and possess interesting electrochemical and optical properties^{190,191}. Those derived from primary amines are susceptible to elimination reactions to yield isothiocyanates.

One important feature of dithiocarbamate ligands is their ability to stabilise high formal oxidation states (e.g. iron(IV), copper(III) and nickel(IV))¹⁹². This is as a result of the high delocalisation that the ligand provides (Figure 50) and the consequential high electron density the sulphur donors provide¹⁹³ (Figure 50 - Resonance Structure III).

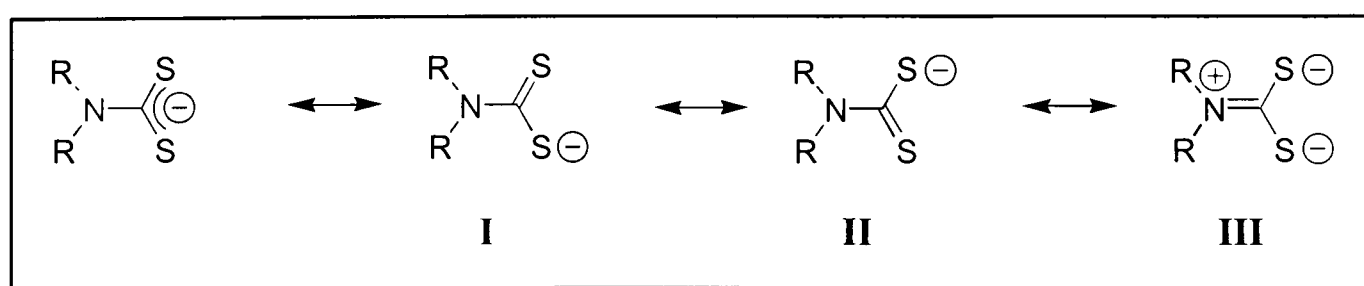


Figure 50 Resonance structures of the dithiocarbamate ligand

The reaction of diamines with carbon disulphide in basic solution has been shown to form bis-dithiocarbamate salts¹⁹⁴. Despite the availability of these multidentate ligands, their well-documented coordination chemistry and useful optical and electrochemical properties, it is somewhat surprisingly that only recently the dithiocarbamate anion has been exploited for metal-directed self-assembly^{195,196}.

9 Aims of the Project

The aim of the research described in this thesis is to investigate the metal-directed self-assembly of transition metal dithiocarbamate-derived complexes. A variety of ligands are prepared in order to generate a range of novel architectures and host molecules. Where appropriate, the binding of cationic, anionic or neutral guests is investigated.

Chapter Two describes the generation of a variety of novel metallomacrocycles. Their structures are investigated by NMR, UV-vis, electrospray mass spectrometry, EPR, electrochemical techniques and X-ray crystallography.

Chapter Three outlines the synthesis of nano-dimensional tetradithiocarbamate-derivatised resorcinarene complexes. The binding of large guests is studied by electrochemistry, NMR and electrospray mass spectrometry.

Chapter Four discusses the synthesis of gold(III) dithiocarbamate based complexes. A range of mono- and multinuclear complexes are generated by both direct and transmetallation reactions. The transmetallation reaction is studied by the use of X-ray crystallography and UV-vis kinetic studies.

Chapter Five highlights the formation of interpenetrating dithiocarbamate-based species. The formation of these structures is described from the use of pre-formed macrocyclic complexes. A range of mixed-metal and mixed-ligand architectures are prepared and investigated by electrospray mass spectrometry and electrochemistry.

Chapter Six centres on the formation of gold and silver nanoparticles. Their preparation is explored in the presence of dithiocarbamate-based templates and the non-covalent linking of nanoparticles is also attempted.

Chapter Seven explores the formation of ruthenium(II) bis-bipyridyl derived dithiocarbamate complexes. The synthesis of hosts designed to bind cations and anions is described and their subsequent binding and sensing properties are investigated via NMR, electrochemical and X-

ray crystallographic techniques.

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Chapter Two

Dithiocarbamate-based Macrocyclic Complexes

Chapter Two: Dithiocarbamate-Based Macrocyclic Complexes

1 Introduction

Metal-directed self-assembly has been shown to be a powerful method of creating a range of polymetallic architectures (Chapter One). Complex structures, such as macrocycles, cages, tubes and polyhedra, are able to be generated by means of the linking of a small number of relatively simple ligands with suitable metal centres^{1,2}. Much of the work so far within this field has concentrated on the well-known palladium(II)- and platinum(II)-pyridyl interactions to generate a variety of two- and three-dimensional architectures^{3,4}. The work described within this Chapter, however, describes the synthesis of novel dinuclear macrocyclic complexes based upon the transition metal-dithiocarbamate motif.

The coordination chemistry of the dithiocarbamate ligand is well established^{5,6}; however, it is only recently that this ligand has begun to be exploited in the field of metal directed self-assembly, with the publication of the first examples of macrocyclic complexes synthesised incorporating copper(II), nickel(II) and zinc(II) metal centres^{7,8}. The aim of this Chapter is to exploit further the properties of the dithiocarbamate ligand to prepare a range of predominantly square-planar transition metal dinuclear macrocyclic complexes. New bimetallic systems are designed via the separation of aromatic moieties. The nature of these dictate the size of the internal cavity, and their planarity preorganises the ligand for macrocyclic formation. A lipophilic side chain (R) confers solubility to the macrocycle in a range of organic solvents and the choice of transition metal centre allows spectroscopic probes to be employed for both structural elucidation and the potential monitoring of guest binding. A general design for the target complexes is shown in Figure 1.

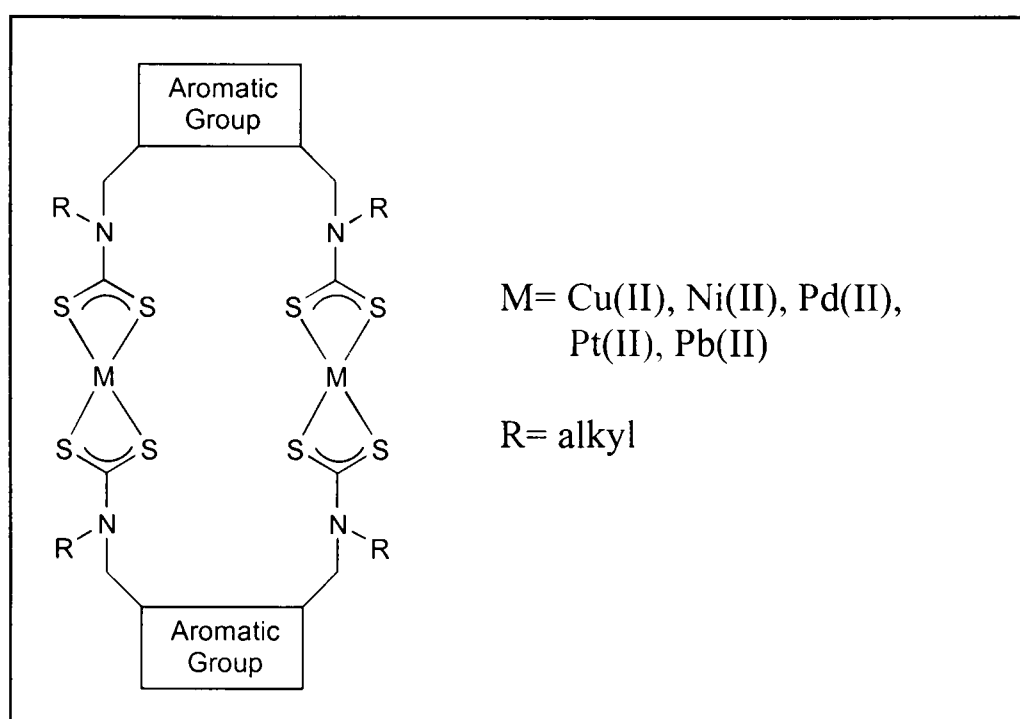


Figure 1 Schematic representation of target complexes

The synthesis and characterisation of these novel metallomacrocycles will be described within this Chapter, as well as preliminary cation binding studies. The subsequent investigation into the formation of interlocked molecules with these macrocycles is described in Chapter Five.

2 Synthesis

The synthetic strategy employed to generate new macrocyclic binuclear dithiocarbamate complexes, involved initial preparation of various secondary bis-amines separated by an aromatic spacer group. Amines were produced via the nucleophilic substitution of a bis-halogenated aromatic compound, resulting in the formation of secondary amines. These were subsequently used for dithiocarbamate formation.

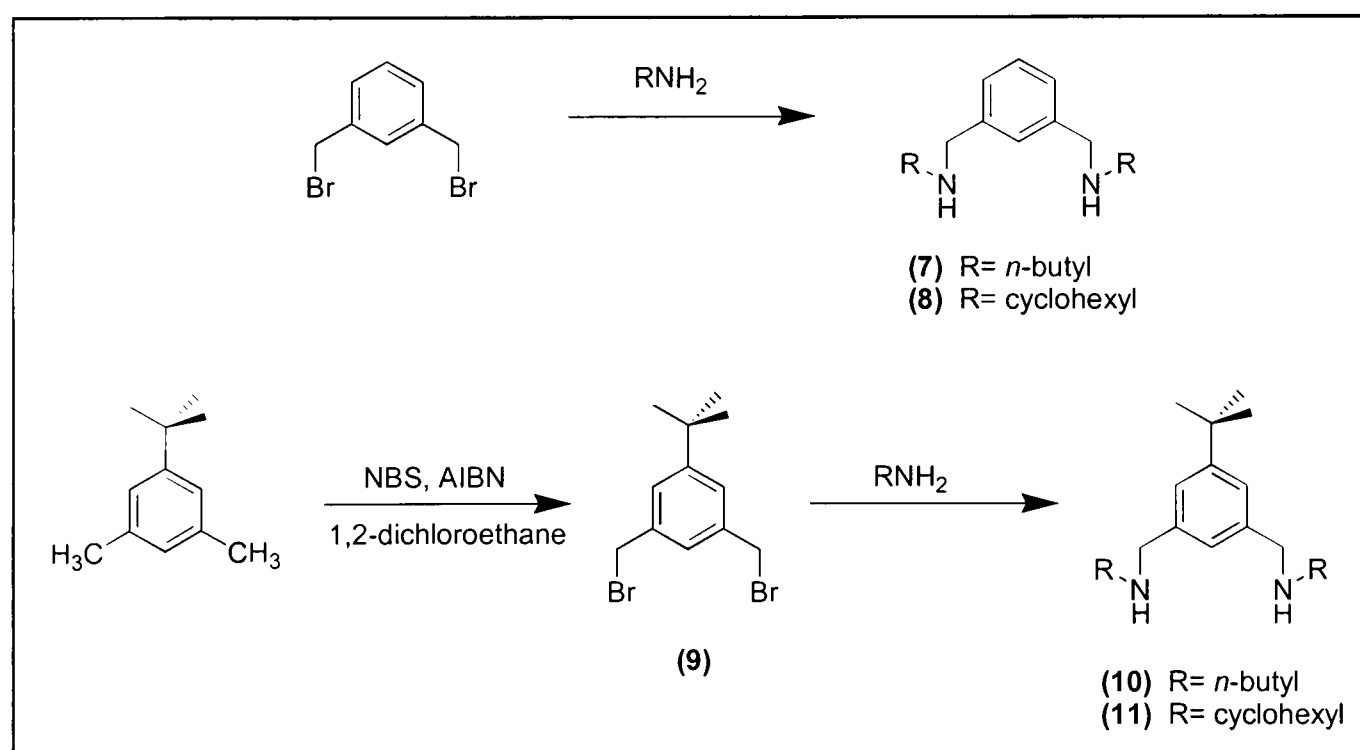
2.1 Ligand Formation

2.1.1 *m*-Xylyl Derivatives

m-Xylyl spaced bis-amines were prepared through the amination of commercially available α - α' -dibromo-*m*-xylene and 1,3-bis-bromomethyl-5-*tert*-butylbenzene (**9**). Radical bromination of 1-*tert*-butyl-3,5-dimethyl-benzene, using *N*-bromosuccinimide (NBS) and catalysed by

2,2'-azobis(2-methyl-propionitrile) (AIBN) afforded **(9)** in 46% yield⁹ (Scheme 1). It was hoped that the introduction of a *tertiary*-butyl group to the aromatic framework, would result in greater solubility of the resultant dithiocarbamate complexes in organic solvents.

The parent secondary bis-amines were subsequently synthesised by nucleophilic substitution of bis(bromomethyl)-aromatic synthons with neat primary amine in an almost instantaneous reaction (Scheme 1). The primary amines, *n*-butylamine and cyclohexylamine, were chosen for this reaction. The use of cyclohexyl chains is designed to confer a greater degree of solubility upon the resultant dithiocarbamate complexes due to the branched nature of the alkyl chain. Yields for this process are high, typically quantitative, and the resulting bis-amines **(7)**, **(8)**, **(10)** and **(11)** were fully characterised by ¹H and ¹³C NMR, electrospray mass spectrometry and elemental analysis.

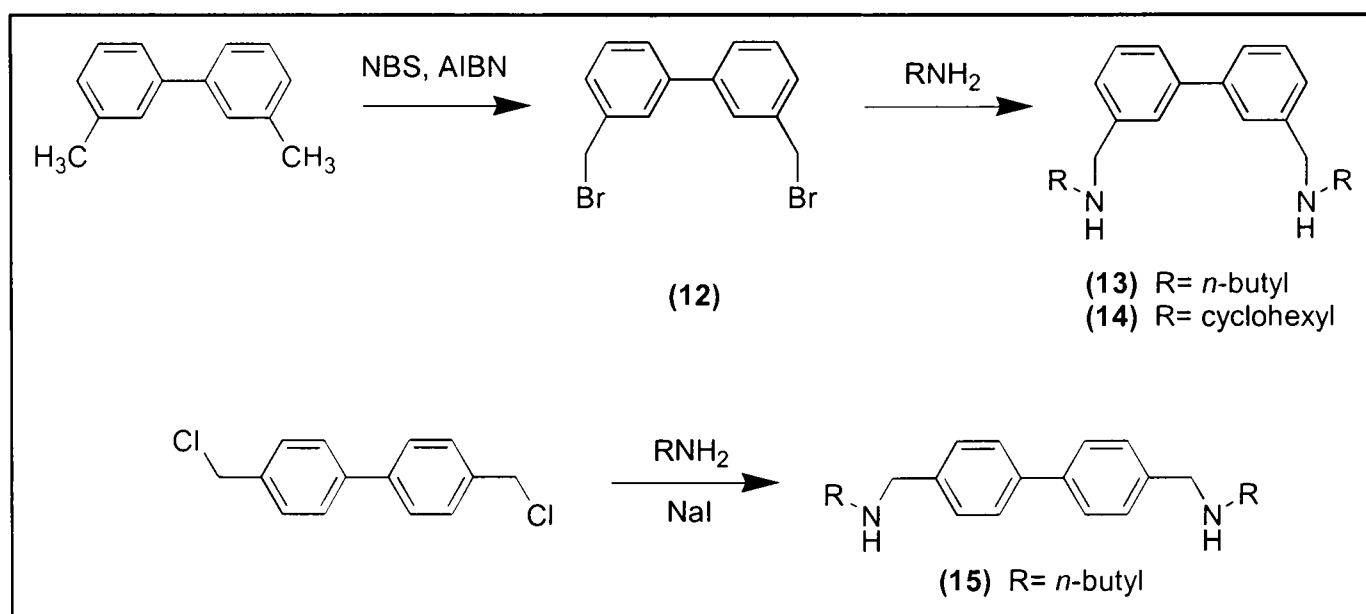


Scheme 1 Synthesis of *m*-xylyl spaced bis-amines

2.1.2 Biphenyl Derivatives

Two biphenyl spaced bis-amines were also prepared for metal-directed self-assembly. 3,3'-Bis-bromomethyl-biphenyl (**(12)**) was prepared via radical bromination of 3,3'-dimethylbiphenyl using *N*-bromosuccinimide. This was converted to the corresponding bis-

amine through its portionwise addition to excess *n*-butylamine and cyclohexylamine to give **(13)** and **(14)** respectively (Scheme 2).



Scheme 2 Synthesis of biphenyl spaced bis-amines

Similarly, the reaction of 4,4'-bis(chloromethyl)-biphenyl with excess *n*-butylamine afforded the 4,4'-bis-amine **(15)**. However, due to chloride being a poorer leaving group, in comparison to bromide, it was found that the reaction was considerably slower. It was therefore necessary to both heat the reaction mixture and add sodium iodide as a nucleophilic catalyst. In the absence of the catalyst a significant amount of the side product **(15a)** was also formed (Figure 2).

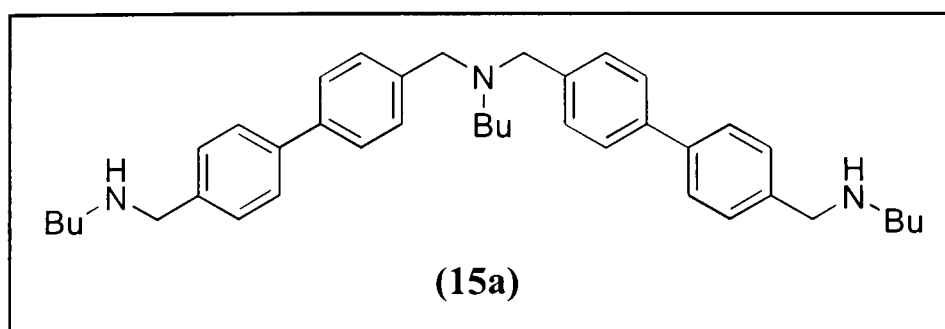
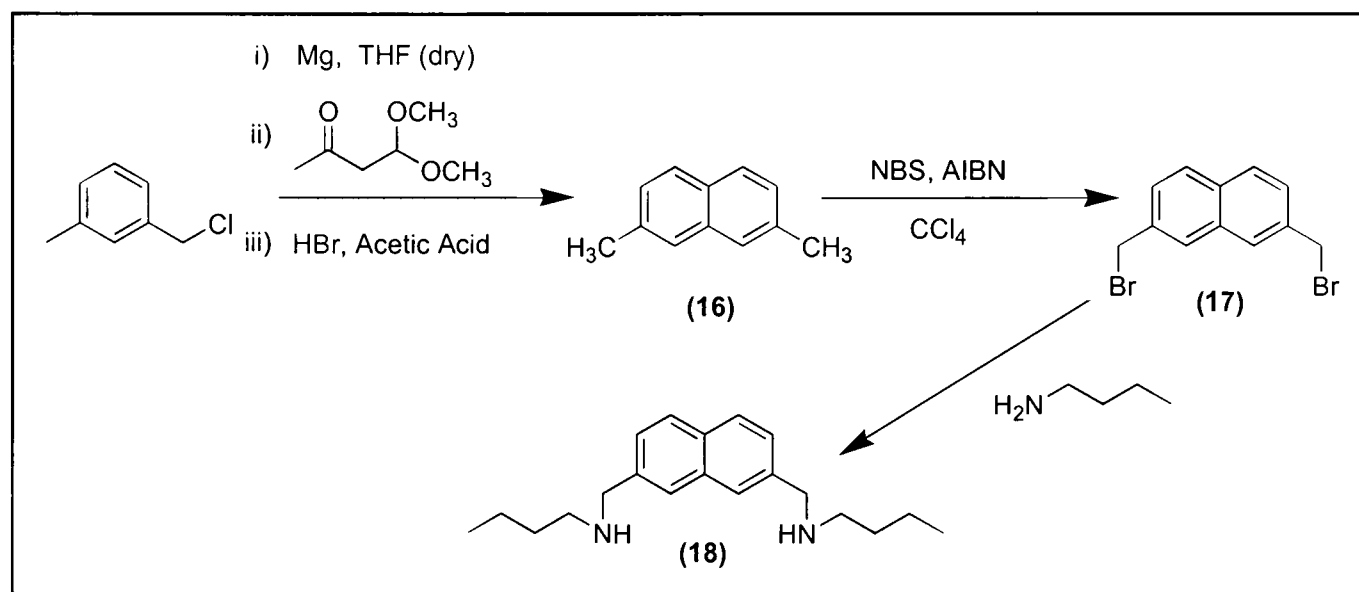


Figure 2 Side product formed in the absence of sodium iodide

2.1.3 Naphthyl Derivatives

A rigid 2,7-naphthylene spacer was also utilised for metal-directed self-assembly. Initially, 2,7-dimethylnaphthylene **(16)** was synthesised following a literature procedure¹⁰. This was

subsequently brominated using *N*-bromosuccinimide and 2,2'-azobis(2-methyl-propionitrile). Whereas previous bromination reactions were undertaken in 1,2-dichloroethane, it was found by ^1H NMR spectroscopy and electrospray mass spectrometry, that the reaction in this solvent resulted in the formation of numerous by-products. The electrophilic attack of the aromatic system by bromine was found to be one of the major side-products in this reaction¹¹. However, the employment of carbon tetrachloride as a solvent suppressed these side reactions and recrystallisation of the crude product from hot ethanol, finally gave the desired bis-brominated product (**17**) in 33% yield (Scheme 3).



Scheme 3 Synthesis of naphthyl-spaced bis-amine

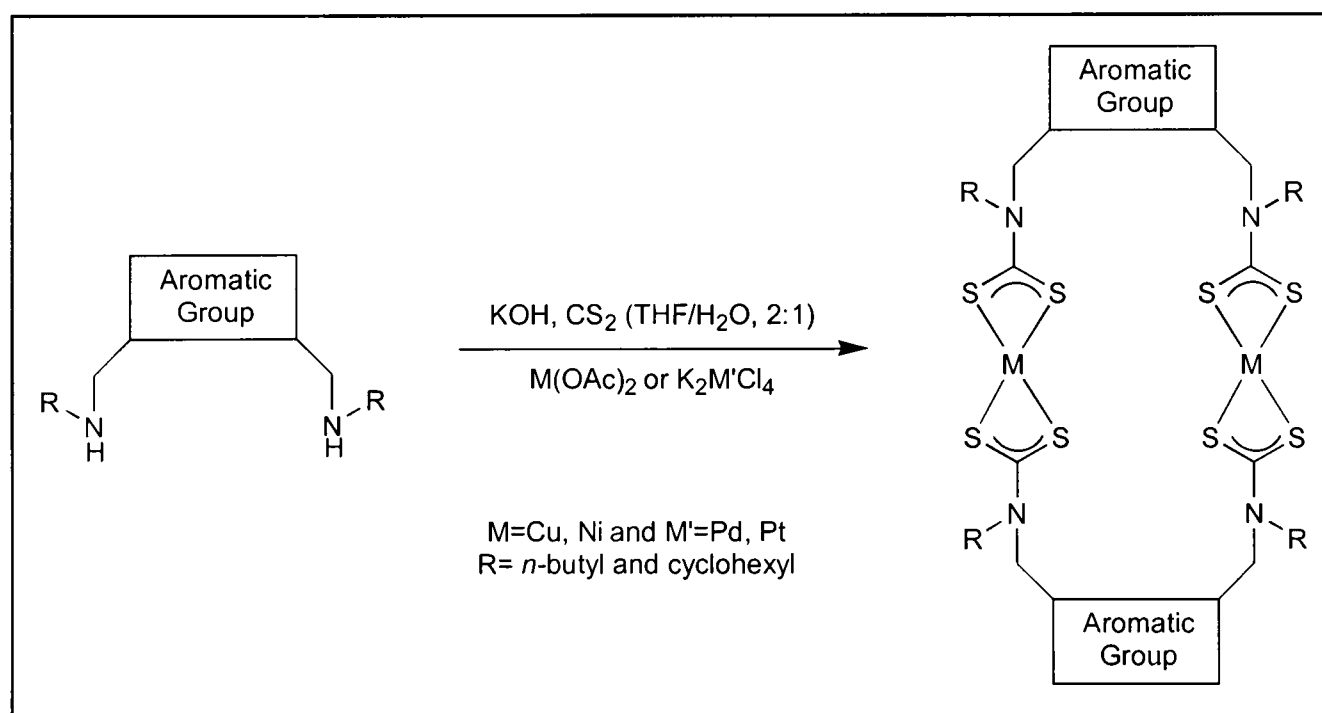
The corresponding bis-amine (**18**) was generated through reaction with excess *n*-butylamine and isolated in quantitative yield.

2.2 Metal-Directed Self-Assembly

Metal-directed self-assembly of dinuclear macrocyclic dithiocarbamate systems was performed initially via the reaction of the secondary bis-amines with carbon disulphide with potassium hydroxide as a base. This generated the potassium dithiocarbamate salt, which was not usually isolated. Addition of a transition metal salt to this solution resulted in the formation of the desired dithiocarbamate complex. Typically, the reactions were carried out in a tetrahydrofuran/water (2:1) solvent system as this was found to solubilise the reagents and

intermediates, whilst slowly precipitating out the final product. Preliminary experiments in ethanol or methanol-based solvent systems proved only moderately successful due to the nucleophilic attack of the alcoholic solvent upon carbon disulphide, resulting in the formation of competing xanthate complexes¹².

Metal-directed self-assembly was attempted with the bis-dithiocarbamate salts of all the above bis-amines through the addition of copper(II) acetate, nickel(II) acetate, potassium tetrachloropalladate and potassium tetrachloroplatinate (Scheme 4). The solutions were stirred at room temperature overnight and the resulting solids isolated via filtration. The crude products were dissolved in dichloromethane and layered with ethanol in order to affect crystallisation. The results of these experiments and the subsequent labelling of these products are displayed in Table 1 and their structures shown in Figure 3.



Scheme 4 Synthesis of bimetallic macrocyclic dithiocarbamate-based complexes

Ligand	Metal Centre			
	Cu(II)	Ni(II)	Pd(II)	Pt(II)
(7)	(7-Cu)	(7-Ni)	insol	insol
(8)	(8-Cu)	(8-Ni)	(8-Pd)	(8-Pt)
(10)	(10-Cu) [*]	(10-Ni)	(10-Pd) [*]	(10-Pt)
(11)	(11-Cu)	(11-Ni)	(11-Pd) [*]	(11-Pt) [†]
(13)	(13-Cu) [*]	(13-Ni)	(13-Pd) [*]	(13-Pt) [†]
(14)	(14-Cu)	(14-Ni)	(14-Pd)	(14-Pt)
(15)	(15-Cu) [*]	(15-Ni) [*]	(15-Pd) [*]	insol
(18)	(18-Cu) [*]	insol	insol	-

Table 1 Representation of the Cu(II), Ni(II), Pd(II) and Pt(II) dinuclear macrocyclic systems generated
insol represents product was insoluble in organic solvents, - reaction was not attempted, * product further
purified by column chromatography on silica gel 60 eluted with chloroform collecting the forerunning
band, † product further purified through precipitation with hexane

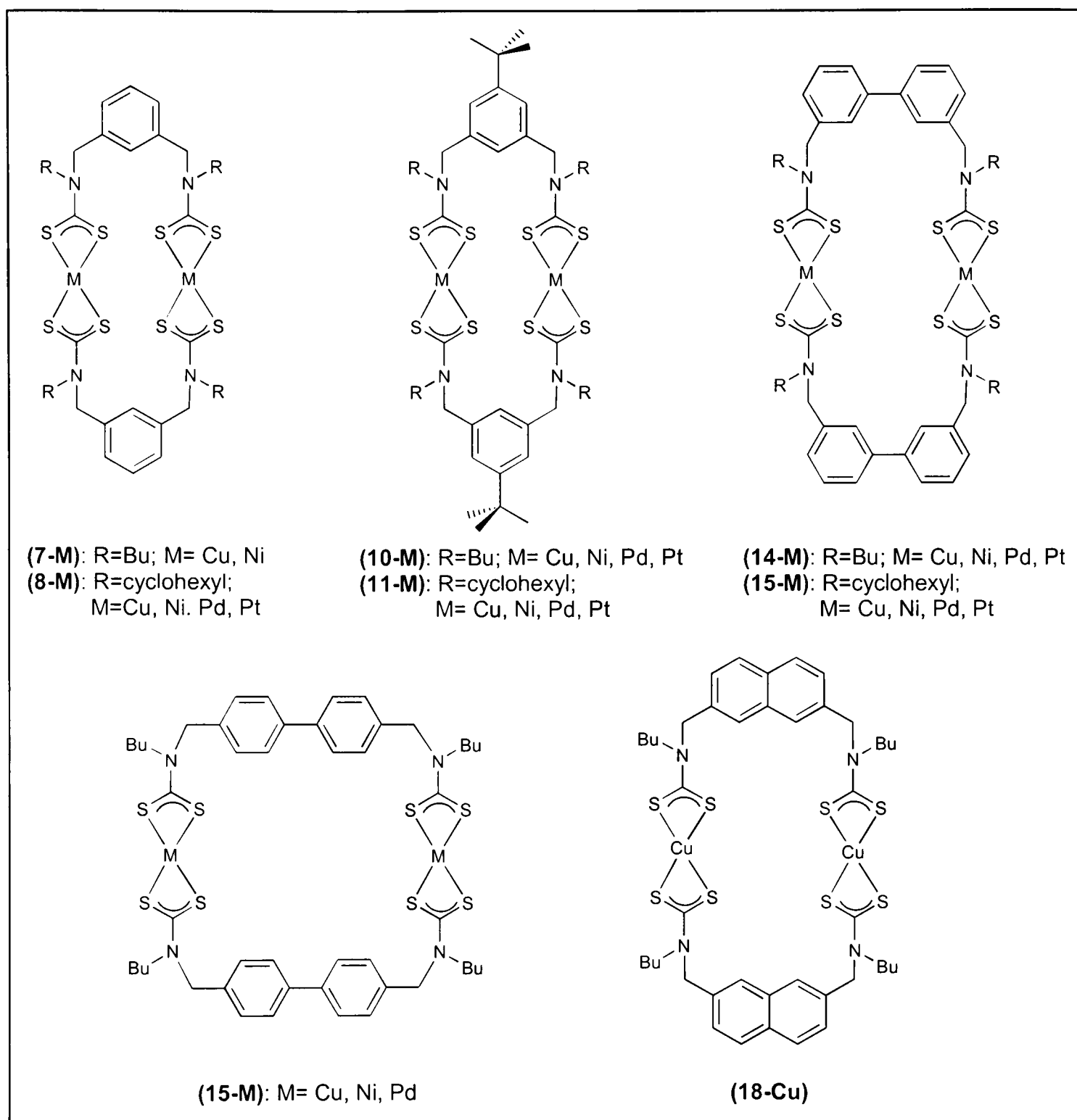


Figure 3 Synthesised dinuclear dithiocarbamate-based macrocyclic complexes

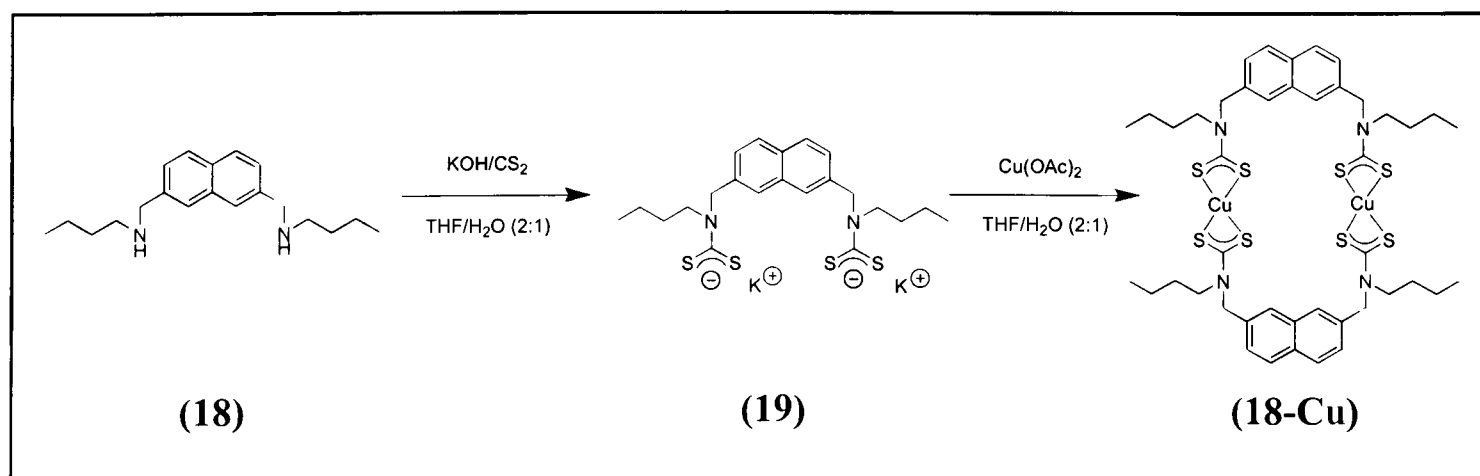
Where stated, further purification was undertaken and the product recrystallised again until the samples were elementally pure. Isolated yields for these reactions varied greatly from 94% for the synthesis of **(14-Ni)** to just 3% for the synthesis of **(13-Pd)**. Unfortunately, attempts to improve the yields through the use of high-dilution methods proved unsuccessful.

As can be seen from Table 1, the employment of both the branched cyclohexyl side chains and the incorporation of a *tertiary*-butyl group in the *m*-xylyl spacing groups did have the desired effect of increasing the solubility of the resultant dithiocarbamate complexes (as

shown by the formation of **(8-Pt)** and **(10-Pt)** but not **(7-Pt)** or **(7-Pd)**). It is noteworthy that the solubility of these complexes was found to decrease upon descending the Group 10 elements. In a number of cases it was not possible to isolate the platinum(II) structures, due to their poor solubilities. In addition, the products generated from the naphthyl spacer **(18)** also displayed poor solubilities in organic solvents from this one-pot reaction.

2.2.1 Improved Synthesis of **(18-Cu)**

In an attempt to discover whether the isolation of the intermediate potassium bis-dithiocarbamate salt could improve the yield of the metal-directed self-assembled product, the preparation of **(18-Cu)** was repeated. The potassium bis-dithiocarbamate salt was prepared via the reaction of **(18)** with two equivalents of potassium hydroxide and carbon disulphide in a tetrahydrofuran/water (2:1) solvent mixture. The resulting solution was redissolved in the minimum amount of methanol, filtered and **(19)** precipitated as a white solid on addition of diethyl ether, in 75% yield (Scheme 5). The solid was characterised by ^1H and ^{13}C NMR and elemental analysis. The presence of a peak at 209.9 ppm in the ^{13}C NMR revealed the formation of the desired dithiocarbamate salt. Addition of copper(II) acetate to a solution of **(19)** generated **(18-Cu)** in 78% yield after recrystallisation with dichloromethane/ethanol.



Scheme 5 Synthesis of **(18-Cu)** via the isolation of the intermediate bis-potassium dithiocarbamate salt

Interestingly, this two-step procedure gave a greater overall yield (59%) than the corresponding one-pot reaction. This is possibly due to the suppression of competing side-

reactions. This method also produced a crude product that could simply be purified through recrystallisation, negating the use of column chromatography purification process required in the initial synthesis.

2.2.2 Reference Compounds

In addition to the macrocyclic hosts, reference bis-(*N,N'*-diethyldithiocarbamate) transition metal complexes were also prepared. These were synthesised according to literature procedures through the addition of sodium *N,N'*-diethyldithiocarbamate to ethanolic solutions of the appropriate transition metal salt and purified from a dichloromethane/ethanol solvent system to yield crystalline solids **(20)** - **(23)** (Figure 4).

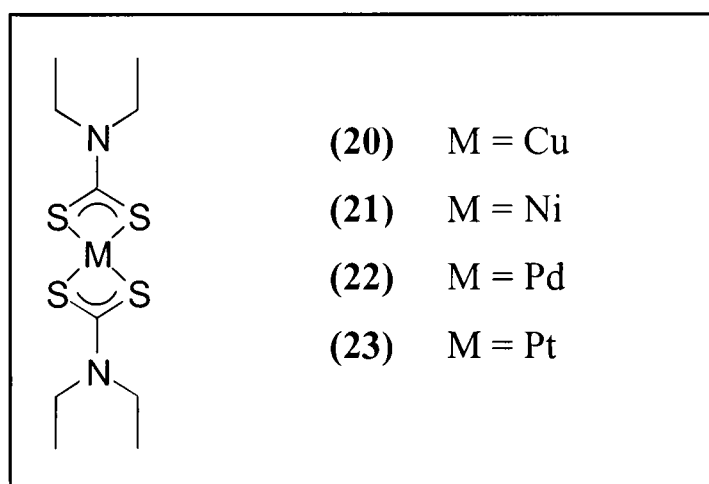


Figure 4 Bis-(*N,N'*-diethyldithiocarbamate) reference complexes

3 Characterisation of Dinuclear Transition Metal Dithiocarbamate-based Macrocyclic Systems

All of the new transition metal dithiocarbamate-based dinuclear macrocyclic assemblies were characterised by a variety of techniques, including ^1H and ^{13}C NMR, elemental analysis, electrospray mass spectrometry, UV-vis spectroscopy, cyclic and square wave voltammetry, electron paramagnetic resonance and X-ray crystallography. This characterisation will now be discussed.

3.1 NMR

The diamagnetic nickel(II), palladium(II) and platinum(II) macrocyclic complexes were studied by ^1H and ^{13}C NMR spectroscopy, revealing spectra consistent with the formation of the desired dinuclear products.

In the ^1H NMR spectra of the macrocyclic complexes, the ArCH_2N and NCH_nCH_2 signals are significantly shifted downfield (~ 1.0 ppm) with respect to the analogous protons on the parent bis-amine. These protons are therefore indicative of dithiocarbamate formation. The resonances often, however, appear broad, a feature probably due to slow rotation processes around the carbon-nitrogen bonds of the metal(dithiocarbamate) $_2$ units, resulting in the presence of numerous stereoisomers (*syn* or *anti*) within the self- assembled product¹³.

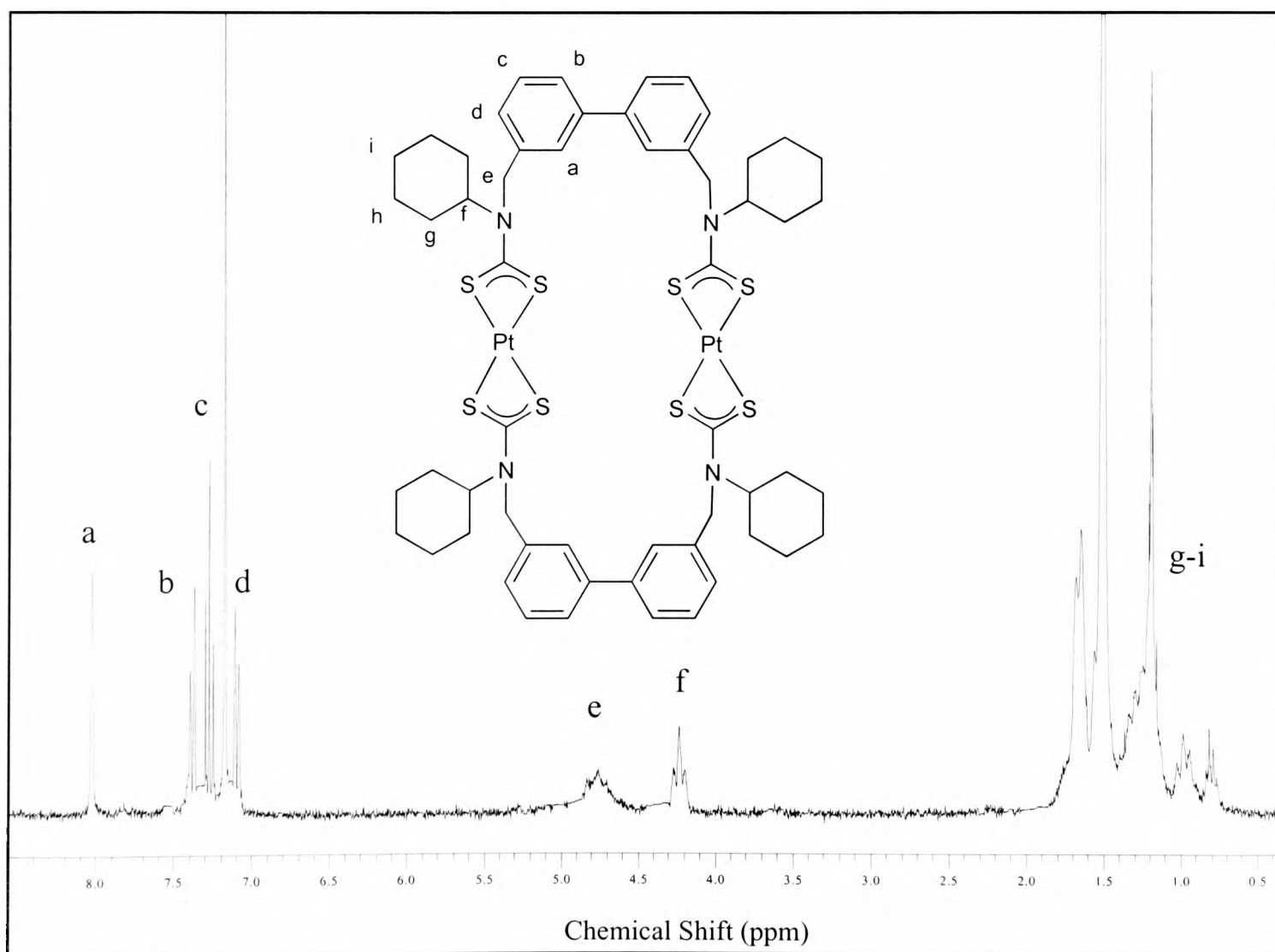


Figure 5 ^1H NMR of (14-Pt) (300MHz, CDCl_3 , 298K)

The ^1H NMR spectrum of macrocycle (14-Pt) (Figure 5) is relatively simple and consistent with the formation of a symmetrical dinuclear product. The spectrum displays four aromatic

peaks: a singlet at 8.09 ppm, corresponding to the aromatic proton (a), which points into the centre of the macrocyclic cavity, and two doublets and a triplet ($J = 7.5$ Hz) from the protons (b - d) on the biphenyl ring. The protons adjacent to the dithiocarbamate ligand (e and f) appear as two broad signals at 4.83 and 4.30 ppm, at significantly higher values than those of the parent amine. The high field resonances are ascribed to the cyclohexyl groups (g - i).

The ^{13}C NMR spectra of the complexes are also in agreement with the proposed structures, with peaks at 208 – 214 ppm confirming the presence of the CS_2 group. Furthermore, the chemical shift position of this peak is indicative of the nature of the metal within the complex¹⁴, with nickel(II), palladium(II) and platinum(II) complexes displaying peaks at 208 – 209 ppm, 211 – 212 ppm and 212 – 214 ppm, respectively.

3.1.1 *m*-Xylyl Complexes

The ^1H NMR spectra of *m*-xylyl spaced macrocycles of the *n*-butyl chained (**7-M**) and (**10-M**) complexes displayed relatively simple patterns consistent with the symmetry of a dinuclear product. However, the introduction of a cyclohexyl side-chain resulted in a more complicated spectrum. Whereas for *n*-butyl chained macrocycles the two protons of the ArCH_2 protons are observed as a singlet, in the cyclohexyl-chained analogues they appear as a broad central singlet and a pair of geminally coupled doublets ($J = 14.4$ Hz) (Figure 6(upper)). The geminal coupling is a result of the prochiral nature of the cyclohexyl side-chain in combination with the conformational rigidity of the *m*-xylyl spacer resulting in the diastereotopic nature of the methylene protons.

Variable temperature experiments were undertaken and showed that lowering the temperature resulted in a decrease in the intensity of the central peak so that at -50°C it was not observed (Figure 6(lower)). This may suggest that this central peak is the result of a second conformation of the complex.

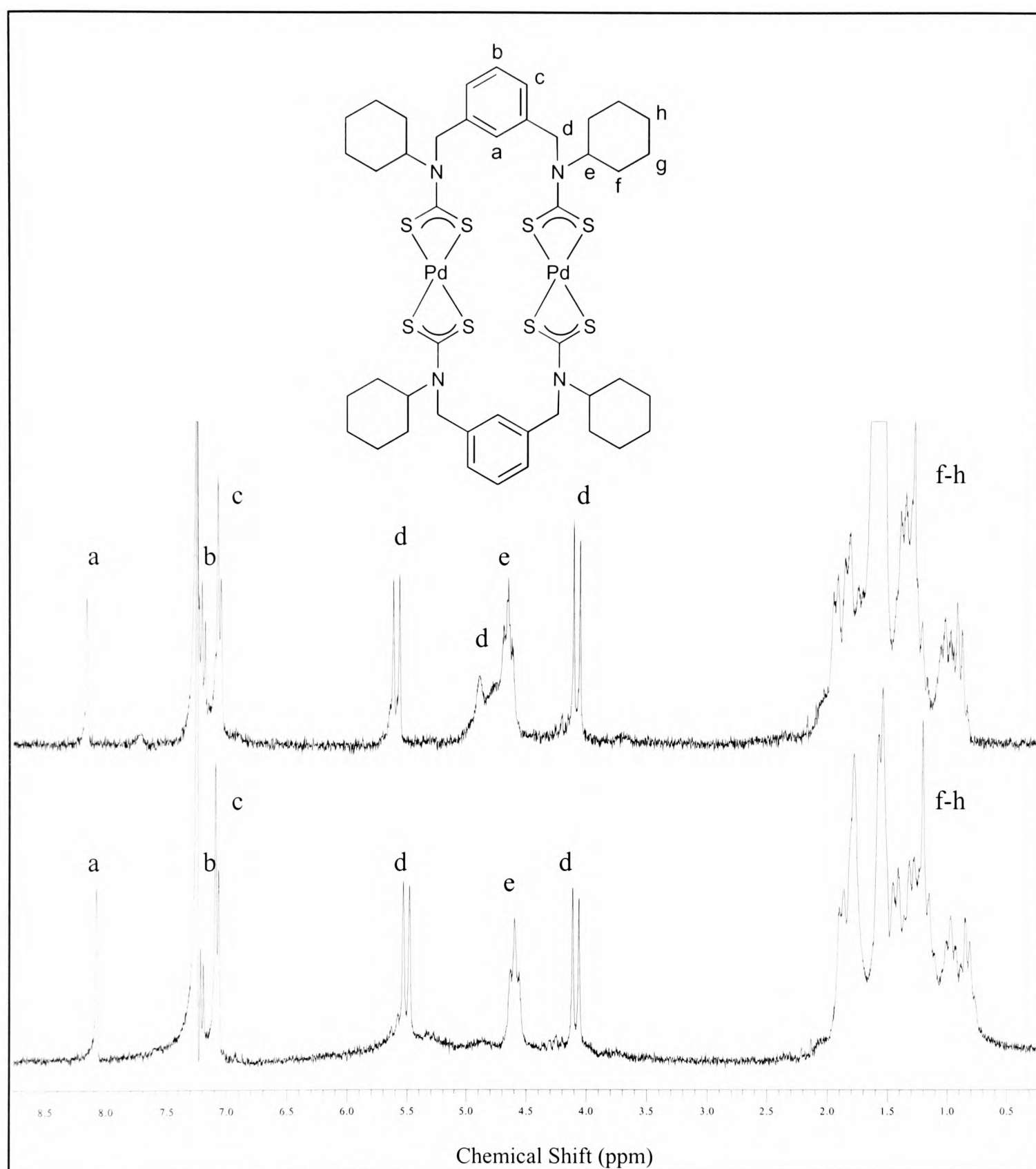


Figure 6 ^1H NMR spectrum of (8-Pd) in CDCl_3 at 298K (upper) and 223K (lower) (300MHz)

Interestingly, the intensity of the geminally coupled doublets was most pronounced for the nickel(II) analogues, with those for the palladium(II) complexes being less prominent and only a minor component for the platinum(II) derivatives. This is possibly a consequence of the increasing metal-sulphur bond length upon descending the series. This allows greater flexibility within the structures, enabling them to adopt a wider range of conformations in solution.

3.2 Electrospray Mass Spectrometry

Whilst NMR techniques are useful in analysing the formation of the metal-directed self-assembled products, they are not able to determine the nuclearity of the ensuing complexes.

For this task, electrospray mass spectrometry was used.

Electrospray mass spectra have been obtained for all of the synthesised products, and these confirm the formation of dinuclear macrocyclic complexes, with no observation of any higher oligomers. In general, the $[M]^+$ (in the case of copper-based architectures¹⁵) or $[M+H]^+$ peaks were observed as the base peaks, with isotopic patterns in good agreement with theoretical calculations. Adducts with sodium and potassium ions were frequently observed, especially at higher cone voltages. Co-injection of the sample with sodium or potassium hexafluorophosphate resulted in the significant increase in the intensity of these peaks, such that they often became the base peaks in the spectra. The electrospray mass spectrum of **(10-Ni)** is displayed in Figure 7, and this shows adduct formation with both sodium and potassium cations.

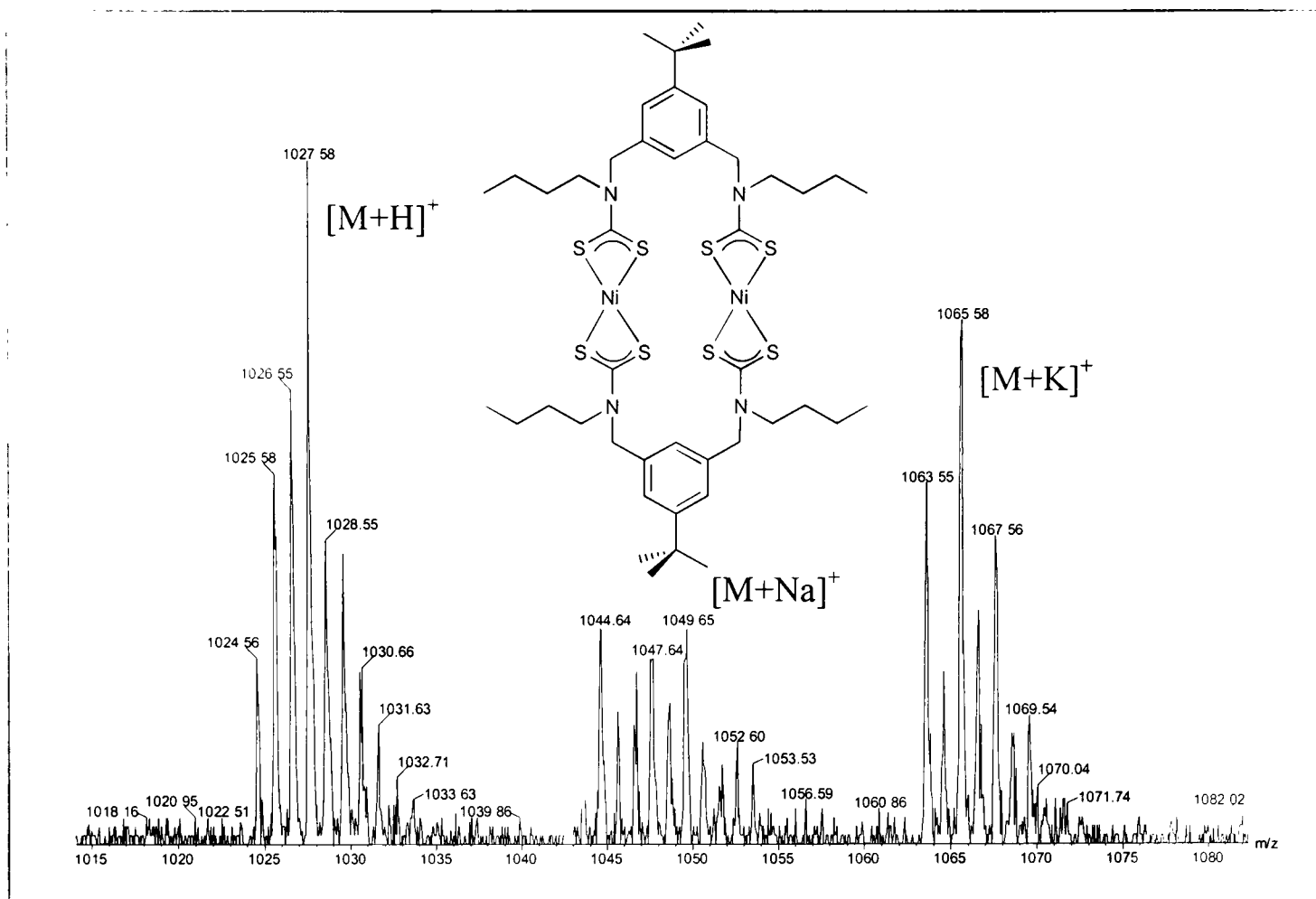


Figure 7 Electrospray mass spectrum of (10-Ni) upon coinjection with sodium and potassium hexafluorophosphate

Copper (II) macrocycles could also be oxidised *in situ* on addition of nitrosium tetrafluoroborate¹⁶. This generates the doubly-charged copper(III) systems, with very high ion counts, which are clearly observable in the spectra due to the half-integral splitting of its peaks. In addition to the dicationic $[M]^{2+}$ peaks, often tetrafluoroborate adducts $[M.BF_4]^+$ were also observable. The electrospray mass spectrum of (8-Cu) is displayed in Figure 8, clearly showing the peak corresponding to the dicationic macrocycle, and its excellent match with its predicted isotopic pattern (Figure 8(inset)).

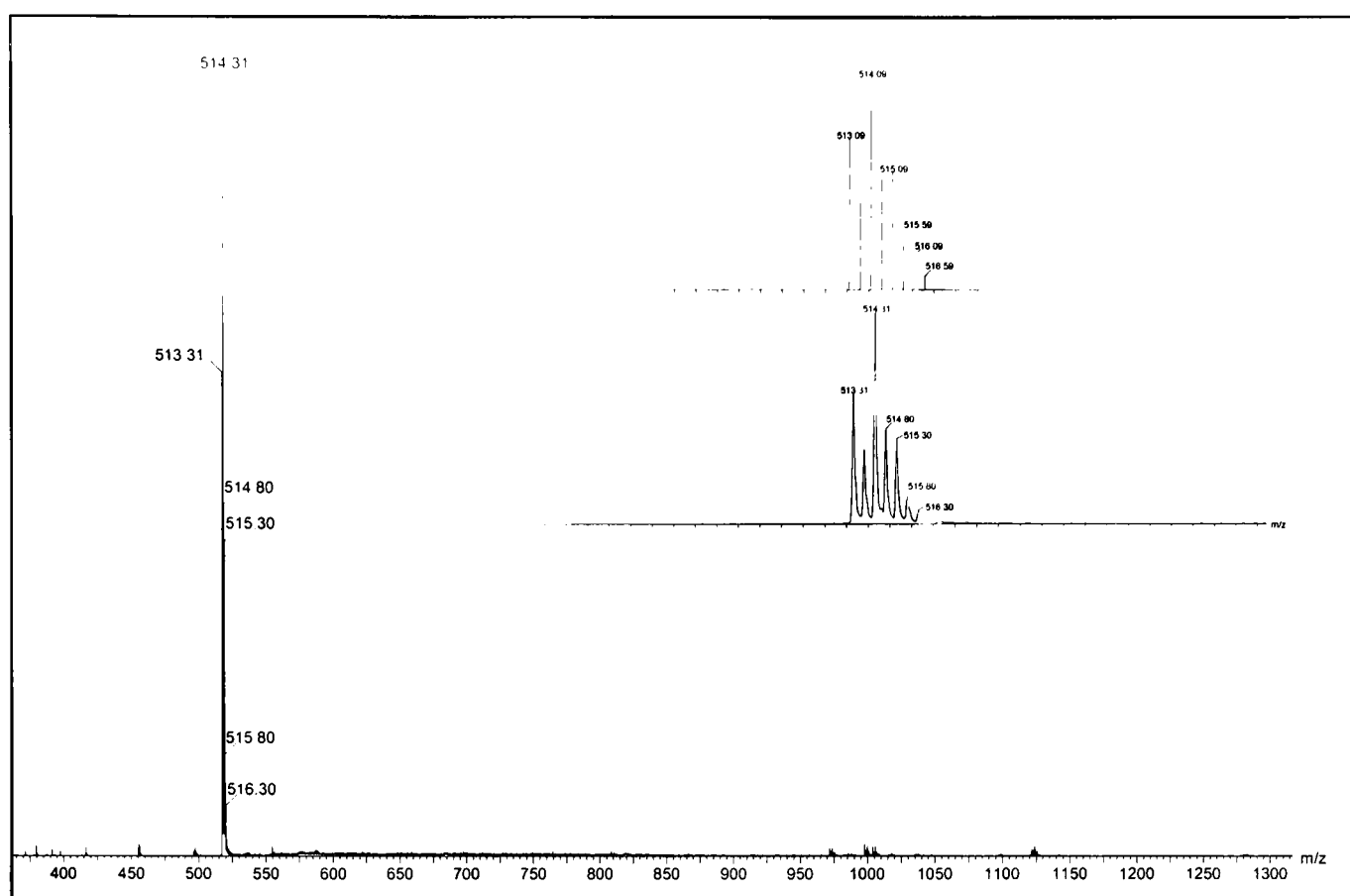


Figure 8 Electrospray mass spectrum of (8-Cu) (Inset: predicted (upper) and actual isotope model of $[M]^{2+}$ peak)

3.3 UV-vis Spectroscopy

One of the appealing properties of transition metal dithiocarbamate complexes is their electronic absorption spectral characteristics. This results in the formation of distinctively coloured complexes: black/brown, green, orange and yellow/orange for copper(II), nickel(II) and palladium(II) and platinum(II) respectively.

The UV-vis spectra of all of the synthesised macrocycles were recorded in dichloromethane solution for characterisation purposes. All of the complexes gave distinctive spectra, with Figure 9 highlighting the spectrum of (10-Ni). The wavelengths λ (nm) of the peak maxima and corresponding extinction coefficients (ϵ , $M^{-1}cm^{-1}$) are displayed in Table 2.

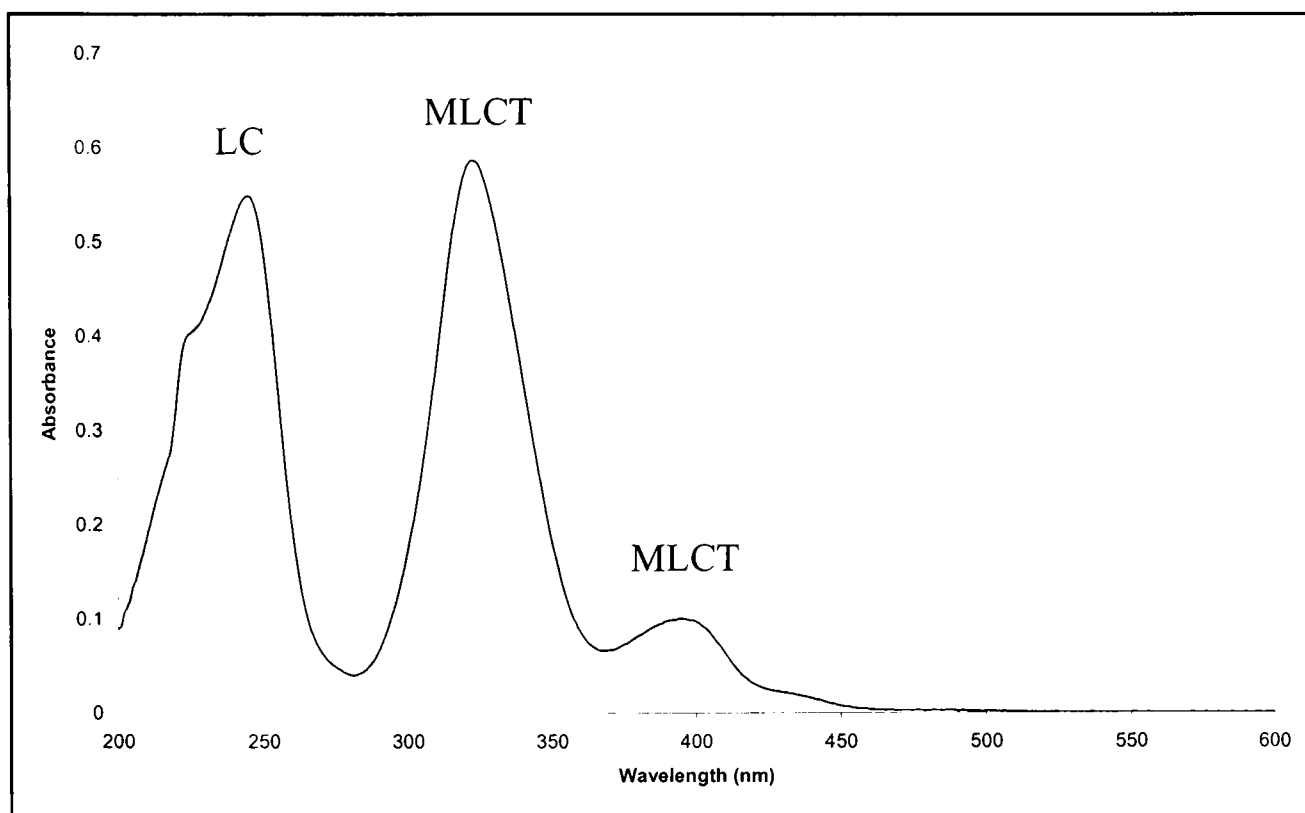


Figure 9 UV-vis spectrum of (10-Ni) recorded in CH_2Cl_2 at $1 \times 10^{-5} \text{ M}$ and 293K

The copper(II) containing metallomacrocycles typically exhibit three bands in their UV-vis spectra. These can be assigned to a ligand to metal charge transfer (LMCT) band¹⁷ at $\sim 430 \text{ nm}$, and two ligand centred (LC) $\pi\text{-}\pi^*$ transitions¹⁸ at $\sim 270 \text{ nm}$ and $\sim 290 \text{ nm}$ (Table 2)¹⁹.

Nickel(II) dithiocarbamates exhibit characteristic electronic absorption spectra containing three intense charge-transfer bands^{20,21}. Two metal to ligand charge transfer (MLCT) bands at around 390 nm and 330 nm are observed, with the one at lower wavelength being more intense. A ligand centred band at approximately 260 nm is also seen (Figure 9). The spectra for platinum(II) compounds are similar to those observed for nickel(II)-based complexes²². The palladium(II) complexes, however, show only two peaks, with the absence of the MLCT band at higher wavelength²³.

M		$\lambda(\epsilon, 10^{-3}\text{M}^{-1}\text{cm}^{-1})$
Cu	(20)	269 (33.8), 289 (17.0), 435 (14.2)
	(7-Cu)	229 (59.5), 275 (47.7), 434 (13.9)
	(8-Cu)	228 (51.4), 275 (43.8), 435 (13.4)
	(10-Cu)	227 (24.2), 271 (64.2), 429 (26.6)
	(11-Cu)	230 (19.4), 272 (58.2), 432 (21.9)
	(13-Cu)	225 (103.8), 271 (64.5), 430 (17.9)
	(14-Cu)	228 (87.4), 269 (49.5), 437 (14.6)
	(15-Cu)	226 (56.0), 270 (95.4), 439 (19.1)
	(18-Cu)	228 (94.7), 271 (66.5), 433 (20.4)
Ni	(21)	240 (39.3), 324 (40.2), 389 (6.1)
	(7-Ni)	246 (77.2), 275 (99.1), 400 (10.1)
	(8-Ni)	242 (72.9), 274 (138.3), 321 (62.1), 400 (10.5)
	(10-Ni)	245 (62.5), 325 (63.9), 397 (11.4)
	(11-Ni)	244 (51.9), 324 (34.0), 398 (10.5)
	(13-Ni)	242 (50.1), 274 (58.9), 401 (39.8)
	(14-Ni)	244 (24.2), 280 (40.9), 398 (19.8)
	(15-Ni)	247 (33.2), 276 (38.9), 397 (16.8)
Pd	(22)	236 (24.5), 300 (73.2), 347 sh (11.2)
	(8-Pd)	237 (31.7), 302 (93.4)
	(10-Pd)	236 (36.4), 299 (129.5)
	(11-Pd)	238 (38.7), 302 (111.9)
	(13-Pd)	240 (48.6), 307 (105.8)
	(14-Pd)	238 (40.9), 304 (89.5)
	(15-Pd)	236 (38.0), 300 (101.7)
Pt	(23)	219 (25.5), 255 (47.2), 347 (25.7)
	(8-Pt)	221 (44.2), 258 (86.8), 353 (42.8)
	(10-Pt)	222 (20.4), 256 (63.5), 352 (32.8)
	(11-Pt)	224 (28.5), 257 (67.5), 352 (35.5)
	(13-Pt)	223 (65.2), 256 (114.8), 351 (39.7)
	(14-Pt)	223 (51.5), 254 (88.8), 354 (29.7)

Table 2 UV-vis spectroscopic data for macrocyclic receptors in CH_2Cl_2 at $1 \times 10^{-5}\text{M}$ and 293K
(Errors for extinction coefficients estimated at $\pm 10\%$)

3.4 X-Ray Crystallography

The solid-state structures of a number of macrocyclic complexes were determined via single-crystal X-ray structural analysis. These structures will now be discussed.

3.4.1 *m*-Xylyl Spaced Macrocycles

Crystals, suitable for X-ray structural analysis, of a range of *m*-xylyl spaced dinuclear dithiocarbamate macrocycles, were grown by layering dichloromethane or chloroform

solutions of the complex with ethanol. The resulting structures have been solved by Professor M. Drew, University of Reading and Dr R. Paul, University of Oxford.

A single crystal of **(7-Cu)** was obtained through recrystallisation from dichloromethane/ethanol and its structure is highlighted in Figure 10.

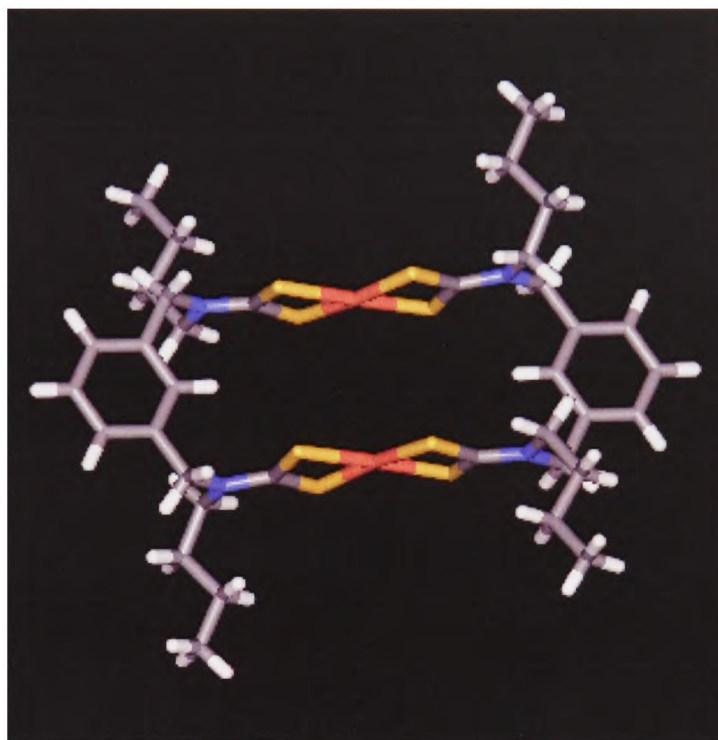


Figure 10 X-ray crystal structure of **(7-Cu)** (Key: C - grey, H - white, N - blue, S - yellow, Cu - red)

As determined by electrospray mass spectrometry, in solution, the X-ray crystal structure confirms the formation of the desired dinuclear dithiocarbamate complex. The metallomacrocycle possesses a centre of symmetry, so the two ends of the molecule are crystallographically identical. The near-planar copper(II) dithiocarbamate groups are coplanar with respect to each other and separated in space through the spacing *m*-xylyl group resulting in a cavity being formed in the centre of the molecule. The bridging *m*-xylyl groups are also coplanar with respect to each other and perpendicular to the plane of the dithiocarbamate moieties. Consequently, they appear *trans* to each other across the copper(II) dithiocarbamate group. The alkyl chains point away from the central cavity and appear on the opposite side of the dithiocarbamate linkage with respect to the *m*-xylyl group.

Similar structures are also adopted in the solid state by complexes **(8-Cu)**, **(8-Ni)** and **(8-Pd)**.

The structure of (**8-Pd**) is displayed in Figure 11 and selected crystallographic parameters are highlighted in Table 3.

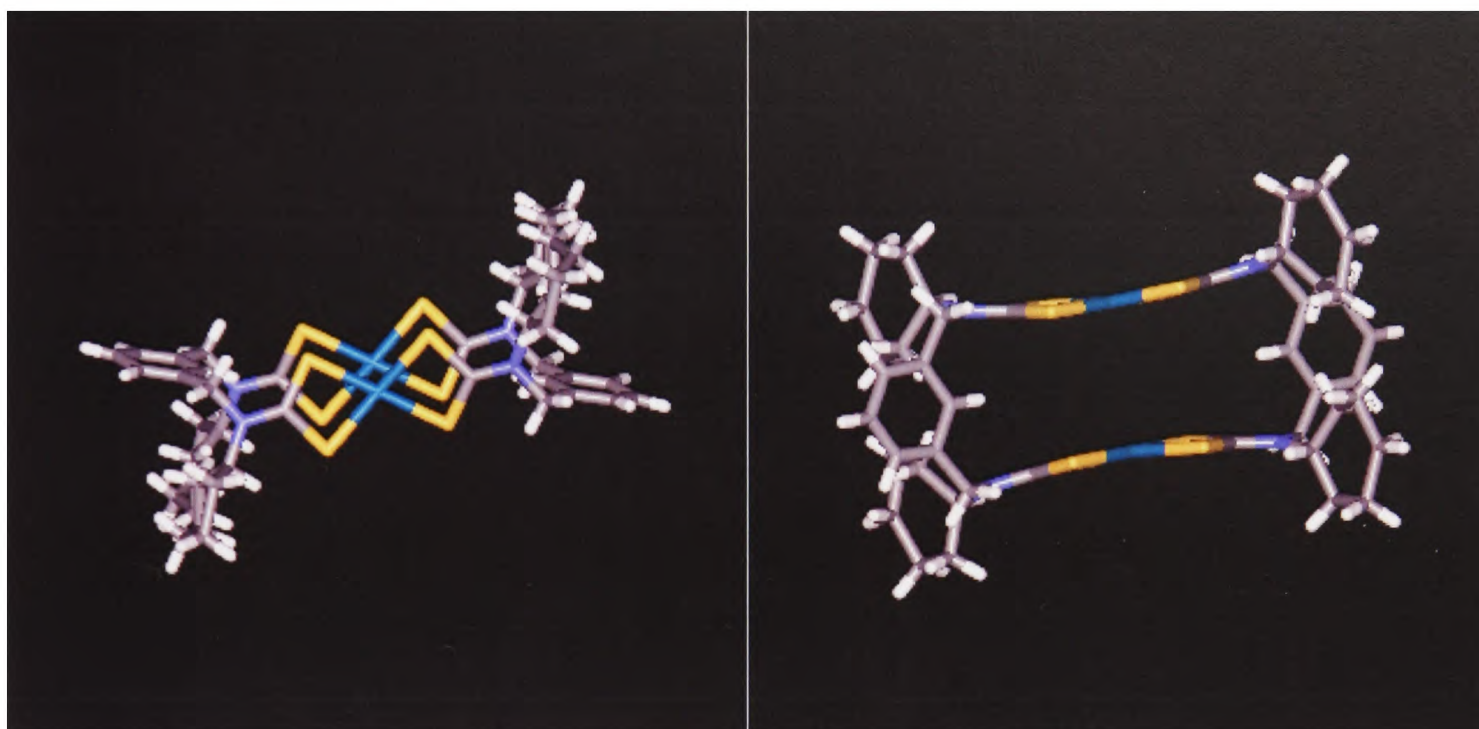


Figure 11 X-ray crystal structure of (**8-Pd**) (Key: C - grey, H - white, N - blue, S - yellow, Pd - turquoise)

	(7-Cu)	(8-Cu)	(8-Ni)	(8-Pd)
d(M-S) Å	2.28, 2.29, 2.30, 2.31	2.27, 2.30	2.20, 2.20, 2.21, 2.22	2.34
d(N-C(S ₂)) Å	1.33	1.31	1.39	1.31
d(M-M) Å	4.54	4.45	4.36	4.24
d(ArH ⁴ -ArH ⁴) Å	8.14	8.19	8.38	8.54
θ (S-M-S _{adj})°	77.5, 77.7	77.7	79.4	75.2
θ (S-M-S _{opp})°	174.7, 178.4	164.8, 174.2	172.5, 178.3	172.8, 179.1
θ (N-N-M)°	3.3	5.1	5.0	5.2

Table 3 Selected crystallographic parameters for (**7-Cu**), (**8-Cu**), (**8-Ni**) and (**8-Pd**)

Similar to (**7-Cu**), all three complexes have the *m*-xylyl spacing group separating the coplanar metal-dithiocarbamate groups through a *trans* arrangement across this linkage. Interestingly,

the variation of metal centre does not alter the overall structure of the complex, with each metal centre adopting a pseudo-square planar geometry.

The metal employed does, however, dictate the dimensions of the macrocycle, with copper(II)-sulphur and palladium(II)-sulphur bonds being considerably longer than those of nickel(II). This feature is also reflected in the length of the nitrogen-carbon bond of the dithiocarbamate linkage. This distance is considerably less than would be expected for a typical single carbon-nitrogen bond ($1.47\text{\AA}$) and closer to that of a carbon-nitrogen double bond ($1.28\text{\AA}$)²⁴. This demonstrates the significant double bond character between the two atoms due to the effective delocalisation of charge about the dithiocarbamate group. This delocalisation is most apparent for **(8-Cu)** and **(8-Pd)** where the nitrogen-carbon bond is $1.31\text{\AA}$, indicating a high degree of covalency within the metal-sulphur bonds.

The distance between the (ArH^4) hydrogen atoms of the *m*-xylyl spacers determines the length of the cavity, with distances varying from $8.14\text{\AA}$ for **(7-Cu)** to $8.54\text{\AA}$ for **(8-Pd)**. The metal-metal distance controls the width of the cavity; this varies from $4.24 - 4.54\text{\AA}$ for the structures. Despite these seemingly large cavity dimensions, Corey-Pauling-Koltun (CPK) space-filling representations of the X-ray crystal structure of **(8-Cu)** (Figure 12) reveals little room within the central cavity for potential guest inclusion.

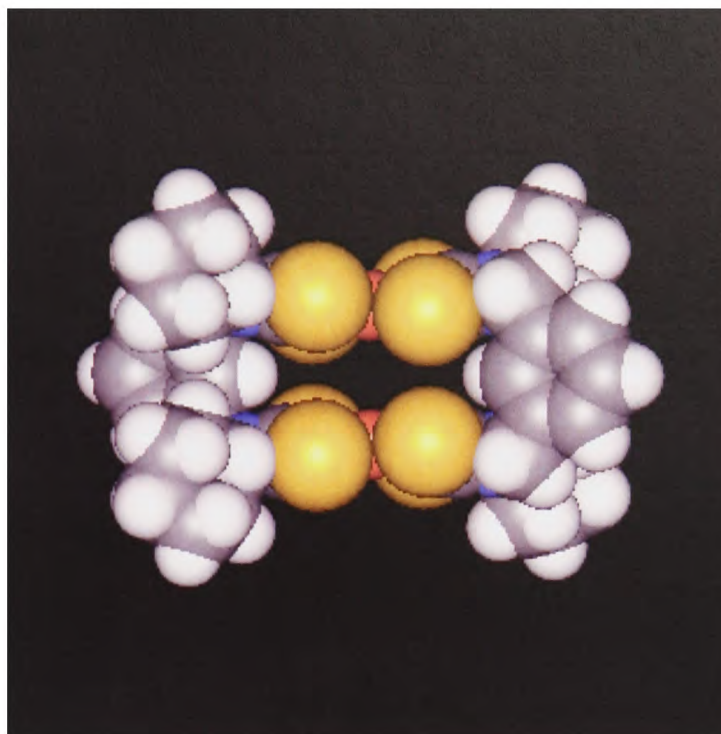


Figure 12 CPK representation of the X-ray crystal structure of **(8-Cu)**

The N-N-M angle is an indication of the degree by which the metal ion lies out of the dithiocarbamate plane. These values are generally low, although there does appear to be a preference for the metals to bow towards each other pointing into the central cavity. This characteristic is maximised for **(8-Pd)** where the metals lie 5.2° above the dithiocarbamate plane (Figure 9), possibly indicative of a weak long range metal-metal interaction. A further feature of the metal-dithiocarbamate group is it twisting so that it is no longer planar. This is observed for **(8-Cu)** where a 7.4° angle is observed between the planes of the dithiocarbamate ligands either side of the metal centre. This is most likely to be a result of the release of steric strain within the relatively small macrocycle.

Crystals of **(11-Ni)**, suitable for X-ray analysis, were grown through recrystallisation from a dichloromethane/ethanol solution. Initially green crystals were formed **(11-Ni(a))**, although over time brown crystals **(11-Ni(b))** also appeared from the green solution. The two resulting structures transpired to be that of the same complex in different conformations. These are highlighted in Figure 13.

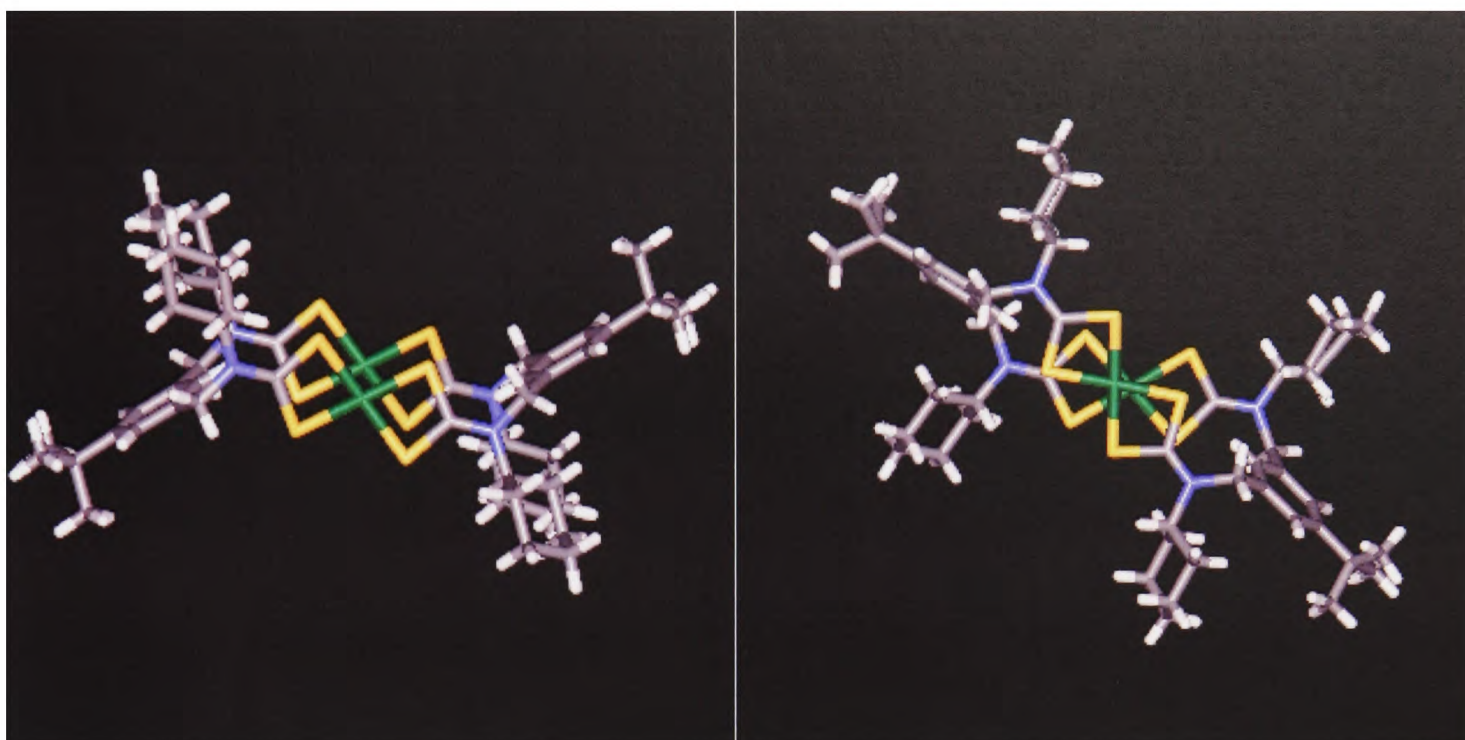


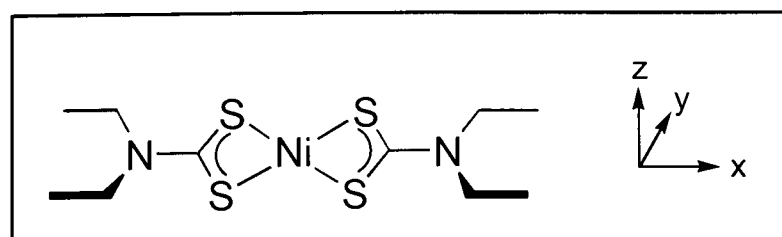
Figure 13 X-ray crystal structures of (left) (11-Ni(a)) (green crystals) and (right) (11-Ni(b)) (brown crystals) (Key: C - grey, H - white, N - blue, S - yellow, Ni - green)

The green crystals of **(11-Ni(a))** reveal the macrocycle adopting a similar conformation to that of **(8-Ni)**, with the cyclohexyl chains *cis* with respect to the spacing aromatic group and the nickel(II) dithiocarbamate groups aligned across the cavity. **(11-Ni(b))**, however, assumes a different conformation. In this case, the cyclohexyl groups appear *trans* to the *m*-xylyl linkage with the nickel(II) dithiocarbamate moieties no longer aligned but adopting approximately a 40° angle to each other. Selected crystallographic parameters for the two structures are highlighted in Table 4.

	(11-Ni(a))	(11-Ni(b))
colour	green	brown
d(Ni-S) Å	2.20, 2.21	2.22, 2.23
d(N-C(S ₂)) Å	1.32	1.32, 1.35
d(Ni-Ni) Å	3.99	4.24
d(ArH ¹ -ArH ⁴) Å	8.16	8.09
θ (S-Ni-S _{adj})°	79.2, 79.4	78.9, 79.2
θ (S-Ni-S _{opp})°	172.6, 176.7	173.1, 178.3
θ (N-N-Ni)°	6.8	4.3

Table 4 Selected crystallographic parameters for (11-Ni(a)) and (11-Ni(b))

The variation of the colours of the crystals is best discussed with reference to nickel(II) bis-(*N,N'*-diethyldithiocarbamate) (**21**) (Figure 14). In solution, as has already been seen (Table 2), the UV-vis spectrum of the nickel(II) complex exhibits three intense peaks, resulting in a green solution. However, examination of a single crystal of (**21**) with polarised light reveals that it is anisotropic, with the crystal appearing green if viewed along the x-axis, but orange/brown if observed along the y- or z-axes²⁵. This is a result of the required symmetries of the relevant transitions. In the case of (**11-Ni(b)**) it is likely that due to the non-alignment of the nickel(II) dithiocarbamate groups along the x-axis, the low energy transition required for the green colouration is absent.

Figure 14 Nickel(II) bis-(*N,N'*-diethyldithiocarbamate) (**21**)

Both **(11-Ni)** macrocycles display small cavity sizes, with the nickel-nickel distance only 3.99 Å for **(11-Ni(a))**. This is partially due to the large bend displayed in the dithiocarbamate plane for this structure, leading to the metal being 6.8° out of the plane of the dithiocarbamate nitrogens. Most importantly, however, the presence of two different structures demonstrates the flexibility of the macrocycles and their ability to adopt energetically similar conformations. This observation is also in agreement with the study of ^1H NMR spectroscopic data, which suggests the presence of more than one conformation of the macrocyclic complexes in solution (Figure 6).

X-ray quality single crystals of **(10-Cu)** and **(10-Pd)** were also obtained through recrystallisation from dichloromethane/ethanol. The resulting structure of **(10-Pd)** is displayed in Figure 15, and crystallographically important parameters are outlined in Table 5.

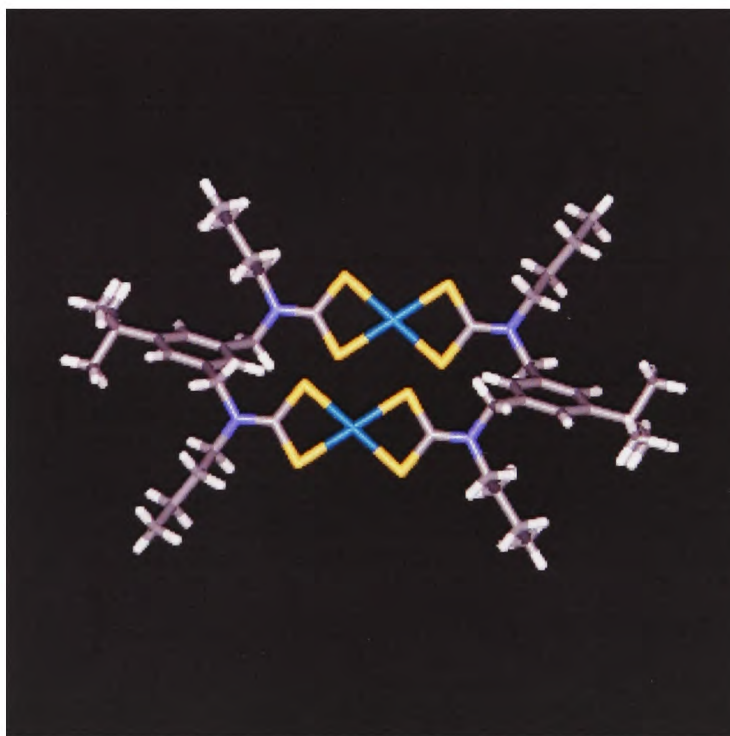


Figure 15 X-ray crystal structure of **(10-Pd)** (Key: C - grey, H - white, N - blue, S - yellow, Pd - turquoise)

Both structures adopted a similar structure, although **(10-Cu)** had two crystallographically distinct macrocycles, (a) and (b), in the unit cell. The structures are related to that of **(11-Ni(b))** in that the *n*-butyl chains appear *trans* to the *m*-xylyl linkage, although the nickel(II) dithiocarbamate moieties do remain aligned, although this alignment is offset. This results in

the metal-metal distances being significantly greater than has previously been observed, up to 5.97 Å in **(10-Cu(a))**.

	(10-Cu)	(10-Pd)
d(M-S) Å	a) 2.30, 2.30, 2.32, 2.36 b) 2.30, 2.32	2.31, 2.32, 2.32, 2.33
d(N-C(S ₂)) Å	a) 1.31, 1.35 b) 1.28, 1.35	1.32, 1.34
d(M-M) Å	a) 5.97, b) 5.59	5.90
d(ArH ⁴ -ArH ⁴) Å	a) 7.92, b) 8.06	7.98
θ (S-M-S _{adj})°	a) 77.5, 77.7 b) 76.9, 77.2	75.6, 75.8
θ (S-M-S _{opp})°	a) 173.7, 177.6 b) 168.4, 176.9	177.7, 179.7
θ (N-N-M)°	a) 0.4, b) 4.6	0.3

Table 5 Selected crystallographic parameters for **(10-Cu)** and **(10-Pd)**

In conclusion, X-ray structural analysis has unequivocally proved the formation of dinuclear macrocyclic *m*-xylyl dithiocarbamate-based complexes. These structures do not vary greatly with the choice of metal, suggesting it is the ligand and the side chains that dictate the conformation adopted in the solid state. Furthermore, the occurrence of different conformers of the same complex **(11-Ni)** reveals the flexibility of the macrocycles and their ability to adopt several conformations in the solid state. This flexibility is also demonstrated in solution, where ¹H NMR studies have also suggesting the formation of flexible, multi-conformational architectures.

3.4.2 3,3'-Biphenyl Spaced Macrocycle (13-Cu)

X-ray quality single crystals were grown from the copper(II) 3,3'-biphenyl spaced macrocycle, (13-Cu) from both dichloromethane/diethyl ether and dichloromethane/ethanol solutions. The resulting structure, solved by Professor M. Drew, University of Reading, turned out to be the unexpected compound which is shown below in Figure 16 and selected parameters are displayed in Table 6.

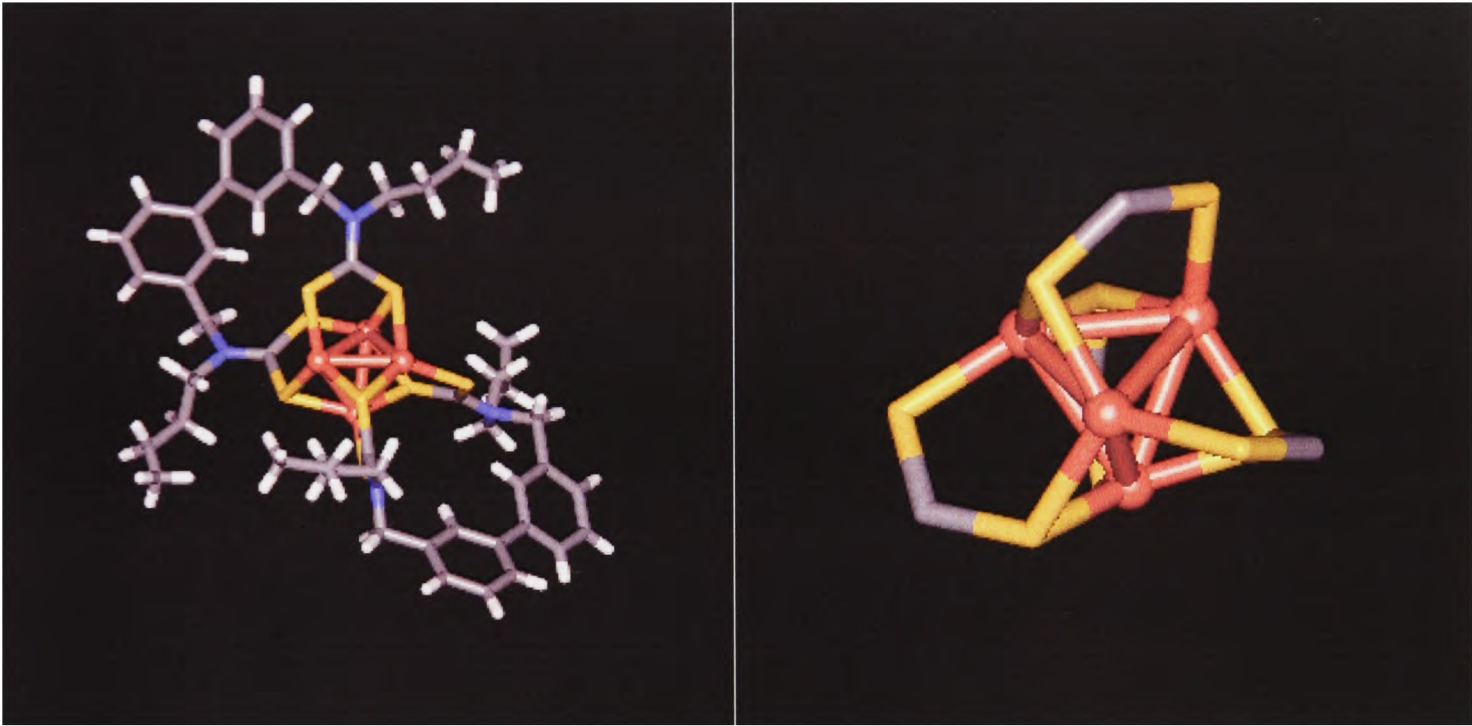


Figure 16 X-ray crystal structure of (13-Cu₂) (right) view of central (CS₂Cu)₄ tetrahedral core (Key: C - grey, H - white, N - blue, S - yellow, Cu - red)

	(13-Cu ₂)
d(Cu-S _{unidentate}) Å	2.24
d(Cu-S _{monodentate}) Å	2.30
d(N-C(S ₂)) Å	1.31, 1.32
d(Cu-Cu) Å	2.54, 2.71 2.80, 2.89

Table 6 Selected crystallographic parameters for (13-Cu₂)

Surprisingly, the copper has been formally reduced to copper(I), forming a central Cu₄

tetrahedral cage (**13-Cu₂**) containing a crystallographic two-fold axis. Each metal is coordinated to three different sulphur donors, in addition to three other copper centres. This results in a distorted octahedral geometry about each copper. The dithiocarbamate ligands coordinate unsymmetrically to different three metal atoms; one sulphur binds to one metal (metal-sulphur distance = 2.24Å) and the other to two copper centres (metal-sulphur distance = 2.30Å) (Figure 16(right)). There are four unique copper-copper bond lengths; 2.54, 2.71, 2.80 and 2.89Å, of which the first is significantly shorter than the other three. Indeed, the short bond length is comparable to those in the metal phase of the element (2.56Å). The dithiocarbamate carbon-nitrogen bonds are 1.31 and 1.32Å, also suggesting a high covalent character for this complex. It is further noteworthy, that the biphenyl rings are not coplanar, with the two rings twisted at a 29.2° angle.

This tetrameric cage-like structure is as would be expected for a copper(I) dithiocarbamate complex. The crystal structure of copper(I) tetra-(*N,N'*-diethyldithiocarbamate) is also shown to adopt this structure (Figure 17).

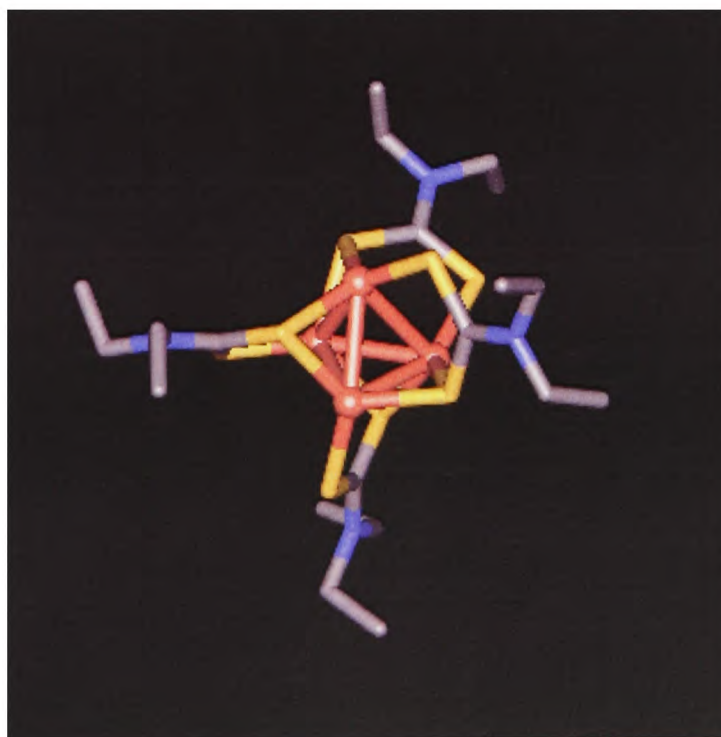


Figure 17 X-ray crystal structure of Cu(I) tetra-(*N,N'*-diethyldithiocarbamate)

It is very surprising that the copper(I) dithiocarbamate species has crystallised since they are

relatively difficult to synthesise. The electrochemistry of copper(II) bis-(*N,N'*-diethyldithiocarbamate) (**20**) shows a reversible reduction at -0.96V in forming a copper(I) dithiocarbamate species²⁶. They have previously been formed by treatment of sodium dithiocarbamate salts with copper(I) oxide in an inert atmosphere²⁷, oxidation of copper, bronze or metallic copper with tetraalkylthiuram disulphides in non polar solvents²⁸ and aqueous reactions of alkali metal *N,N'*-dialkyldithiocarbamates with a cuprous halide²⁹, however, frequent contamination with the corresponding cuprous salts are observed³⁰.

Examination of the ^1H NMR of the crude product revealed the presence of a paramagnetic product. Furthermore, electrospray mass spectrometry and elemental analysis also demonstrated the presence of the copper(II) dithiocarbamate complex. This shows the reduction must have occurred during the recrystallisation stage of the process, although since two different solvent systems resulted in the formation of the same copper(I) product, it is unclear what the reducing agent may have been. This is also uncertain as the recrystallisations were undertaken open to the atmosphere (refer also to Section 4 for further discussion).

3.4.3 Naphthyl Spaced Macrocycle (18-Cu)

A single crystal of (**18-Cu**) suitable for X-ray analysis was prepared from a dichloromethane/ethanol solution and its structure solved by Dr. R. Paul, University of Oxford. The structure, displayed in Figure 18, exists with disordered dichloromethane solvent molecules occupying half the cavities of the macrocyclic complexes. Selected crystallographic parameters for the structure are highlighted in Table 7.

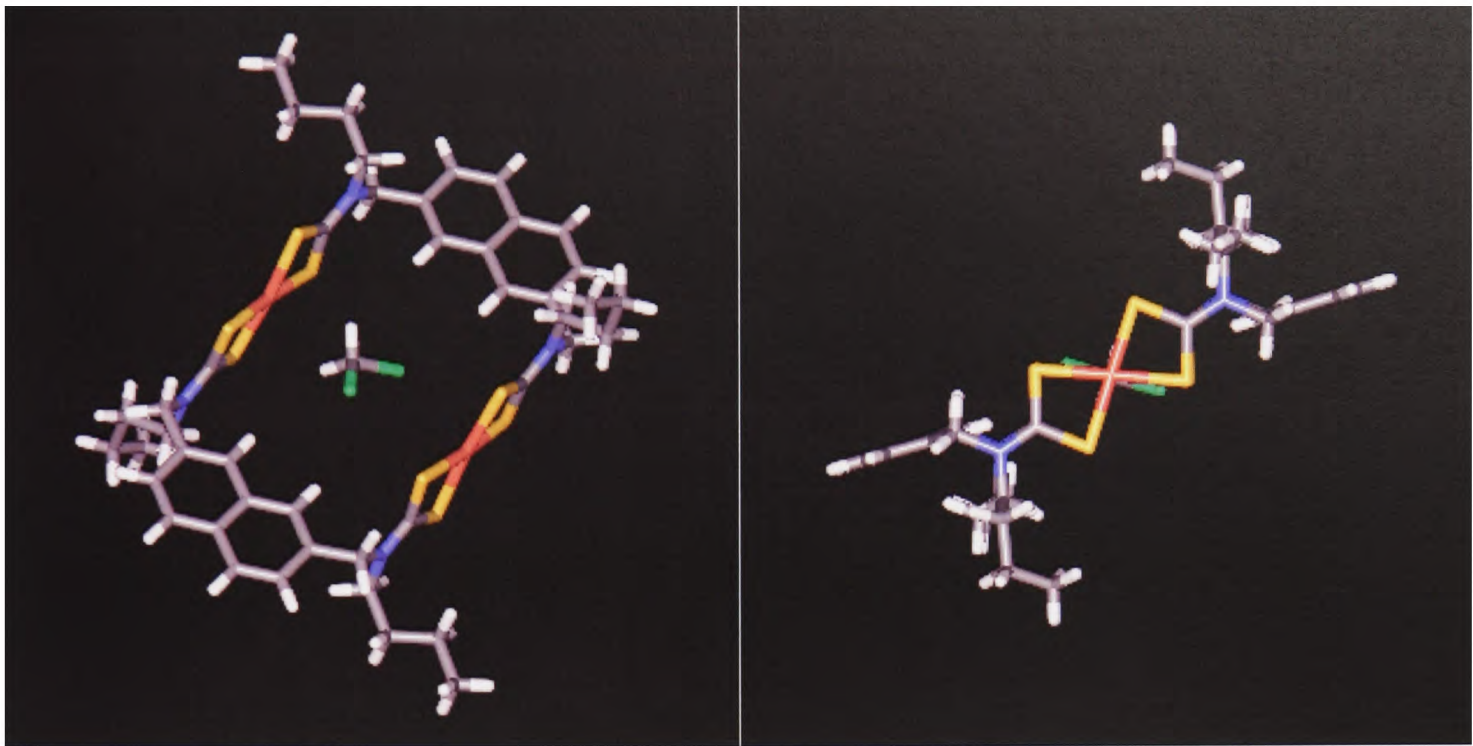


Figure 18 X-ray crystal structure of (18-Cu.½CH₂Cl₂) (Key: C - grey, H - white, N - blue, S - yellow, Cl – green, Cu - red)

	(18-Cu)
d(Cu-S) Å	2.29, 2.30
d(N-C(S ₂)) Å	1.32, 1.33
d(Cu-Cu) Å	7.62
d(ArH ¹ -ArH ^{1'}) Å	8.09
θ(S-Cu-S _{adj})°	77.6
θ(S-Cu-S _{opp})°	174.1, 175.7
θ(N-N-Cu)°	0.8

Table 7 Selected crystallographic parameters for (18-Cu)

The macrocycle adopts a similar structure to that of (7-Cu) with the near-planar copper(II) dithiocarbamate groups coplanar to each other and separated in space through the spacing 2,7-disubstituted naphthylene group. The bridging aromatic groups are coplanar to each other and perpendicular to the plane of the dithiocarbamate moieties. This has the result that they appear

trans to each other across the copper(II) dithiocarbamate group. The alkyl chains point away from the central cavity and appear on the opposite side of the dithiocarbamate linkage with respect to the naphthyl spacer (Figure 18(right)).

The resultant cavity of the molecule possesses a similar length to the previously discussed *m*-xylyl spaced macrocycles (8.09 Å), but the use of a larger aromatic spacer means the cavity is much wider (7.62 Å). This larger width comfortably allows the inclusion of suitably sized guest species, such as dichloromethane, into the structure. The metal dithiocarbamate group is considerably less bowed than in the examples of the *m*-xylyl spaced macrocycles, with the copper centre only 0.8° out of the plane and considerably less twisted also. This is possibly a result of less steric strain in the larger macrocycle and also a consequence of an absence of possible metal-metal interactions in the smaller macrocycles.

3.5 Electrochemistry

The electrochemical properties of copper(II) dithiocarbamate complexes have been well-established^{31,32}. They have been shown to undergo two metal-based, one-electron redox processes, corresponding to a copper(II/III) oxidation and a copper(II/I) reduction. The copper(II/III) oxidation process is reversible, predominantly a consequence of the preservation of the square planar geometry of the copper centre upon its oxidation^{33,34}.

The electrochemical properties of the copper(II/III) redox couple of the copper(II) dithiocarbamate macrocyclic complexes have been investigated by both cyclic and square wave voltammetry. The electrochemical properties of the acyclic analogue (**20**) were also recorded as a comparison to the dinuclear complexes.

If the redox process is reversible and is diffusion controlled (i.e. electron transfer is fast in comparison with diffusion of species from the bulk solvent to the electrode surface) then the cyclic voltammetry waves satisfy the following criteria³⁵:

- i) The anodic and cathodic peak currents are the same;
- ii) The separation between the anodic and cathodic wave potentials is about $59/n$ mV (n = the number of electrons transferred);
- iii) Wave potentials are independent of scan rate;
- iv) Current is proportional to the square root of the scan rate.

If only some of these criteria are met then the system is said to be quasi-reversible.

The electrochemical properties of the complexes were examined in a dichloromethane/ acetonitrile (4:1) solvent mixture containing 0.1M tetra-*n*-butylammonium tetrafluoroborate as a background electrolyte. The cyclic voltammograms of the macrocycles were recorded at varying scan rates and the results with (10-Cu) are displayed in Figure 19.

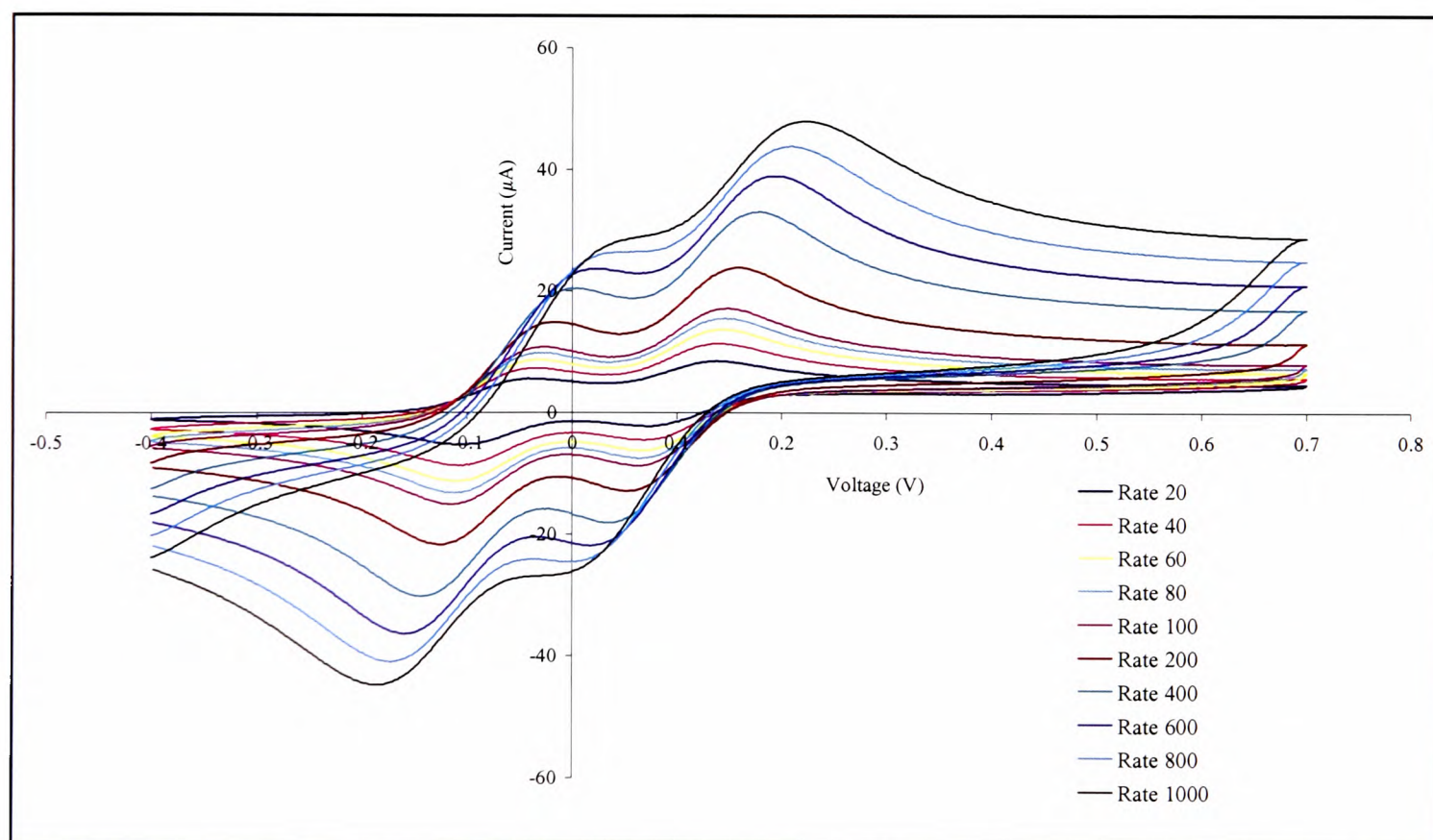


Figure 19 Cyclic voltammograms of the Cu(II/III) oxidation couple of (10-Cu) at varying scan rates (mVs^{-1}), performed in $\text{CH}_2\text{Cl}_2/\text{MeCN}$ (4:1) containing 0.1M TBABF₄ with reference to Ag/AgNO₃ at 293K. Working electrode – glassy carbon (Errors $\pm 5\text{mV}$)

Peak currents of this oxidation process were found to be proportional to the square root of the scan rate (Figure 20), but since the wave potential also varied with increasing scan rate the copper(II/III) couple can only be described as quasi-reversible.

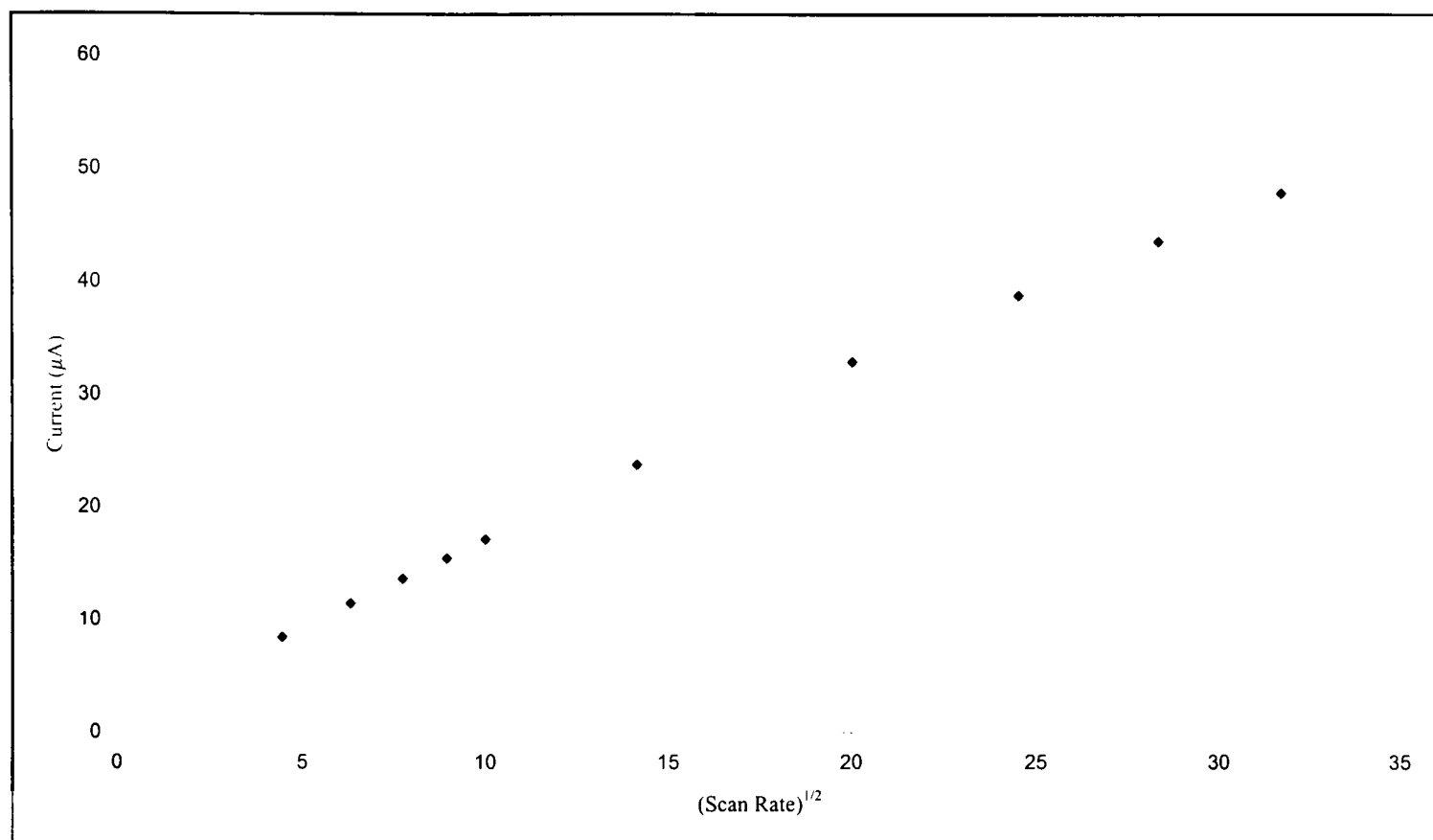


Figure 20 Variation in the square root of the scan rate with the current of the first Cu(II/III) oxidation peak of (10-Cu) in CH₂Cl₂/MeCN (4:1) containing 0.1M TBABF₄ at 293K. Working electrode – glassy carbon

The voltammograms for the copper(II) dithiocarbamate macrocycles all display quasi-reversible oxidation copper(II/III) redox couples at similar potentials (Table 4). As expected, one oxidation wave is observed for the copper(II) bis-(*N,N'*-diethyldithiocarbamate) mononuclear complex (**20**). However, two redox couples are observed for the *m*-xylyl spaced macrocycles (**7-Cu**), (**8-Cu**), (**10-Cu**) and (**11-Cu**). In these cases, the two copper centres are in close proximity to each other through space (for example, just 4.45 Å in the crystal structure of (**8-Cu**)). On electrostatic grounds, therefore, the oxidation of one copper(II) centre perturbs the subsequent oxidation of the other, resulting in an anodic shift in the second oxidation potential. The metal centres are therefore said to be electrochemically coupled. The square wave voltammogram of (**8-Cu**) is displayed in Figure 21, and clearly shows the two oxidation waves for the copper couple.

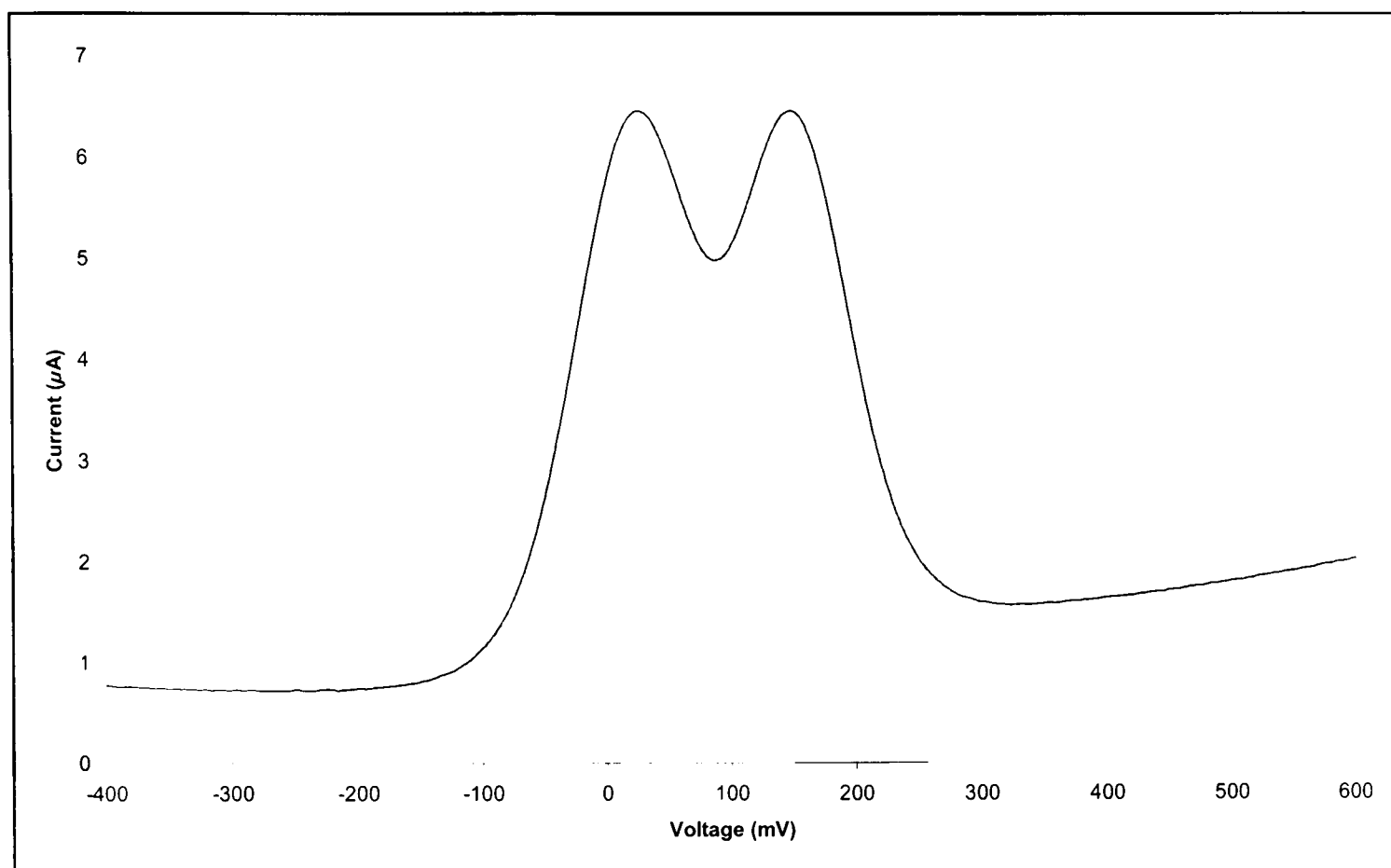


Figure 21 Square wave voltammogram of (8-Cu) (frequency = 5Hz) performed in $\text{CH}_2\text{Cl}_2/\text{MeCN}$ (4:1) containing 0.1M TBABF_4 with reference to Ag/AgNO_3 at 293K. Working electrode – glassy carbon

Similarly, the cyclic and square wave voltammograms of the 3,3'-biphenyl spaced complexes (**13-Cu**) and (**14-Cu**), also display two redox waves, although they do appear broader than those of the *m*-xylyl spaced macrocycles. This is also due to the metal centres electrochemically coupling through space, which is somewhat surprising considering the longer distance between the metal centres³⁶ (refer also to Section 4).

In contrast, the 4,4'-biphenyl and naphthyl spaced macrocyclic complexes (**15-Cu**) and (**18-Cu**), only show one, albeit broad, redox process in their cyclic and square wave voltammograms. This suggests that both copper(II) centres are oxidised at very similar potentials and are sufficiently far apart from one another to behave independently. This is a result of the greater metal-metal distances in the structures (7.62Å in the crystal structure of (**18-Cu**)), and a lack of flexibility in the ligands to allow communication. Electrochemical data related to the copper(II) dithiocarbamate-based macrocycles are displayed in Table 8.

	$E_{1/2}$ (V)	E_{pa} (V)	E_{pc} (V)
(20)	0.08	0.15	0.01
(7-Cu)	0.01, 0.16	0.06, 0.20	-0.03, 0.11
(8-Cu)	0.03, 0.16	0.07, 0.23	-0.01, 0.14
(10-Cu)	-0.07, 0.11	-0.03, 0.15	-0.12, 0.07
(11-Cu)	-0.06, 0.12	-0.02, 0.16	-0.11, 0.08
(13-Cu)	0.01, 0.14	0.04, 0.18	-0.03, 0.09
(14-Cu)	-0.02, 0.09	0.00, 0.14	-0.07, 0.04
(15-Cu)	0.08	0.12	0.03
(18-Cu)	0.13	0.20	0.07

Table 8 Electrochemical data of Cu(II) dithiocarbamate-based macrocycles in CH₂Cl₂/MeCN (4:1) with 0.1M TBABF₄ as the supporting electrolyte using glassy carbon as the working electrode and Ag/AgNO₃ reference electrode, sample 1x10⁻³M. Scan rate 100 mVs⁻¹, frequency 5Hz, T=293K, Errors ±5mV

The variation of the alkyl chain has little effect on the electrochemical properties of the macrocycles. However, the presence of a *tert*-butyl group on the *m*-xylyl spacer results in a significant cathodic shift in the oxidation potential compared to those in the absence of the group (90mV in the case of the first redox couple of **(11-Cu)** compared to that of **(8-Cu)**). This is likely to be the result of an alkyl inductive effect helping to stabilise the electron-deficient copper(III) oxidation state.

3.6 Electron Paramagnetic Resonance

Electron paramagnetic resonance (EPR) has been of great value in studying the binding of transition metal complexes containing unpaired electrons^{37,38}. The investigation into copper-based complexes has been particularly prevalent due to the variations in g-values and hyperfine coupling constants revealing much information about the bonding of the metal

ion³⁹. The EPR spectra of simple copper(II) dithiocarbamate complexes has previously been examined, revealing structural and coordination information of the structures^{40,41}. A series of studies were therefore undertaken on a variety of copper-based dithiocarbamate complexes, in collaboration with Dr J. P. Maher at Bristol University (refer to Appendix Three).

The EPR spectrum of the mononuclear complex, **(20)** at 296K, displays a characteristic sharp four-line spectrum in dichloromethane (Figure 22). The four lines are a result of hyperfine splitting (A) between the unpaired electron and the copper nucleus ($I = 3/2$). The g-value of **(20)** is close to that of a free electron (2.002), which confirms that the metal-sulphur bond in copper(II) dithiocarbamate complexes have a high degree of covalency (Table 9), a feature also shown through X-ray crystallographic studies. The sharp-line nature of the solution spectrum observed, is evidence that there is little chemical exchange on and off the fifth and sixth coordination sites of the copper, hence very little chemical exchange broadening is seen^{42,43}. There is also a shoulder on the high field peak, which is just resolvable due to isotopic splitting with the copper nucleus ⁶³Cu (69.2%) and ⁶⁵Cu (30.8%).

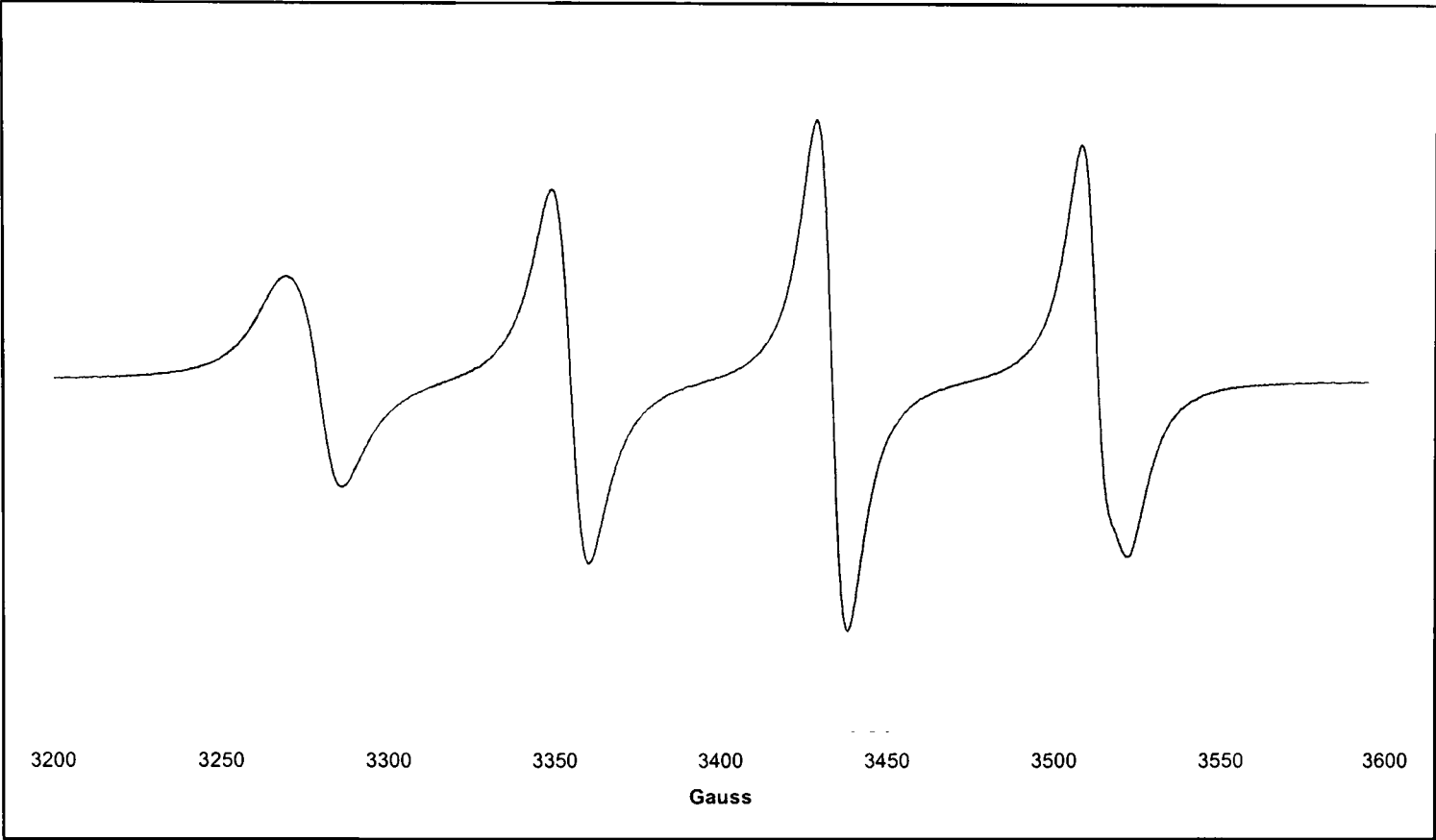
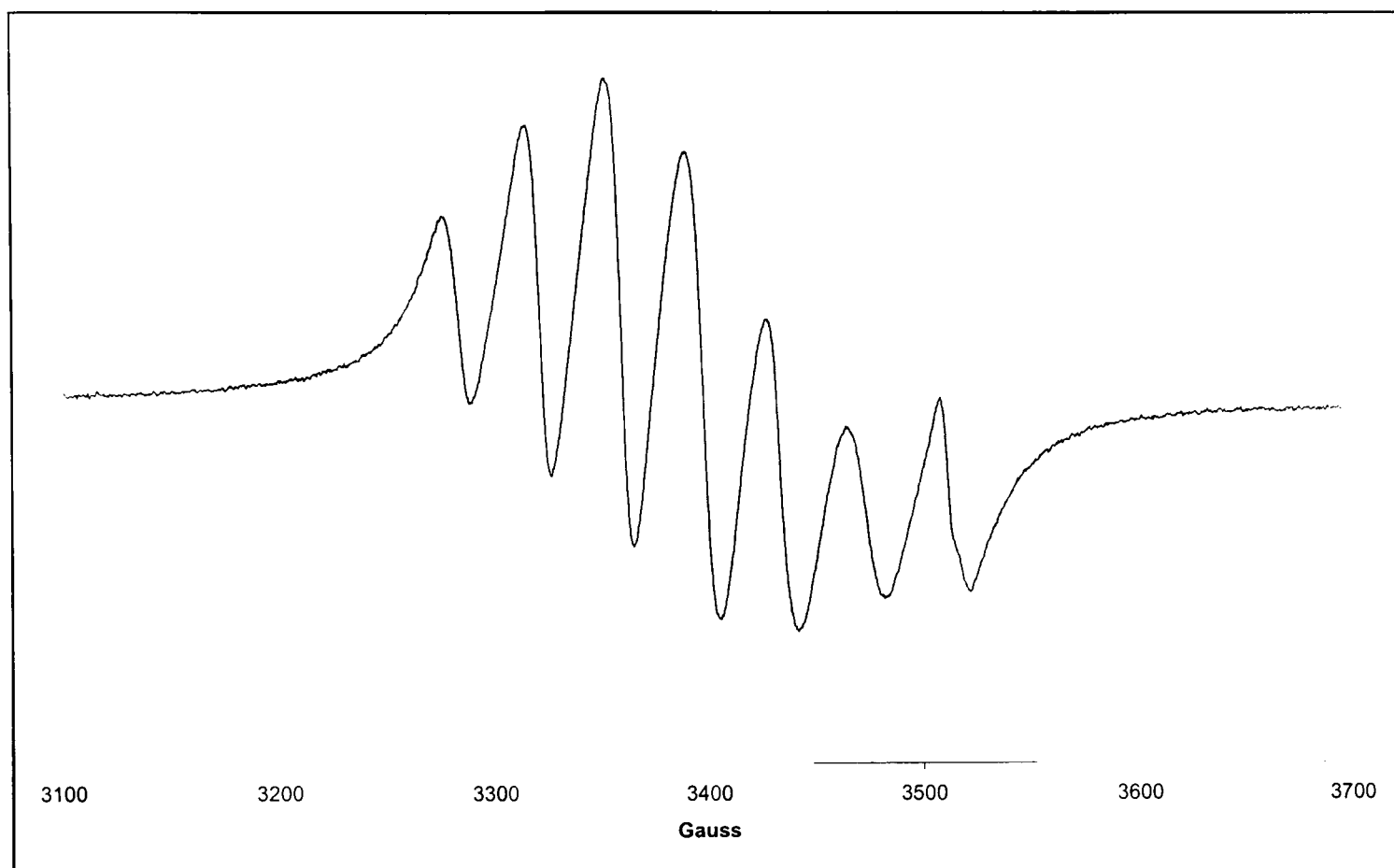


Figure 22 EPR spectrum of mononuclear Cu(II) dithiocarbamate complex (20) in CH₂Cl₂ at 296K

	g_{iso}	A_{iso} (mT)
(20)	2.047	7.90
(7-Cu)	2.046	3.84
(11-Cu)	2.044	3.83
(13-Cu)	2.048	7.90 and 3.90

Table 9 EPR data for mono- and dinuclear Cu(II) dithiocarbamate complexes in CH₂Cl₂ at 296K

In contrast to the four lines observed in the EPR spectrum of (20), the dinuclear copper(II) dithiocarbamate complexes of (7-Cu) and (11-Cu) display seven lines in their spectra. The spectrum of (7-Cu) is highlighted in Figure 23.

Figure 23 EPR spectrum of (7-Cu) in CH₂Cl₂ at 296K

Both of the *m*-xylyl spaced copper(II) macrocycles (**7-Cu**) and (**11-Cu**) display similar spectra. The observed 1:2:3:4:3:2:1 multiplet would be expected from electron hyperfine interactions between two $I = 3/2$ nuclei, indicating that the unpaired electrons on each copper nucleus interact with both copper nuclei. The observed isotropic hyperfine coupling for the dinuclear complex is apparently half that for the monomeric (**20**), a situation that must be due to strong electron-electron through-bond coupling (J-coupling) between the two copper centres, and which causes the observed A-value to be halved. This also shows that $J \gg A$,⁴⁴ and is a feature which has recently been observed in many paramagnetic dinuclear tris(pyrazolyl)boratomolybdenum centres⁴⁵. Thus the A-value for (**7-Cu**) and (**11-Cu**) is 7.6mT, very similar to the A/2 for the monomeric complex (**20**).

The observed isotropic g-values and A-values for the dinuclear complexes are in agreement with published values for other square planar copper(II) bis-(dialkyldithiocarbamates) and other square planar CuS₄ ligand sets. Analysis of the g- and A-parameters in such complexes are consistent with a very strong covalent interaction between the copper and the sulphurs.

and an essentially square planar ground state. The strong covalency of the copper-sulphur bonds allows the hyperfine interaction between the copper nuclei, which occurs via two 12-bond paths through the connecting ligands.

The EPR spectrum of the 3,3'-biphenyl spaced copper(II) dithiocarbamate macrocycle (**13-Cu**) was also recorded in order to observe the effect in varying the aromatic spacer. This spectrum was also recorded in dichloromethane and is displayed in Figure 24.

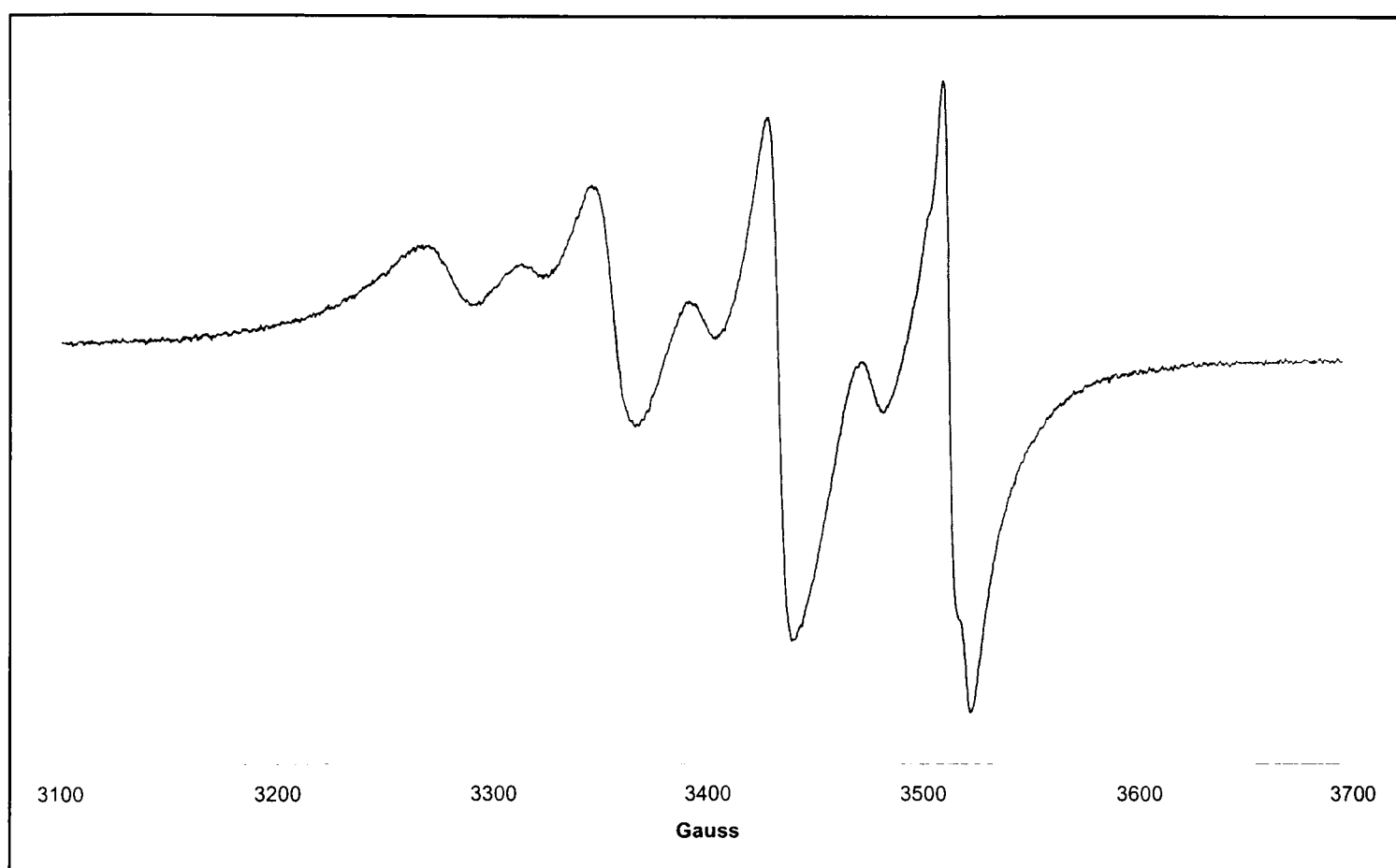


Figure 24 EPR spectrum of (**13-Cu**) in CH_2Cl_2 at 296K

The spectrum of the 3,3'-biphenyl spaced macrocycle (**13-Cu**), appears more complicated than the *m*-xylyl spaced macrocycles (**7-Cu**) and (**11-Cu**). It possesses two different sets of signals, one which shows little or no electronic coupling between the two copper centres (giving rise to four large peaks in the spectrum) and one which does (giving three smaller peaks between the larger ones). The most likely explanation is the existence of different conformations of the macrocycle, with varying degrees of copper-copper interaction occurring, in solution.

This is also in agreement with the electrochemical data, where two peaks are visible in the

cyclic and square wave voltammograms, albeit significantly broader - a possible effect of conformational flexibility.

3.6.1 Low Temperature EPR

The spectra of **(7-Cu)** and **(11-Cu)** were also measured at 10K in dichloromethane- d_2 /toluene- d_8 glasses to see if triplet spectra could be observed. The resulting spectra are displayed in Figure 25.

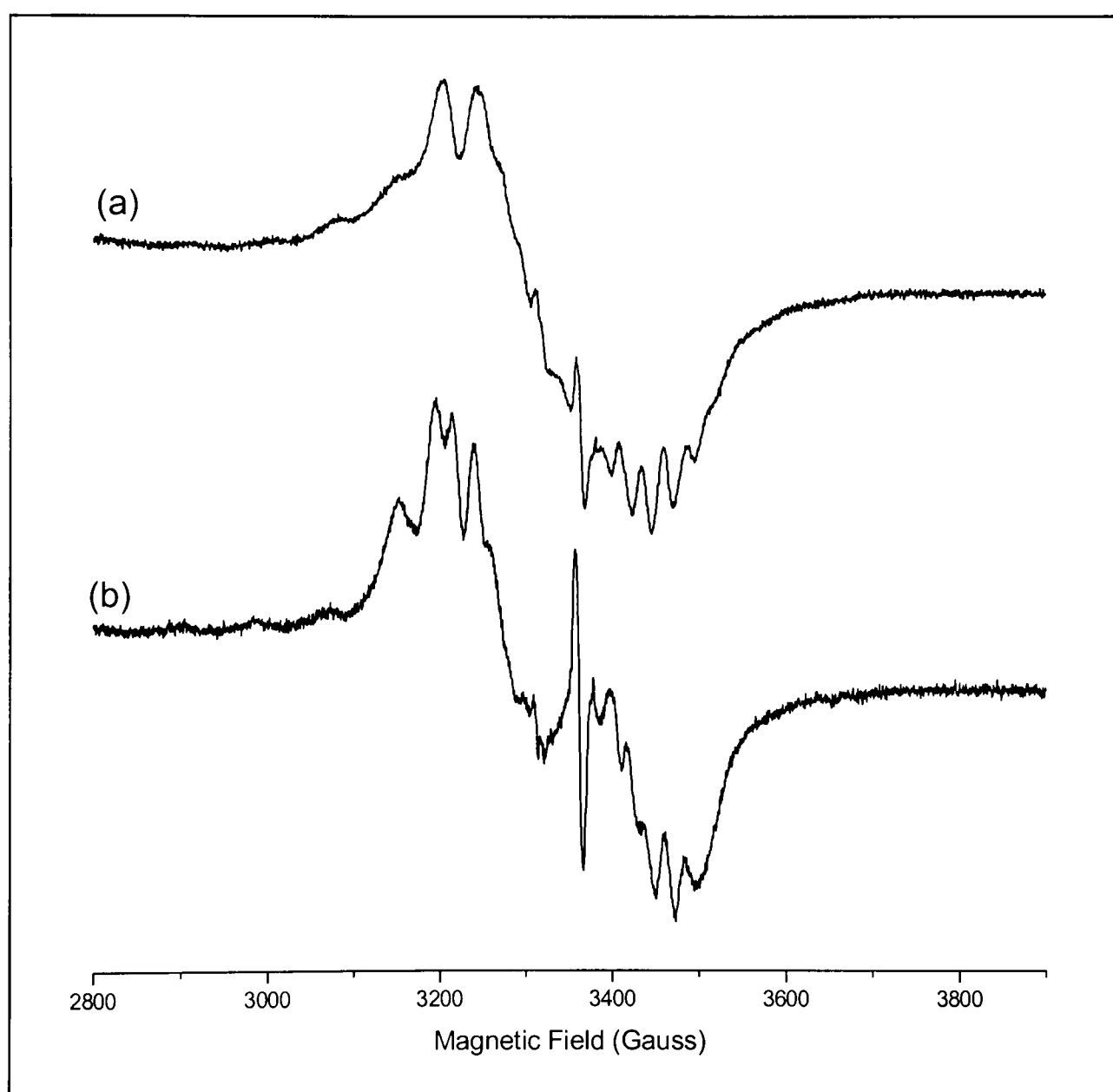


Figure 25 CW EPR spectra, recorded at 10K, of the dimeric Cu(II) dithiocarbamate complexes (a) (7-Cu), and (b) (11-Cu)

The resulting spectra are significantly more complex than those determined at room temperature. For both complexes the $g = 2$ signal is a complex multiplet with copper hyperfine interactions on several of the component absorptions. Depending on the symmetry

of the copper sites, either four or six transitions should be observable⁴⁶, but for neither **(7-Cu)** and **(11-Cu)** are these clearly discernable. The spectrum for **(11-Cu)** is better resolved than that for **(7-Cu)**, and the fact that the spectrum of the former is spread over a larger field range may be evidence for stronger copper coupling in the former complex. In both spectra one side of a 1:2:3:4:3:2:1 multiplet with a hyperfine coupling of about 8.5mT is visible. The single sharp inflection in the middle of both spectra (stronger again for **(11-Cu)** than for **(7-Cu)**) may be due to a free radical impurity, since the spectra were measured in air. In addition, **(11-Cu)** shows an extremely weak ($g = 4$) half-field signal. Since an analogous signal is not observed for **(7-Cu)**, this suggests **(11-Cu)** experiences stronger coupling between the copper centres.

3.6.2 ENDOR

ENDOR (electron-nuclear double resonance) is an extension to the technique of electron paramagnetic resonance (EPR)⁴⁷. It may be considered as a form of EPR that combines the high resolution and nuclear selectivity of an NMR experiment with the sensitivity of an EPR experiment⁴⁸. Such experiments often lead to an increase in spectral resolution and decrease in complexity in comparison to standard EPR techniques. ENDOR has already been used to provide an insight into the bonding of paramagnetic transition metal complexes^{49,50}. ENDOR measurements have been performed on a variety of copper(II)-based macrocyclic complexes by Dr R. Farley and Dr D. Murphy, Cardiff University.

To our knowledge no ENDOR measurements have been made for copper(II) dithiolates such as these, even as monomers. ENDOR measurements were therefore attempted on these complexes to see whether evidence for long range ^1H couplings could be observed. The ENDOR spectrum of the mononuclear copper(II) dithiocarbamate complex, **(20)**, is displayed in Figure 26.

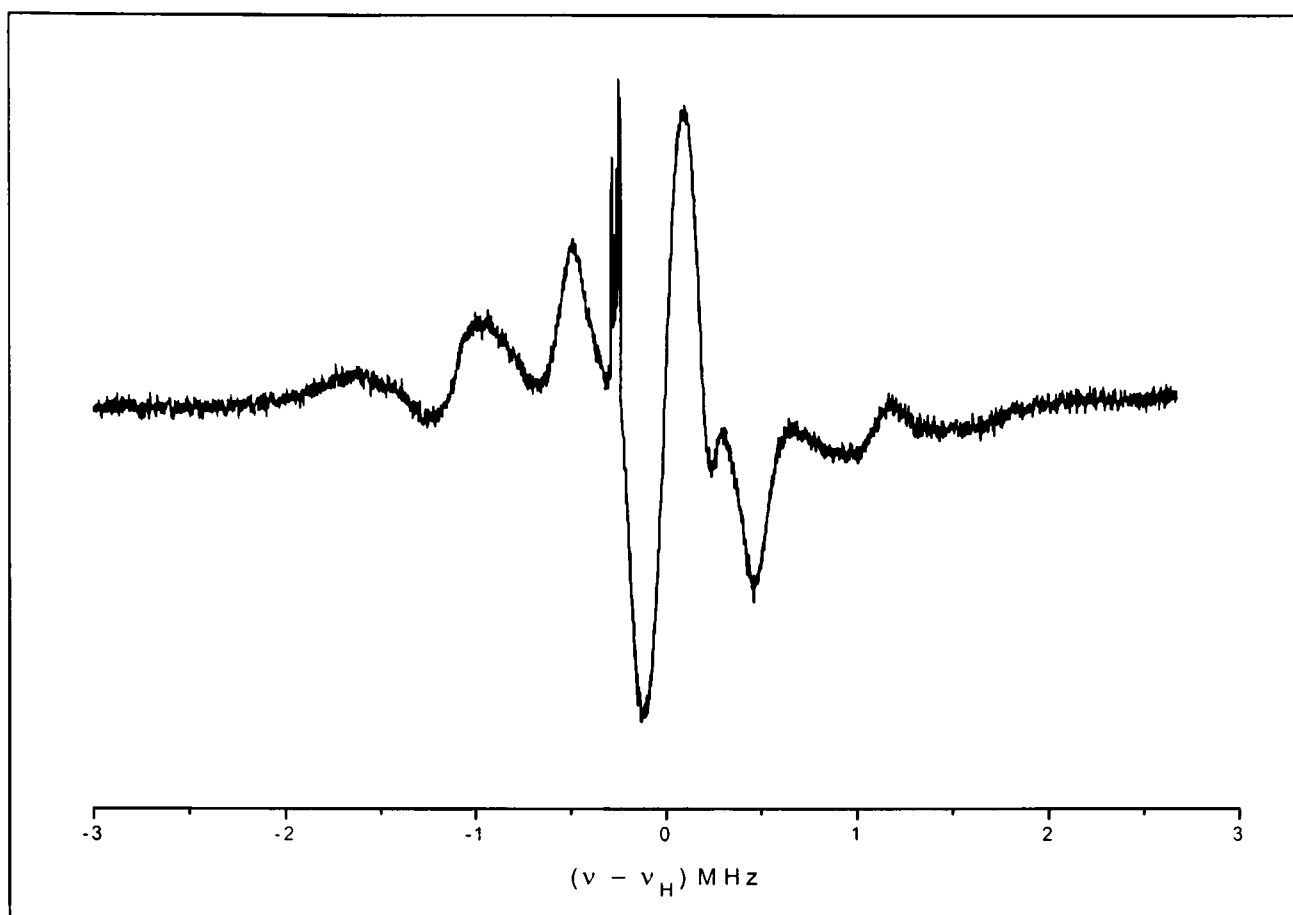


Figure 26 ENDOR spectrum of (20) recorded at 10K at a static field of 3357 G

The mononuclear complex, (20), shows a very clear multiplet ^1H -ENDOR centred at 14MHz due to hyperfine couplings with the C_2H_5 groups, but there is no ^{14}N -ENDOR visible from the nitrogens of the $\text{N}(\text{C}_2\text{H}_5)_2$ groups.

For the dinuclear copper(II) dithiocarbamate-based complexes, (7-Cu), (11-Cu) and (13-Cu) the ^1H -ENDOR consists of some very broad, poorly resolved absorptions on either side of a sharp central peak. The sharp centre peak is probably due to the desired weak long range ^1H interactions. The ^1H -ENDOR from the nearby protons on the N-centre are probably complicated by relaxation effects associated with the triplet. The ENDOR spectrum of (13-Cu) is shown in Figure 27.

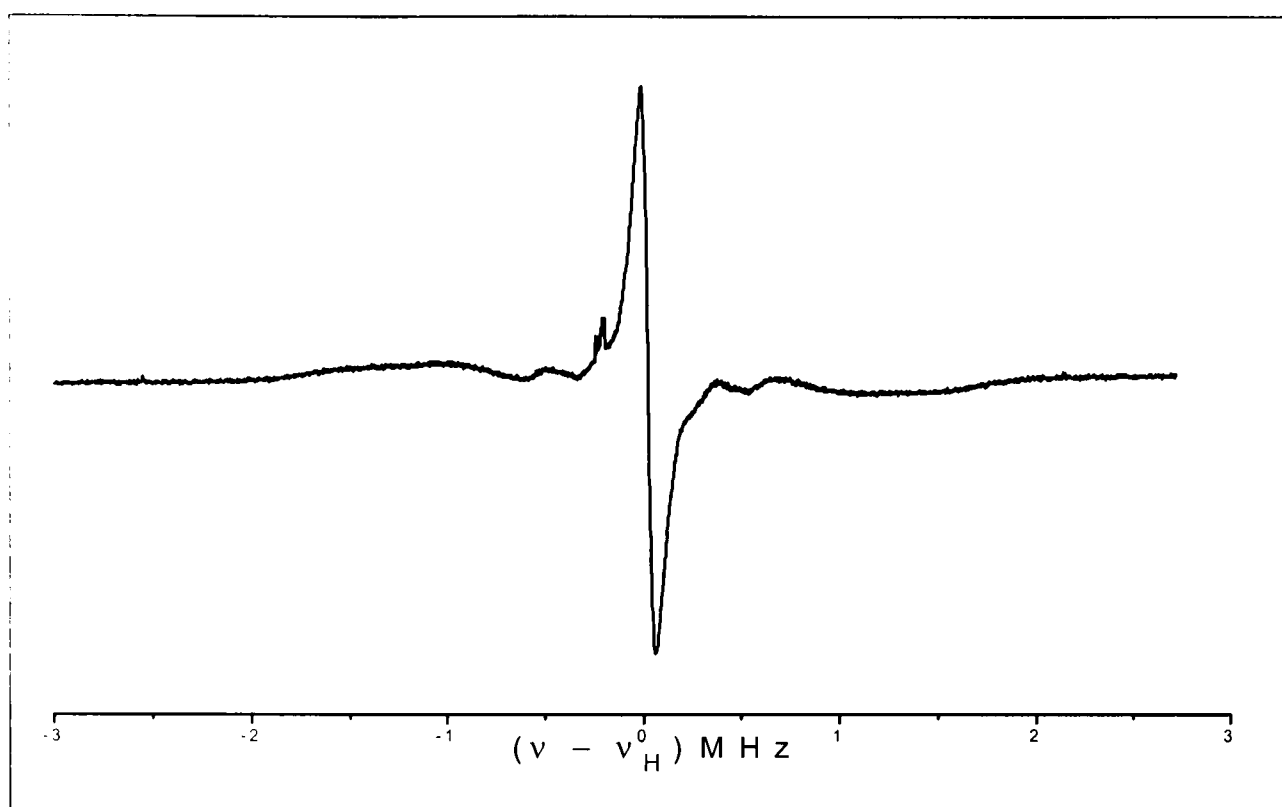


Figure 27 ENDOR spectrum, recorded at 10K, of the dimeric Cu(II) complex (13-Cu) (Static field = 3480 G)

4 3,3'-Biphenyl-Spaced Macrocyclic Complexes

It was originally assumed that the copper(II) dithiocarbamate 3,3'-biphenyl-spaced macrocyclic complexes assumed a dinuclear structure whereby the transition metal dithiocarbamate moieties are separated via a planar aromatic group. This conformation would be in agreement with the X-ray crystal structures of the various *m*-xylyl and naphthyl-spaced complexes that have been solved for these two spacers. Whilst it is not possible to record NMR spectra of the paramagnetic copper 3,3'-biphenyl-based structures, both electrospray mass spectrometry and elemental analysis showed the formation of the desired pure dinuclear products. However, further electrochemical, EPR and X-ray crystallographic studies upon these samples have been difficult to rationalise using this original model.

Firstly, the electrochemical studies of (13-Cu) reveal that the two copper centres are electrochemically communicating, as a broad oxidation wave with two peaks is observed. This is somewhat surprising considering that in the similar sized macrocyclic complex (18-Cu) no such communication is observed, presumably due to the metal centres being too

distant. Similarly, the EPR spectrum of **(13-Cu)** displays two sets of signals suggesting that there may be at least two different conformers of the macrocycle; one where the metals were able to communicate and one where they were not.

The X-ray single crystal structure of **(13-Cu)** was solved and surprisingly revealed the formation of a cage-like copper(I) dithiocarbamate complex. One feature of this structure is the flexibility of the biphenyl-spaced ligand, and its ability to twist out of plane. This suggests that the formation of a range of conformations may be possible with this ligand.

Two possible conformations the macrocycles could adopt are illustrated in Figure 28. This shows the standard dinuclear complex (I) similar to that of **(18-Cu)**, with coplanar aromatic-spacing groups and dithiocarbamate moieties. It also shows a twisted conformation (II), that the flexible ligand may be able to adopt. Here, the molecule adopts a “figure of eight” structure by coordinating via the copper(II) centres to the opposite corner of the other ligand. This would have the effect that the metal centres are close together, and this may in turn be stabilised by favourable axial copper-sulphur interactions.

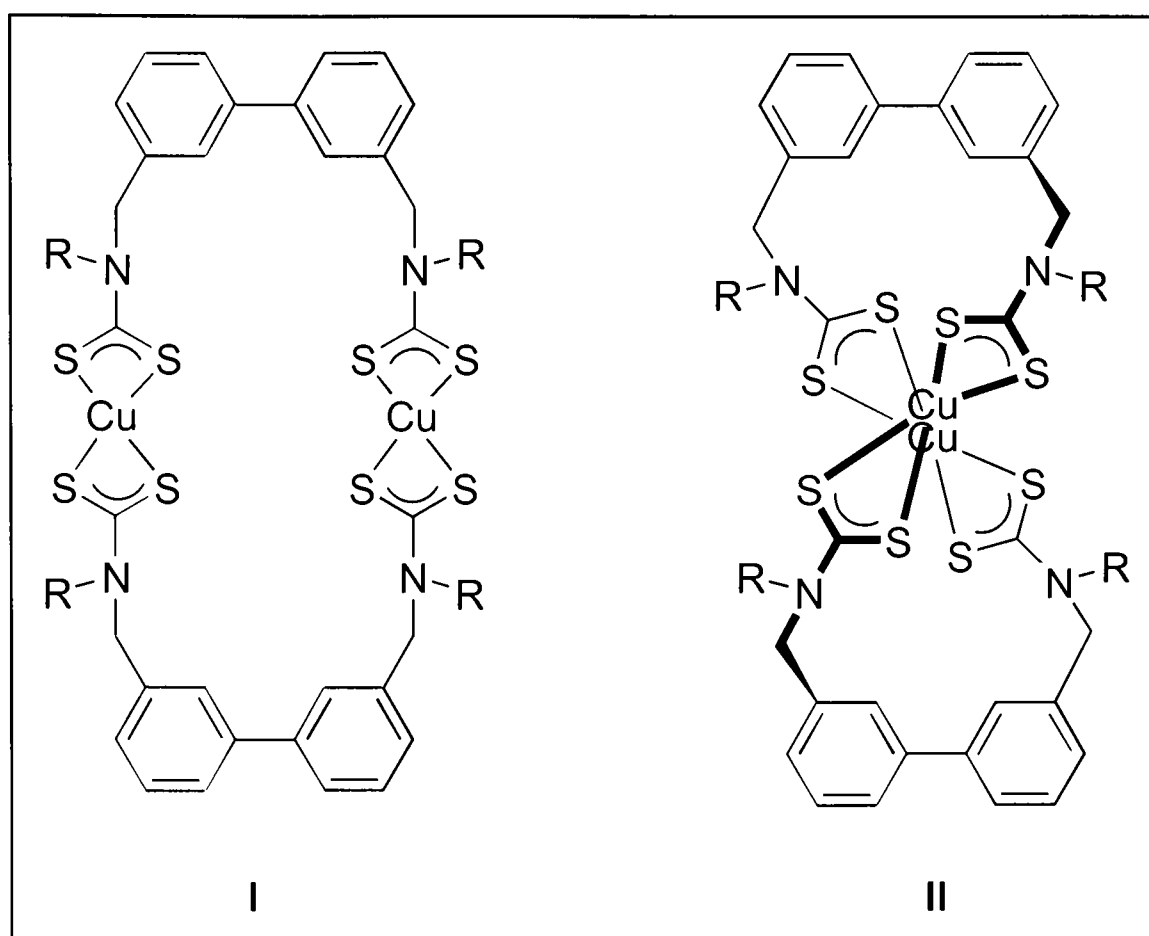


Figure 28 Possible conformations of Cu(II) 3,3'-biphenyl-spaced dinuclear macrocyclic complexes

If the more flexible 3,3'-biphenyl spaced ligand is able to form more than one conformation in solution, then it would explain the variation in both the electrochemical and EPR data. Where the complex adopted conformation II, there would be expected to be significant nuclear coupling, due to their close proximity in space, whereas this would be substantially reduced in conformation I. This difference explains how a mixture of the two conformers would generate the responses seen for these complexes.

In addition, if the molecule were to adopt conformation II in solution, then it could help to explain the formation of the copper(I) cage-like configuration in the X-ray structure of (**13-Cu**). The conformation of the biphenyl-based ligands found in the X-ray crystal structure is similar to that proposed for conformation II. It is possible that the adoption of this conformer preorganises the structure such that, over time, the reduced form of the complex it is able to crystallise out. It is likely that the reduction of the copper(II) to copper(I) may occur via the corresponding oxidation of the liberated dithiocarbamate ligands to thiuram disulphides ($R_2NCS_2S_2NCR_2$) (Figure 29).

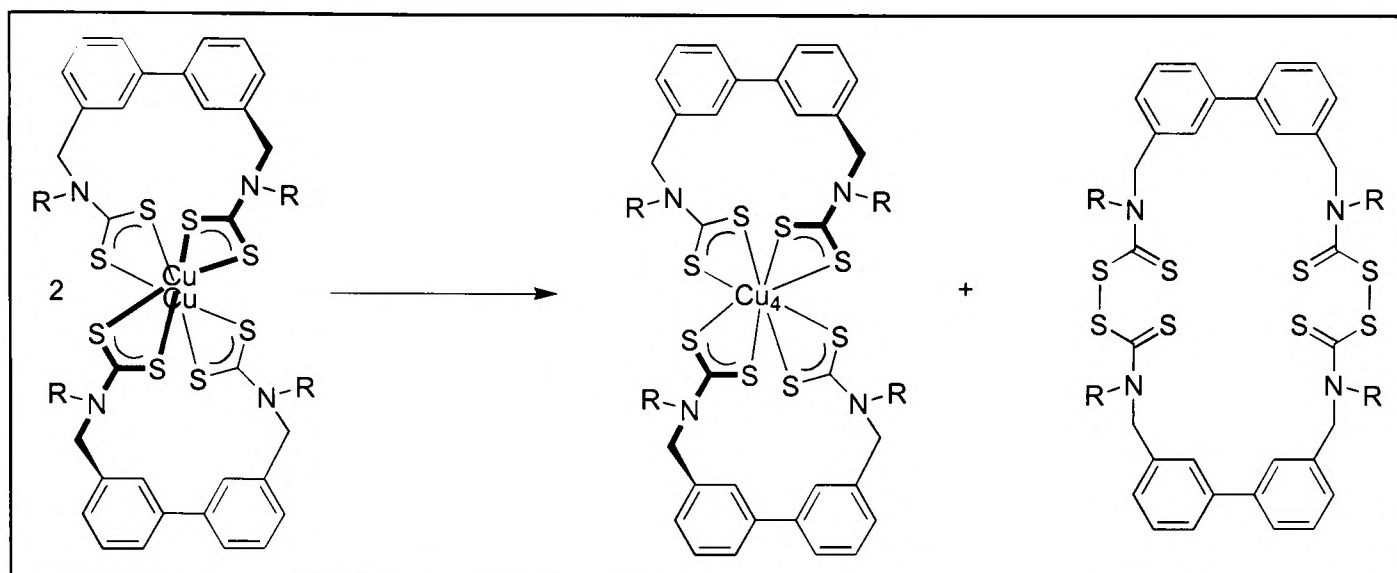


Figure 29 Potential route for the formation of the Cu(I) cage structure

This was further investigated via the examination of the copper(II/I) reduction wave. Whereas this potential was reversible in the acyclic (**20**), the process was found to be irreversible in the case of dinuclear macrocyclic complexes. A variety of dinuclear macrocyclic complexes were studied by square wave voltammetry (Figure 30) and their electrochemical data related to the copper(II/I) reduction potentials are displayed in Table 10.

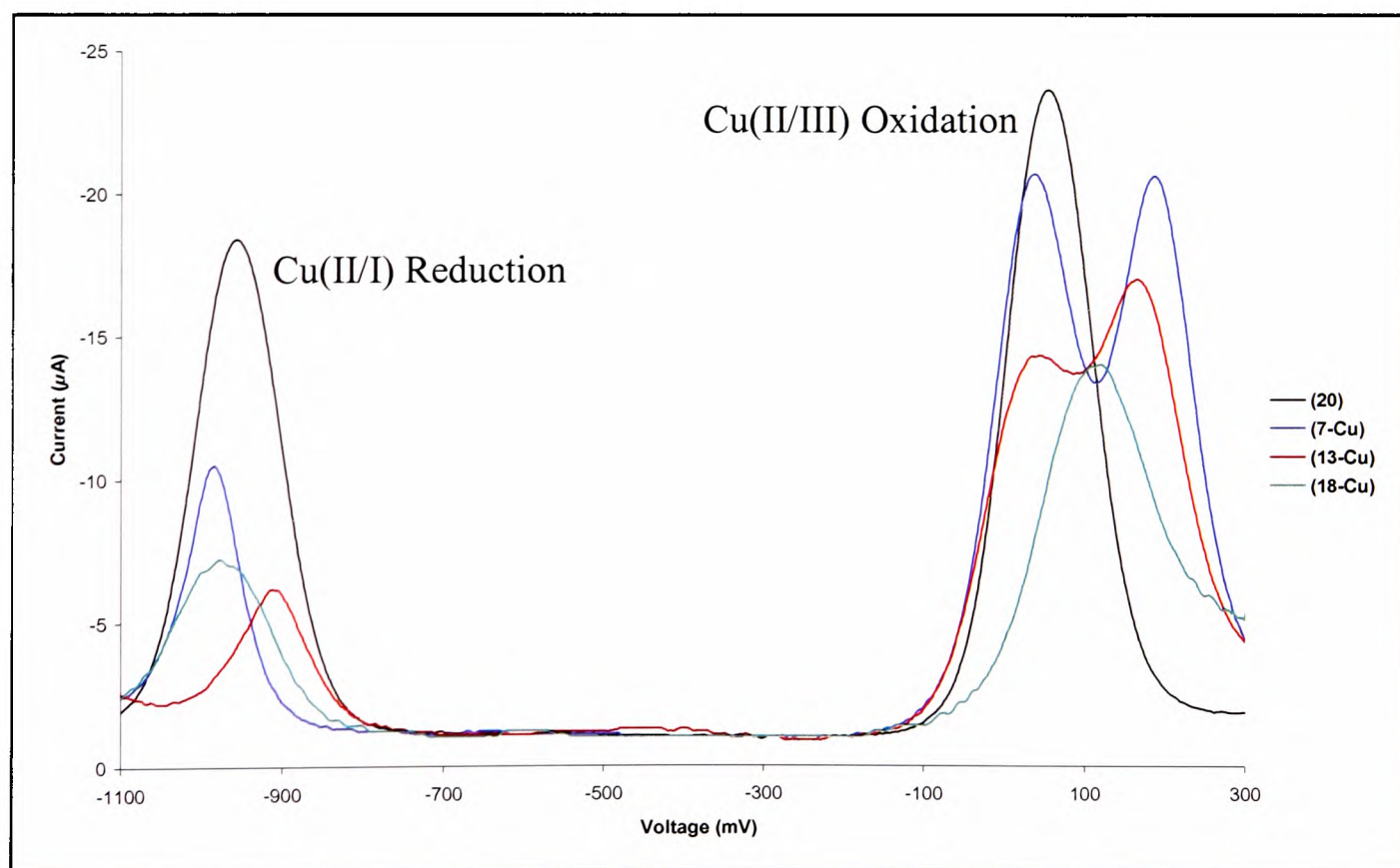


Figure 30 Square wave voltammograms of the Cu(I/II) and Cu(II/III) oxidation waves of (**20**), (**7-Cu**), (**13-Cu**) and (**18-Cu**) (frequency = 5Hz) performed using a glassy carbon working electrode in $\text{CH}_2\text{Cl}_2/\text{MeCN}$ (4:1) containing 0.1M TBABF_4 with reference to Ag/AgNO_3 at 293K, samples $\sim 2 \times 10^{-3}\text{M}$

	$E_{1/2}$ (V) Cu(II/I)
(20)	-0.96
(7-Cu)	-0.98
(13-Cu)	-0.91
(18-Cu)	-0.98

Table 10 Electrochemical data of the Cu(II/I) reduction potential for a range of Cu(II) macrocycles in CH₂Cl₂/MeCN (4:1) with 0.1M TBABF₄ as the supporting electrolyte using glassy carbon as a working electrode and Ag/AgNO₃ reference electrode, sample $\sim 2 \times 10^{-3}$ M, frequency 5Hz, T=293K, errors ± 5 mV

Unlike the copper(II/III) oxidation potential, the copper(II/I) reduction wave occurs as a single peak. Interestingly, the reduction of the 3,3'-biphenyl spaced macrocycle **(13-Cu)** is 50mV easier than the acyclic, mononuclear complex **(20)**. This is in contrast to the *m*-xylyl and naphthyl spaced macrocycles **(7-Cu)** and **(18-Cu)** where the analogous process is observed to be 20 mV more difficult than that of **(20)**. This observation is in agreement with the 3,3'-biphenyl spaced complex being preorganised to form a copper(I) dithiocarbamate-based complex. Similarly, the macrocycles **(7-Cu)** and **(18-Cu)** are too rigid to undergo this intramolecular reduction, and hence their copper(II/I) reduction potentials are significantly greater.

It is therefore possible that the copper(II) 3,3'-biphenyl spaced macrocycles adopt a “figure of eight” conformation, in solution. This structure is allowed due to the flexible nature of the aromatic spacing ligand with its formation being entropically favourable. The wrapping of the dinuclear complex results in the close proximity of the copper(II) centres, leading to electrochemical communication between the metals. In addition, the formation of this conformation preorganises the 3,3'-biphenyl spaced architecture for the reduction to the corresponding copper(I)-based dithiocarbamate complex. This feature is highlighted both by the greater ease in the electrochemical reduction of **(13-Cu)** in comparison to the acyclic

analogue (**20**) and the X-ray crystal structure obtained for the copper(I)-based complex. Examination of the NMR spectra of the analogous nickel(II), palladium(II) and platinum(II) complexes does not suggest the formation of conformationally-variable structures. However, it has previously been seen that the nature of the transition metal employed in the metal-directed self-assembly process does not significantly effect the conformation adopted in dinuclear macrocyclic complexes. It is therefore likely that these complexes also adopt the same “figure of eight” conformation.

5 Further Syntheses

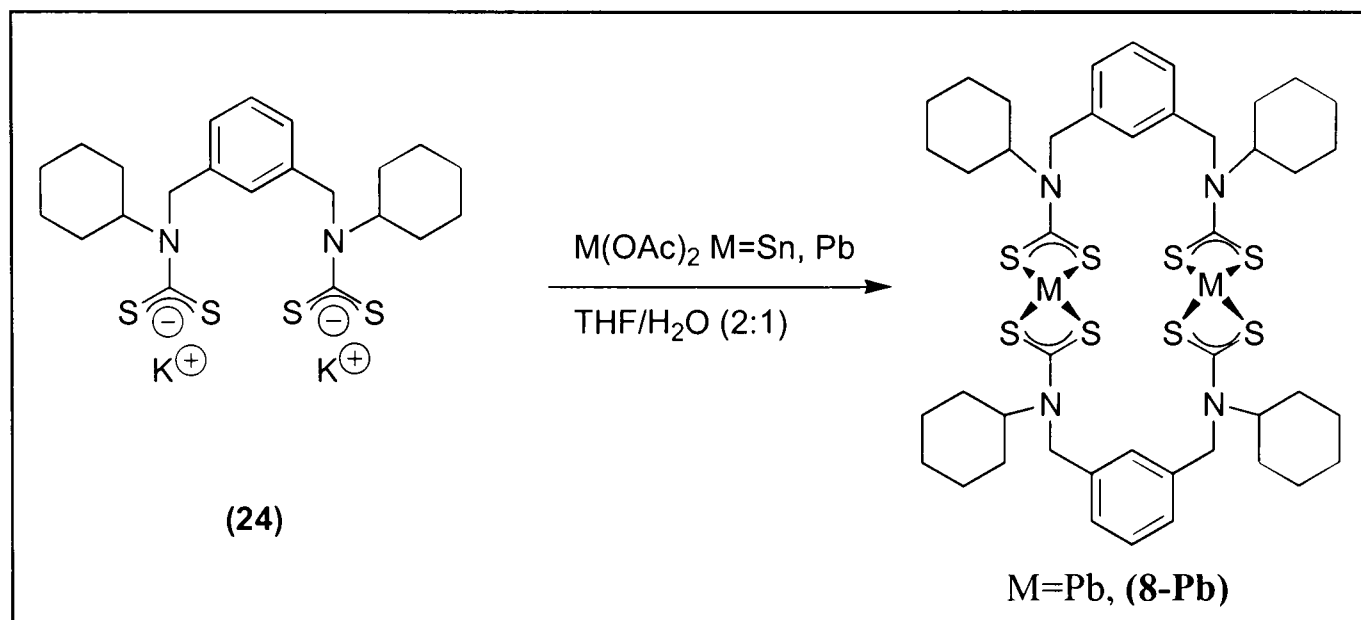
It has been demonstrated that macrocyclic dithiocarbamate complexes can be formed by the incorporation of square planar copper(II) and Group 10 divalent metal ions. Metals with contrasting stereochemical requirements, and the use of different synthetic methods were examined, to determine whether they could also yield macrocyclic complexes.

5.1 Group 14 Metals

Divalent Group 14 metal ions have been shown to form complexes with the dithiocarbamate ligand, with both tin(II) and lead(II) dithiocarbamates possessing a stereochemically active lone pair⁵¹. In the solid state, both complexes adopt a square based pyramidal structure, although that of tin(II) bis-(*N,N'*-diethyldithiocarbamate) is significantly twisted⁵². The availability of these lone pairs offers the possibility of complexing Lewis acidic guests. The synthesis of such species was therefore undertaken.

Tin(II) and lead(II) acetate was added to a tetrahydrofuran/water (2:1) solution of the potassium bis-dithiocarbamate *m*-xylyl spaced salt (**24**) (Scheme 6). Unfortunately, the attempted synthesis of the tin(II) macrocyclic complex failed to afford the desired macrocyclic structure. However, the analogous lead(II) macrocycle (**8-Pb**) could be isolated

in 40% yield, after purification by precipitation with ethanol. The compound was characterised by ^1H and ^{13}C NMR, elemental analysis and electrospray mass spectrometry.



Scheme 6 Synthesis of dinuclear Pb(II) dithiocarbamate macrocyclic complex (8-Pb)

The ^1H NMR is very broad at room temperature, but sharpens upon raising or lowering the temperature (Figure 31). At elevated temperatures the spectrum is extremely broad with one peak observable for the CH_2 signal at 5.2 ppm. Lowering the temperature resulted in the appearance in three broad resonances, which sharpen up to two outer doublets and a central broader singlet (typical of a *m*-xylyl spaced macrocycle possessing cyclohexyl side chains). Further cooling to 223K, results in a decrease in intensity of the central peak. This feature, (also observed for the analogous nickel and palladium-based macrocycles) could be a result of two conformations existing in solution, with one of these either precipitating out of solution or converting to the other conformer at this lower temperature.

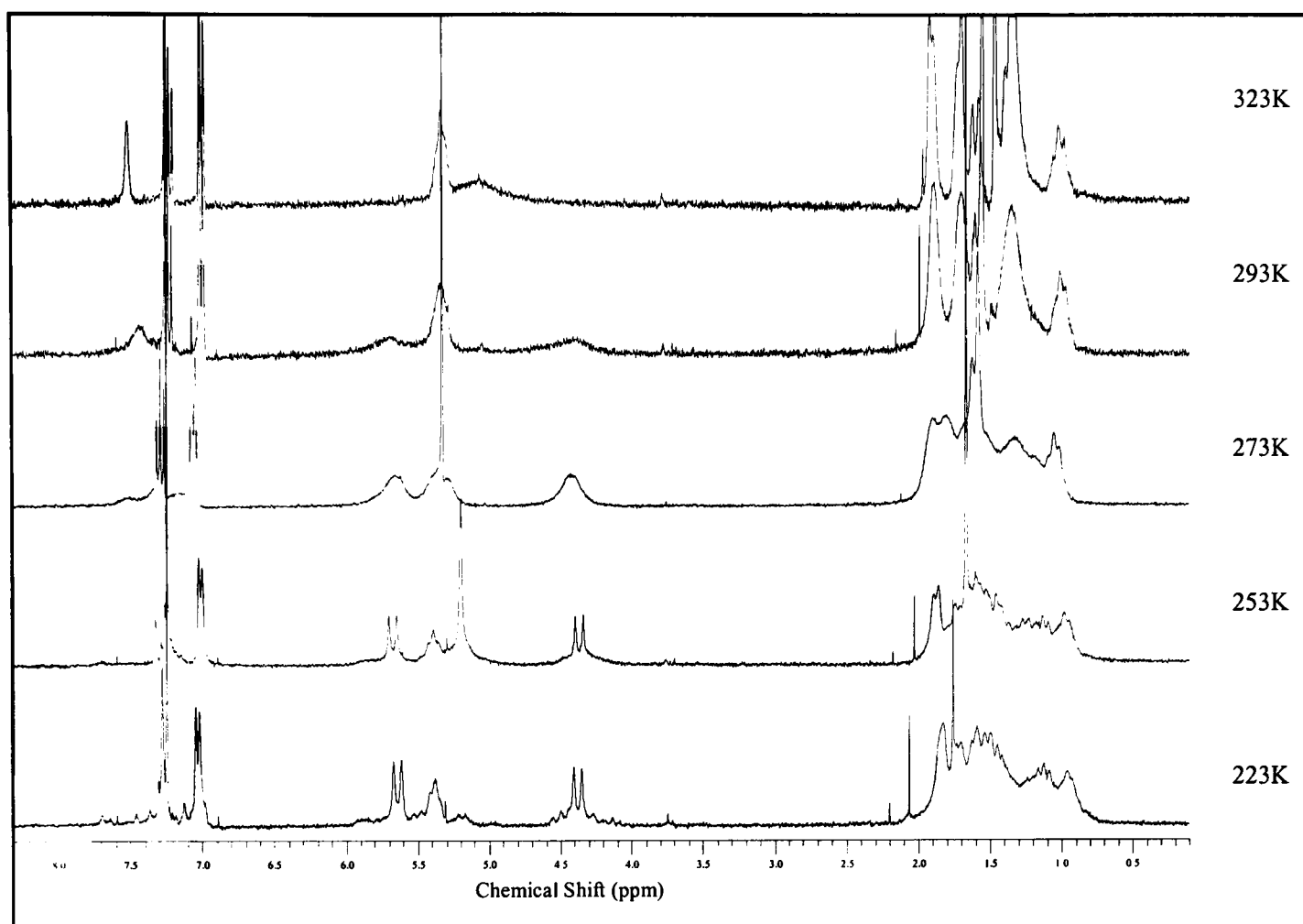


Figure 31 Variable temperature ^1H NMR experiments on (8-Pb) (300 MHz, CDCl_3)

The temperature variation of the ^1H NMR properties of the lead(II) macrocycle, suggest significant lability of the lead-dithiocarbamate bond on the NMR timescale leading to fluxionality within the structure.

5.2 Solventless Reactions

In recent years, research in ‘Green chemistry’ has developed rapidly⁵³. Moving away from the reliance on organic solvents in chemical syntheses is important in the drive towards benign chemical technologies. Organic solvents are high on the list of toxic or otherwise damaging compounds as well as being relatively costly and potentially dangerous to handle in large amounts. These factors have led to a vast expansion in the field of solventless reactions.

Otera and co-workers recently reported that supramolecular self-assembly reactions may also be performed under solvent-free conditions⁵⁴. They demonstrated that multi-nuclear two- and three-dimensional palladium(II)- and platinum(II)-pyridyl based architectures could be

synthesised merely from the grinding together of the constituent parts in a pestle and mortar at room temperature. This method not only resulted in the same products as seen by the analogous reactions in solution, but also gave rise to significantly shorter reaction times and very high yields.

It was investigated as to whether dithiocarbamate complexes could similarly be synthesised through solvent-free conditions. Initially, the synthesis of two simple dithiocarbamate complexes was attempted. This was achieved through grinding together a solid mixture of sodium bis-(*N,N'*-diethyldithiocarbamate) with both copper(II) and nickel(II) acetate, in a pestle and mortar. Upon grinding the solids together, there was an instant brown and green colour change, reminiscent of the formation of the respective dithiocarbamate complexes. Grinding continued for one minute, after which the complex was extracted by the addition of dichloromethane. Subsequent analysis via electrospray mass spectrometry and NMR spectrometry revealed the formation of the desired compounds **(20)** and **(21)**, although their yields of 63 and 78% respectively, are lower than the near quantitative yields achieved for the corresponding solution state reaction. This is primarily due to the ineffective mixing of the solids in this method.

It was further examined to see whether solvent-free reactions could also be used to synthesise a dinuclear macrocyclic dithiocarbamate complex. A similar procedure was therefore undertaken using an equimolar amount of the potassium bis-dithiocarbamate salt **(24)** and copper(II) and nickel(II) acetate. Once again, characteristic colour changes were observed and the resulting residues extracted into dichloromethane. Analysis of the solutions revealed the formation of the desired products **(8-Cu)** and **(8-Ni)**. The ¹H NMR spectrum of **(8-Ni)** is shown in Figure 32.

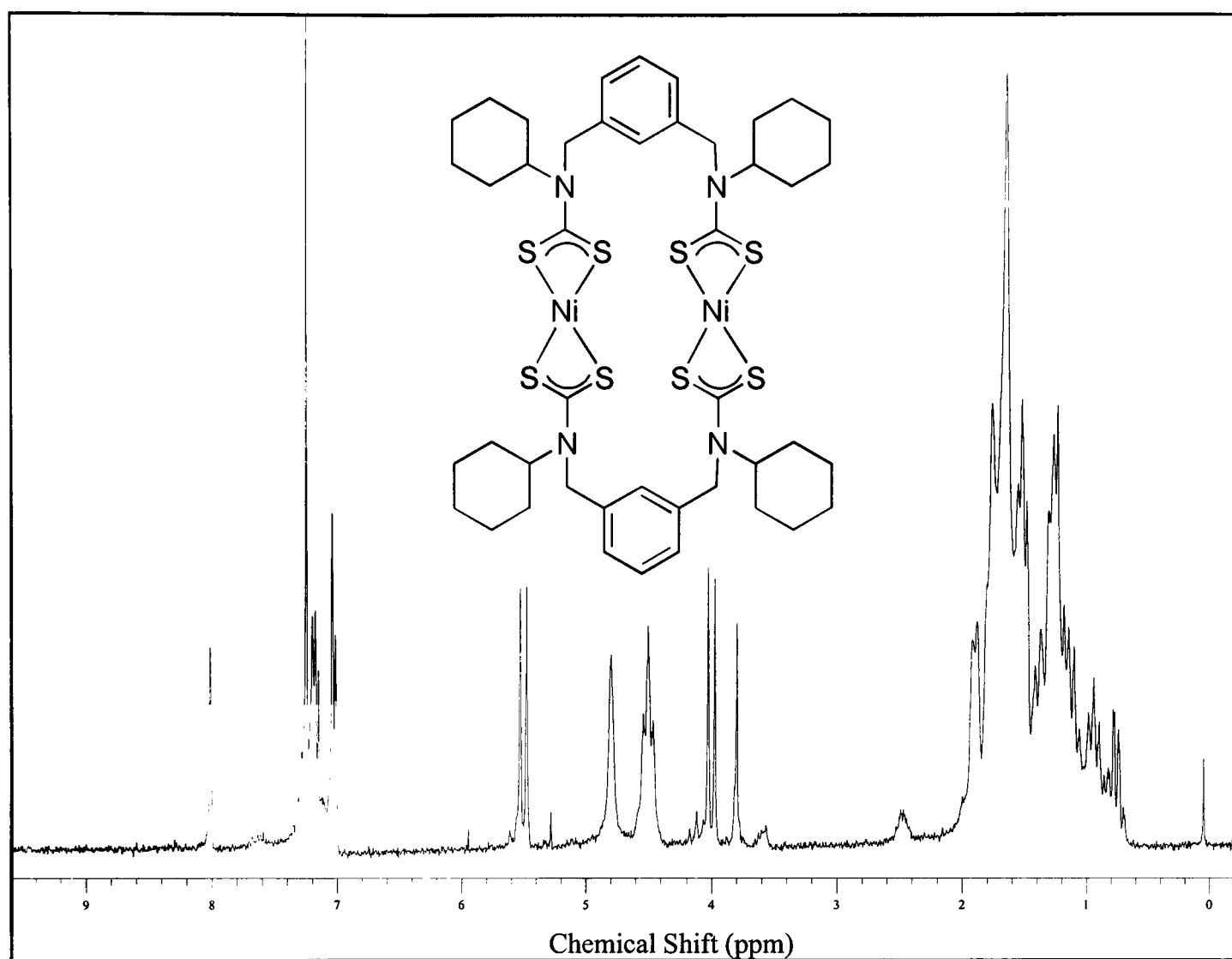


Figure 32 ^1H NMR spectrum of (8-Ni) synthesised from grinding of (24) and $\text{Ni}(\text{OAc})_2$ (300MHz, CDCl_3)

The resulting spectrum shows the characteristic peaks of a *m*-xylyl spaced cyclohexyl chained macrocycle, with the ArCH_2 protons displayed as two geminally coupled doublets astride a central singlet in the mid-field region. This clearly demonstrates the formation of the desired macrocyclic product, although the yields of 34 and 41% for (8-Cu) and (8-Ni) respectively, again are low due to poor mixing of the solid starting materials. Nevertheless, it has been demonstrated that dithiocarbamate complexes may also be synthesised in a solvent-free environment, yielding the same products as the analogous reactions performed in solution.

6 Lability of Dithiocarbamate Complexes

It has been shown that at elevated temperatures, lead(II) dithiocarbamate bonds are highly labile. It has also previously been noted that first row transition metal dithiocarbamate

complexes exhibit a high degree of lability^{55,56} and ligand exchange reactions have been observed⁵⁷.

It was investigated as to whether the lability of dithiocarbamate complexes could be exploited to generate new architectures. This was undertaken using the two *m*-xylene spaced macrocycles **(7-Cu)** and **(10-Cu)**. These were chosen since they contain the same sized aromatic spacing group and identical alkyl chains. As a result, both the structures of the starting materials and that of the desired product would be expected to be very similar. The presence of the *tertiary*-butyl group on **(10-Cu)** would act as a marker, with its mass being used to determine the presence or absence of the new macrocyclic complex. This process was studied through the examination of an equimolar dichloromethane solution of the macrocycles by electrospray mass spectrometry. Samples of the solution were added at regular time intervals to the mass spectrometer and the resulting spectra displayed in Figure 33.

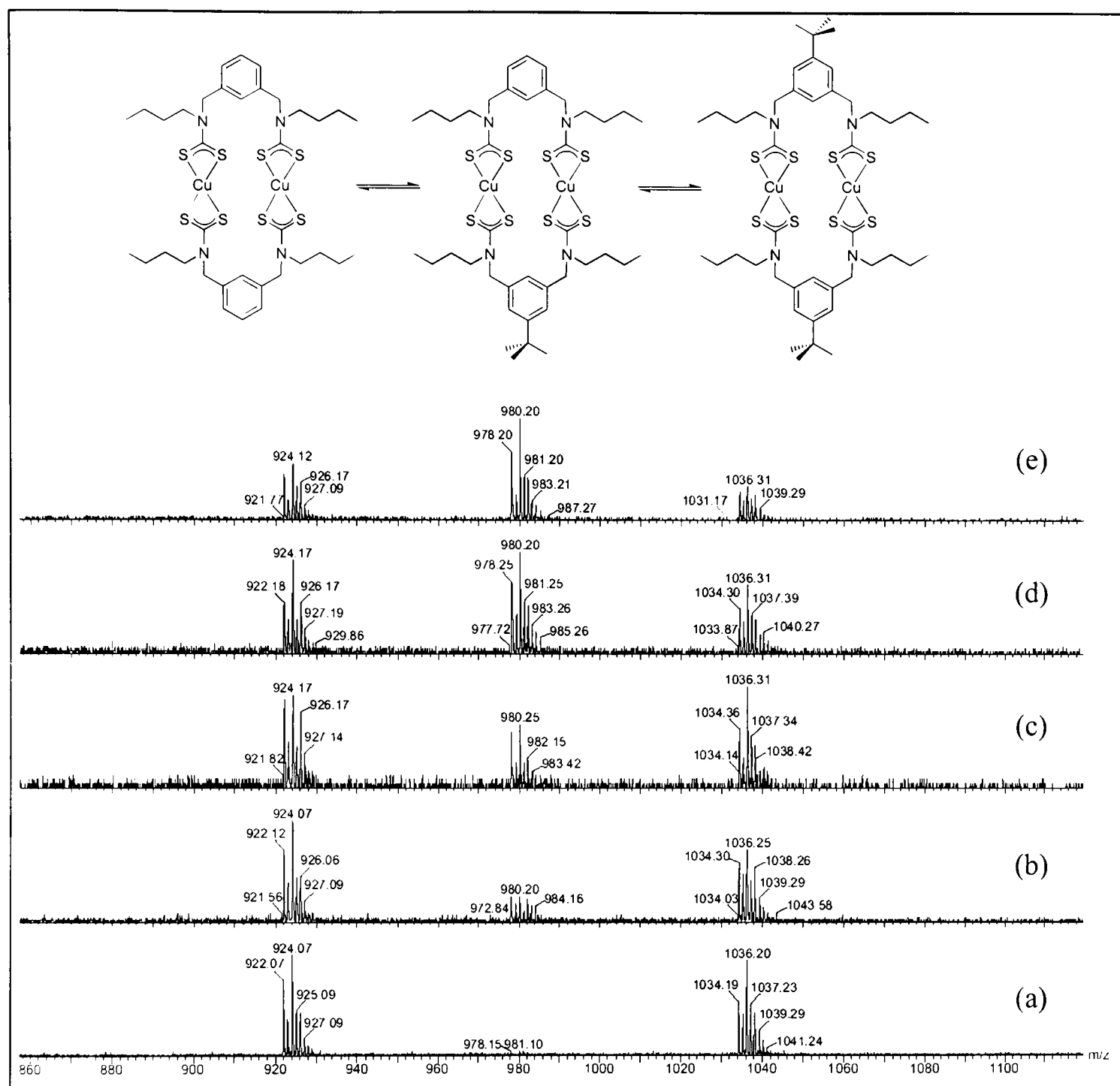


Figure 33 Electro spray mass spectra of the variation of an equimolar solution of (7-Cu) and (10-Cu) over time a) initially, b) 10 minutes, c) 30 minutes, d) 90 minutes, e) 3 hours

Initially two peaks were observed in the spectrum corresponding to the molecular ions of the two copper(II) dinuclear macrocycles, (7-Cu) (m/z 924.1) and (10-Cu) (m/z 1036.2). After time, however, a third peak began to emerge in the spectrum. This additional peak (m/z 980.2) corresponded to a new macrocycle (**25**), the unsymmetrical macrocyclic complex (Figure 34).

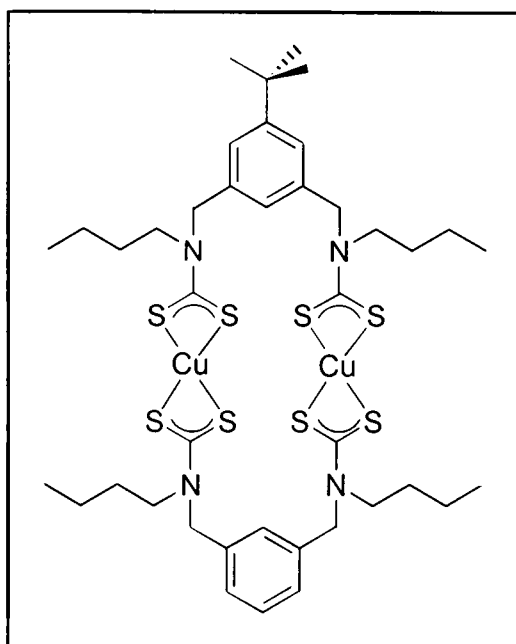


Figure 34 Unsymmetrical macrocyclic complex (25)

The unsymmetrical product **(25)**, is formed through the exchange of ligands from the original macrocycles which illustrates the copper(II) dithiocarbamate bonds are labile. The presence of **(25)** increases in intensity over time, and after three hours the solution has reached the statistical 1:2:1 ((**7-Cu**):(**25**):(**10-Cu**)) equilibrium, after which no further changes are observed in the spectrum.

This highlights the difficulty of synthesising unsymmetrical dithiocarbamate-based macrocycles, as any such systems will rapidly equilibrate in solution. The lability of the transition metal dithiocarbamate bond is exploited in Chapters Three and Five to allow both the inclusion of suitable guests within cage-like structures and also to generate interlocked molecules.

7 Cation Binding Properties of Macrocyclic Complexes

Characterisation of the dithiocarbamate macrocyclic complexes by electrospray mass spectrometry frequently revealed large adducts with univalent metal ions. This suggests that the electron-rich sulphur donors and metal centres may be interacting with cationic guests. Such interactions have been previously observed; for example, the addition of silver perchlorate to platinum(II) bis-(*N,N'*-diethyldithiocarbamate), results in the formation of

$(\{\text{Pt}(\text{S}_2\text{CNEt}_2)_2\}_3\text{Ag}_2)^{2+}$ complex, both in solution and the solid state⁵⁸. Here, the silver(I) ion adopts a tetrahedral geometry, bonding to both the electron-rich sulphur donors and the filled dz^2 orbital of the platinum(II) centre. Similarly, cyclic hosts, such as crown ethers, have previously been demonstrated to form strong complexes with alkali metal cationic guests, due to their coordination to electron-rich oxygen atoms. The extent of cation binding of a range of electron-rich dithiocarbamate-based macrocyclic hosts was investigated by a variety of spectroscopic techniques.

7.1 Electrospray Mass Spectrometry Competition Experiments

A qualitative look at cation binding was carried out initially by performing an electrospray mass spectrometry competition experiment. A 10^{-6} M macrocyclic solution was co-injected into the electrospray mass spectrometer with one equivalent of the perchlorate salts of the univalent sodium, potassium, rubidium and caesium ions in addition to copper(I) iodide. A high cone voltage was employed in order to maintain non-covalent interactions in the experiment. A typical spectrum observed during this experiment is displayed in Figure 35, and the relative intensities of the peaks of a range of macrocycles are highlighted in Table 11.

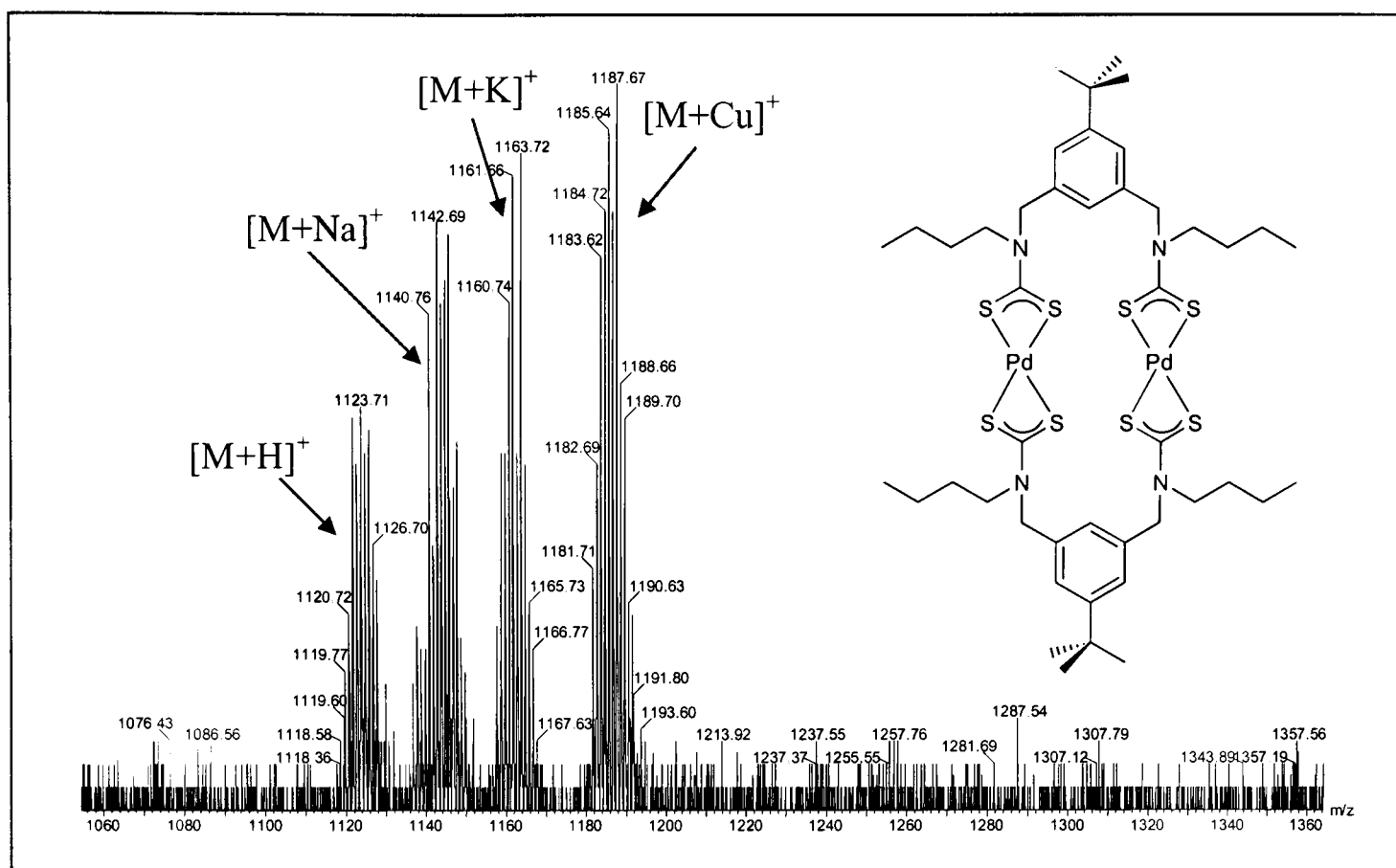


Figure 35 Electrospray competition experiment for (10-Pd) in the presence of 1.0 equivalent of Na, K, Rb, Cs and Cu cations

Intensity of ion (relative to the most intense peak=100)						
	[M] ⁺	[M+Na] ⁺	[M+K] ⁺	[M+Rb] ⁺	[M+Cs] ⁺	[M+Cu] ⁺
(8-Cu)	100	22.7	42.4	-	-	33.7
(8-Ni)	100	78.9	91.6	-		5.0
(8-Pd)	5.6	100	31.2	-		15.4
(8-Pt)	12.4	76.8	100	-		-
(10-Cu)	100	9.6	53.3	2.4	3.0	24.0
(10-Ni)	31.3	43.4	100	-	-	65.1
(10-Pd)	56.3	81.4	91.0	-	-	100
(10-Pt)	96.4	76.6	100	-	-	72.5
(13-Cu)	100	12.0	52.7	-	-	-
(13-Ni)	100	59.3	77.8	-	-	-
(13-Pd)	67.0	46.7	63.5	-	-	-
(13-Pt)	100	100	88.0	-	-	-
(18-Cu)	100	4.7	5.3	-	-	-

Table 11 Relative intensities of adduct peaks during electrospray competition experiments with 1.0 equivalents of Na, K, Rb, Cs and Cu(I) ClO₄ salts, – indicates no adducts were observed

As can be seen, the macrocycles form adducts with numerous univalent cations. The most intense peaks are observed for adducts with sodium, potassium and copper cations and fewer with the larger rubidium and caesium. In addition, the size of the aromatic spacer does not appear to bestow a significant selectivity upon the system, although only copper(I) adducts are observed for the smaller *m*-xylyl spaced macrocycles.

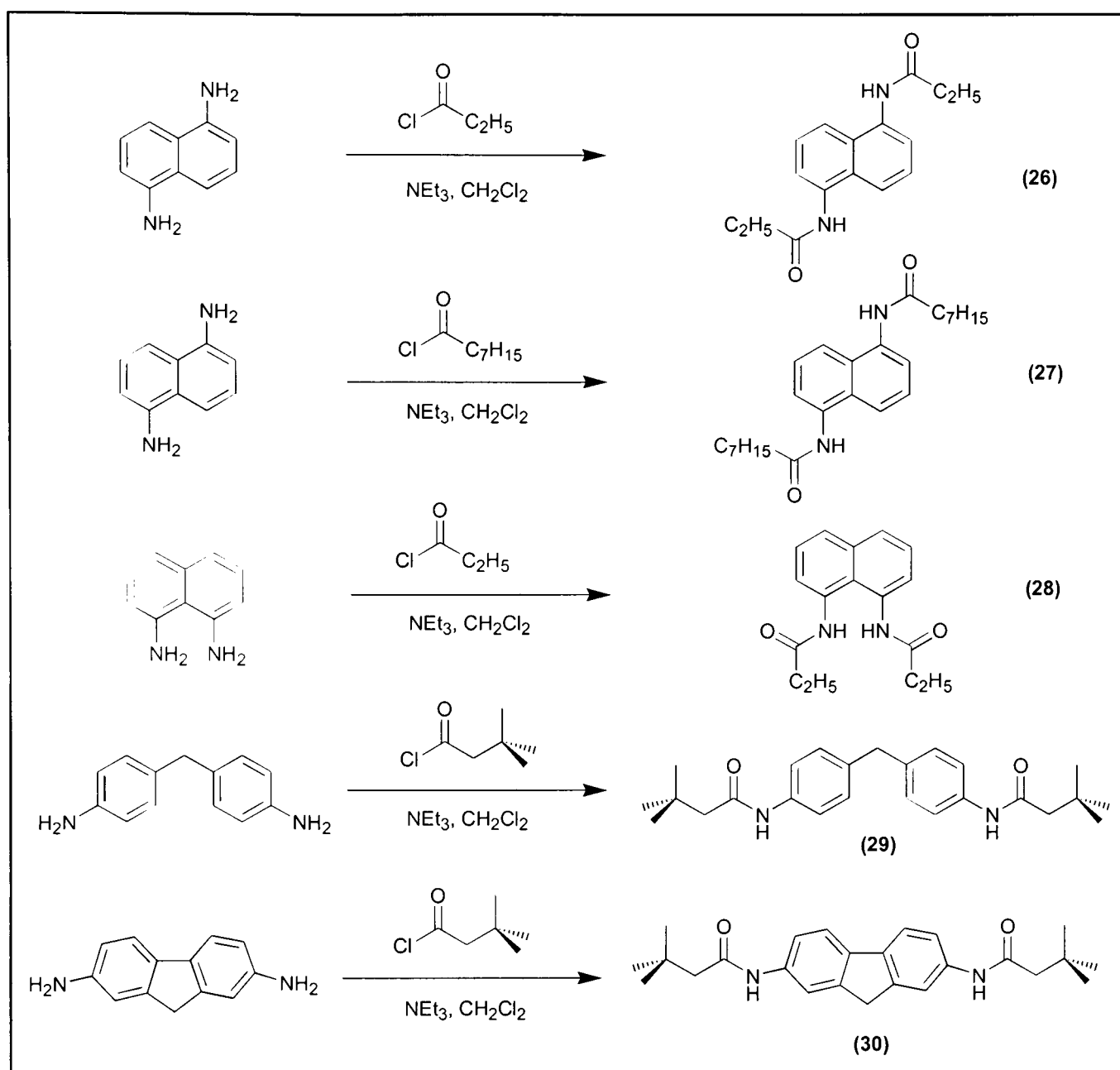
7.2 Other Techniques

The interaction with cations with a range of macrocyclic dithiocarbamate-based receptors was also investigated using UV-vis spectroscopy, electrochemistry and ^1H and ^{13}C NMR. Unfortunately, none of these techniques revealed any significant perturbation in their respective signals upon addition of a univalent cationic guest. This may suggest that any potential binding of these simple cations by the macrocycles is relatively weak. This is possibly a result of the competitive acetonitrile-based solvent systems in which these experiments were performed.

8 Attempted Syntheses

8.1 Aniline-Based Dithiocarbamate Macrocycles

It has been demonstrated that bis-(aminomethyl)-aromatic spacers can be used to generate dithiocarbamate-based macrocyclic architectures. There are, however, numerous commercially available bis-(amino)-aromatic synthons. An investigation as to whether these spacers could also generate similar dithiocarbamate-based macrocyclic complexes was undertaken. Secondary amines were generated from the bis-amines through initial condensation with an acid chloride and subsequent reduction of the resultant amide (Scheme 7).



Scheme 7 Synthesis of bis-amide derivatised aniline-based systems

The bis-amides **(26)** - **(30)** were synthesised through the reaction of the bis-amines with the acid chlorides, *tert*-butyl acetylchloride, propionyl chloride and octanoyl chloride in dry dichloromethane, and a stoichiometric amount of triethylamine. The yields for these reactions are high, typically near-quantitative. The amides were characterised through ^1H and ^{13}C NMR spectroscopy, electrospray mass spectrometry and elemental analysis. The compound **(29)** was further characterised by X-ray crystallography.

A single crystal of **(29)** suitable for X-ray analysis was grown from slow evaporation of a methanol solution, and its structure solved by Dr. A. Cowley, University of Oxford. The resultant structure is displayed in Figure 36.

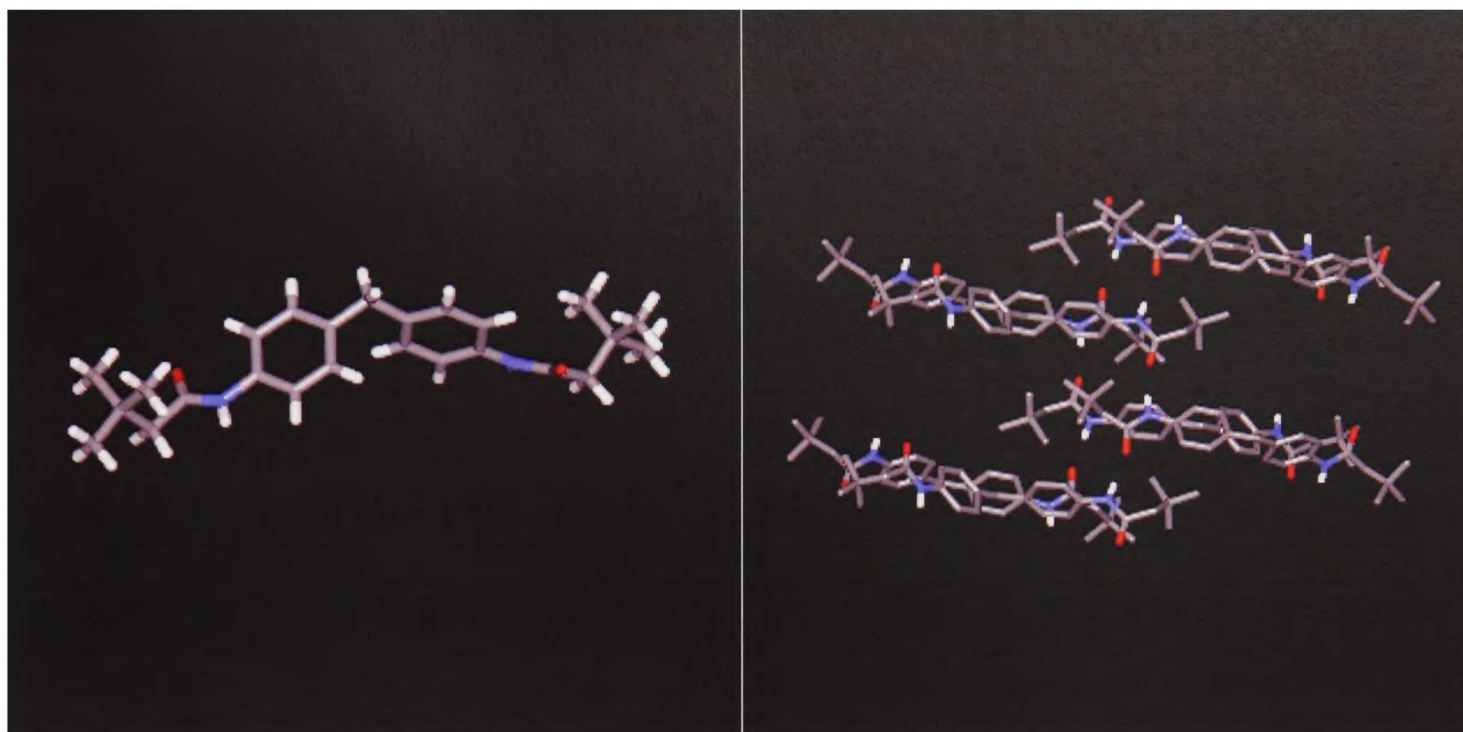


Figure 36 X-ray crystal structure of (27) (right) packing diagram showing intramolecular hydrogen bonding (non-polar hydrogen atoms omitted for clarity)

This shows the formation of the desired bis-amide structure. The molecule has no crystallographic symmetry, but there is an approximate two-fold axis passing through the central methylene carbon. The amide groups each form a hydrogen bond to the oxygen atoms of a different neighbouring molecule (intramolecular nitrogen-oxygen distances are 2.92 and 2.89 Å). These link the molecules to form infinite sheets parallel to the crystallographic *ab*-plane (Figure 36(right)).

Reduction of the amides (29) and (30) to the corresponding amines (31) and (32) was performed through treatment with lithium aluminium hydride in dry tetrahydrofuran (Scheme 8). Amide reduction was achieved in 85% yield in both cases, although was found not to be facile. It was necessary for the hydride source to be used in combination with the Lewis acid, aluminium trichloride. Coordination of this Lewis acid to the amide oxygens activates the amides to nucleophilic attack. In its absence, however, the acidic amide proton may be deprotonated, thus deactivating the amide to reduction⁵⁹. Unfortunately, the analogous reductions with the naphthylene-derivatised amides (26) - (28) were not possible, due to the poor solubility of the aromatic compounds.

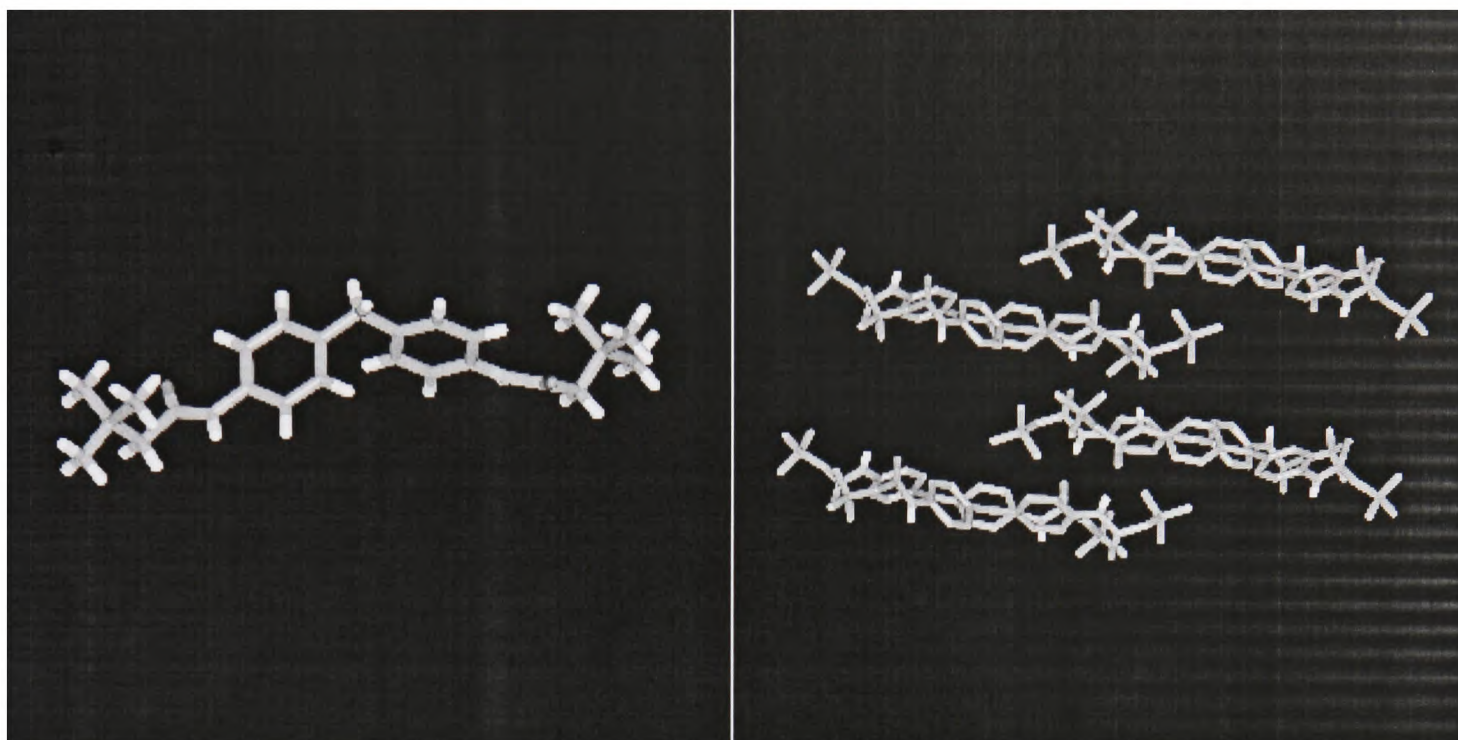
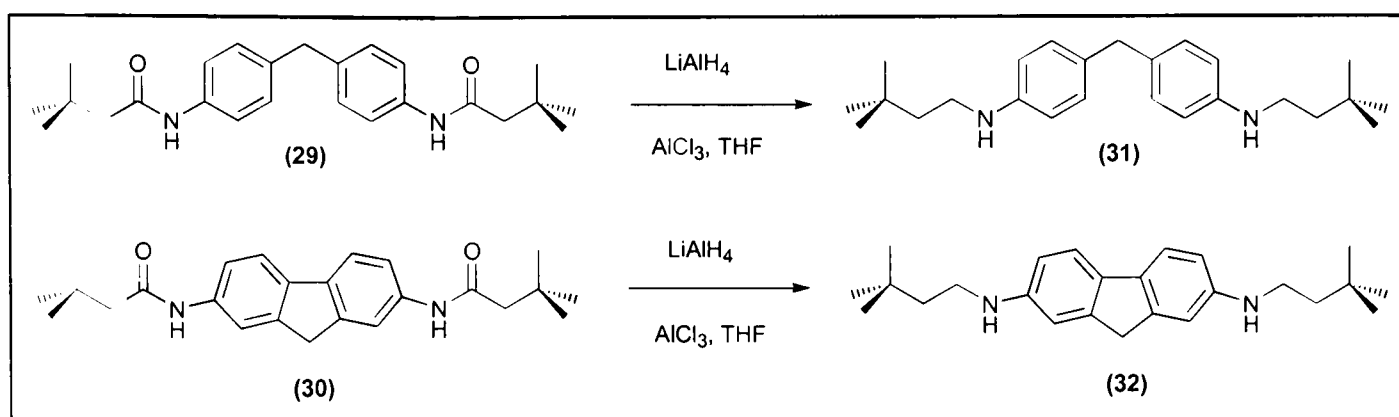


Figure 36 X-ray crystal structure of (27) (right) packing diagram showing intramolecular hydrogen bonding (non-polar hydrogen atoms omitted for clarity)

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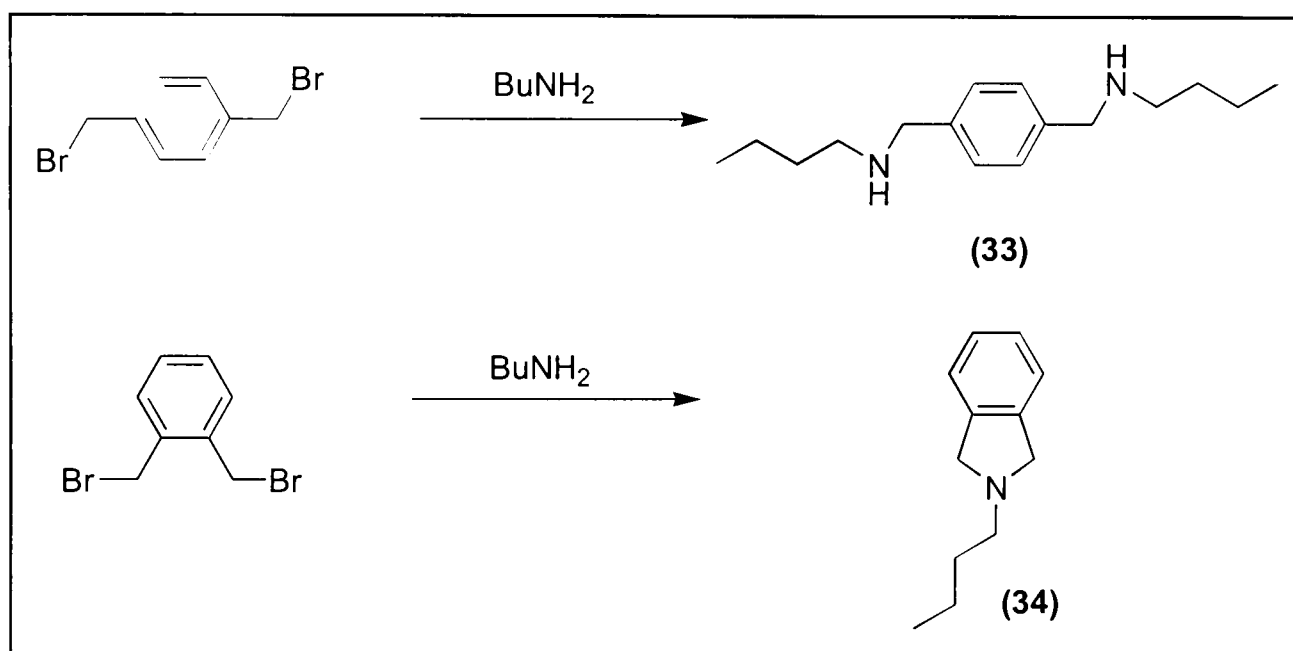
Scheme 8 Synthesis of aniline derivatised secondary bis-amines

The synthesis of copper(II) and nickel(II) bimetallic macrocyclic complexes was attempted with the bis-amines **(31)** and **(32)** via a one-pot reaction. The secondary bis-amines are reacted sequentially with potassium hydroxide, carbon disulphide and copper(II) and nickel(II) acetate in a tetrahydrofuran/water (2:1) solvent system. Standard colour changes were observed and black and green precipitates formed respectively. However, in both cases the resultant solids were only sparingly soluble in organic solvents. Analysis of the soluble products by both electrospray mass spectrometry and NMR spectroscopy failed to reveal the generation of any of the desired products. This is likely to be the result of the reduced coordinating power of the dithiocarbamate ligand when it is adjacent to aromatic systems, allowing its charge to be delocalised over numerous atoms⁶⁰. The weaker metal coordination leads to the increased probability of forming polymeric products.

7.2 *o*- and *p*-Xylyl-Based Macrocycles

After the success of the synthesis of the *m*-xylyl spaced macrocyclic complexes the syntheses of the similar *o*- and *p*-xylyl spaced macrocycles were investigated. This was achieved through an analogous method from commercially available α - α' -dibromo-*o*-xylene and α - α' -dibromo-*p*-xylene. Both compounds were aminated through their portionwise addition to stirred *n*-butylamine. The *p*-xylyl spaced bis-amine **(33)** was isolated as a brown oil in quantitative yield and characterised through ¹H and ¹³C NMR, electrospray mass spectrometry and elemental analysis. However, analysis by ¹H NMR and electrospray mass spectrometry of

the corresponding *o*-xylyl spaced product did not reveal the synthesis of the desired secondary amine, but instead indicated the formation of a cyclic tertiary amine (**34**). In this case, it was found that the intramolecular cyclisation reaction was favoured generating a five-membered ring, despite the huge excess of the reactant *n*-butylamine (Scheme 9).



Scheme 9 Synthesis of *o*- and *p*-xylyl spaced diamines

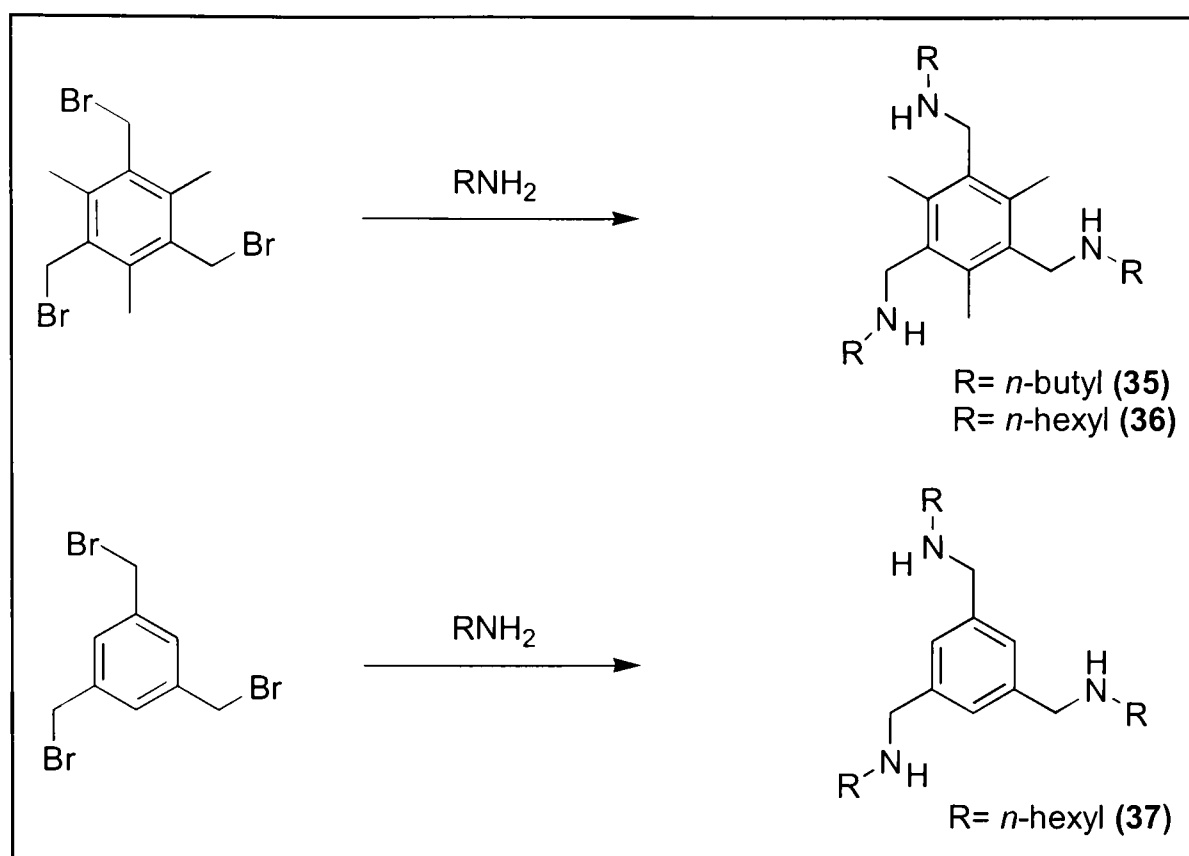
Metal-directed self-assembly of the copper(II) and nickel(II) dithiocarbamate macrocyclic complexes was then attempted with **(33)**. The bis-amine **(33)** was reacted in a one-pot reaction with potassium hydroxide, carbon disulphide and then either copper(II) or nickel(II) acetate added. The resulting brown and green solids were isolated, although their solubility in chlorinated solvents was very poor. Unfortunately, analysis of these solutions failed to reveal any of the desired macrocyclic products. This is likely to be the result of the ligand not being sufficiently preorganised to encourage macrocyclic formation, hence resulting in the formation of polymeric products. It is, however, somewhat surprising that the *p*-xylyl spaced bis-amine **(33)** does not result in successful cyclisation whereas the structurally similar *p*-biphenyl spaced bis-amine **(15)** does. The success of the latter is probably a result of intramolecular π - π stacking interactions between biphenyl groups that template the formation of the macrocyclic structure. It is also likely that replacement of the *n*-butyl chains of **(33)** with a bulkier group would disfavour the polymerisation process and result in the formation

of discrete complexes⁶¹.

7.3 Trimetallic Dithiocarbamate Complexes

It has been previously demonstrated that three-dimensional trinuclear cage structures may be formed through the combination of tris-pyridine ligands with *cis*-protected palladium centres (Chapter One Section 7.2). An investigation as to whether similar trimetallic dithiocarbamate cage type structures could also be formed was undertaken. The generation of simple dithiocarbamate cage complexes would be interesting, since they offer the possibility of utilising the lability of the metal-dithiocarbamate bond to entrap small molecules inside the cavity.

For this task, two starting materials with the appropriate three-fold symmetry were chosen, 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene and 1,3,5-tris(bromomethyl)-benzene. Both of these compounds were converted to the corresponding tris-amines **(35)** - **(37)** via portionwise addition to stirred *n*-butylamine and *n*-hexylamine at room temperature, with the resultant oils being isolated in quantitative yields (Scheme 10).



Scheme 10 Synthesis of tris-amino compounds

The tris-amines (35) - (37) were converted to their analogous tris-dithiocarbamate salts by the addition of potassium hydroxide and carbon disulphide in a tetrahydrofuran/water (2:1) solution. The corresponding copper(II) and nickel(II) complexes were then formed through addition of copper(II) and nickel(II) acetate and the resultant solids collected. Unfortunately, addition of the metal salt to (35) and (36) resulted in the formation of insoluble solids. However, addition of copper(II) and nickel(II) acetate to (37) did lead to the formation of complexes that were soluble in organic solvents. Electrospray mass spectrometry (Figure 37) revealed the formation of trinuclear cage complex for both the copper (38) and nickel (39) products (Figure 38).

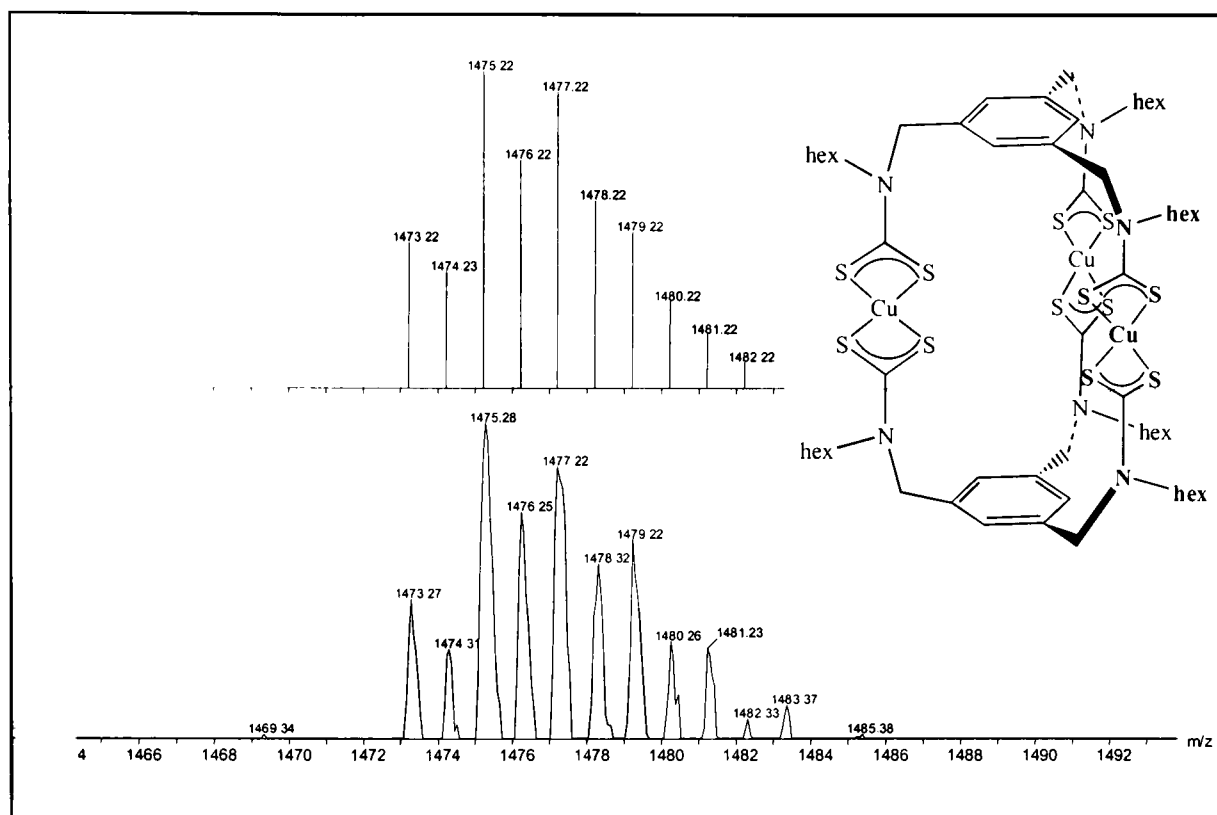


Figure 37 Electrospray mass spectrum of $[M]^+$ peak of trinuclear Cu(II) complex (38) (upper) predicted isotope model

Unfortunately, the nickel complex (39) was unable to be purified to yield a satisfactorily elementally pure product. The analogous copper(II) complex, however, was able to be precipitated from dichloromethane with ethanol to generate a brown solid in 43% yield which was characterised by elemental analysis and electrospray mass spectrometry. The resulting brown solid, exhibited poor solubility. Its electrochemical properties were examined in a *N,N'*-dimethylformamide/dichloromethane (4:1) solution and this revealed a rather broad oxidation wave for the copper(II/III) couple due to the presence of overlapping waves. The resulting cyclic voltammogram is displayed in Figure 38 and the square wave voltammogram shown in Figure 39.

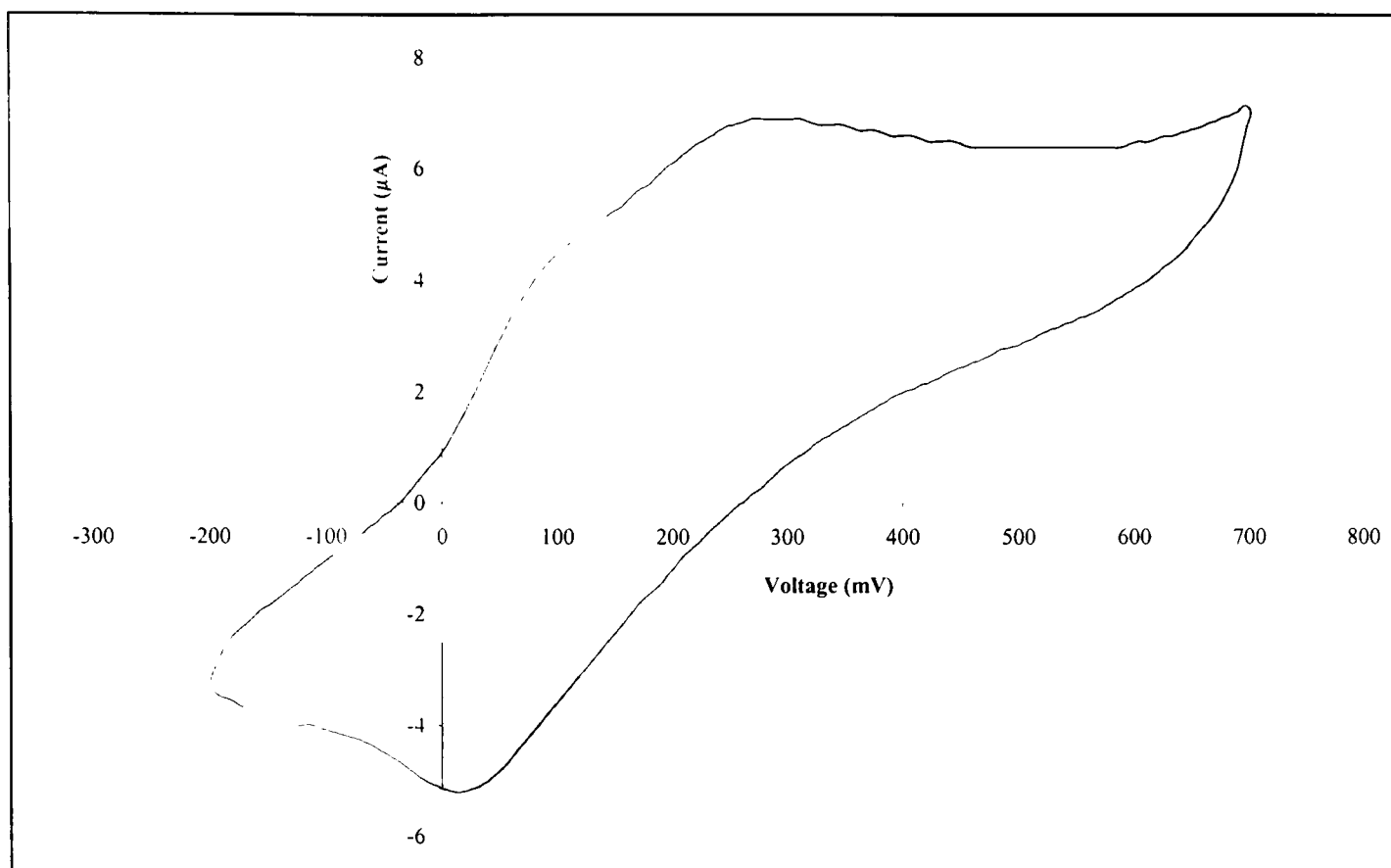


Figure 38 Cyclic voltammogram of the Cu(II/III) oxidation couple of (38) at 100 mVs⁻¹, performed in DMF/CH₂Cl₂ (4:1) containing 0.1M TBABF₄ using a glassy carbon working electrode with reference to Ag/AgNO₃ at 293K (E_{na} 0.27V, E_{nr} 0.02V, errors ± 5 mV)

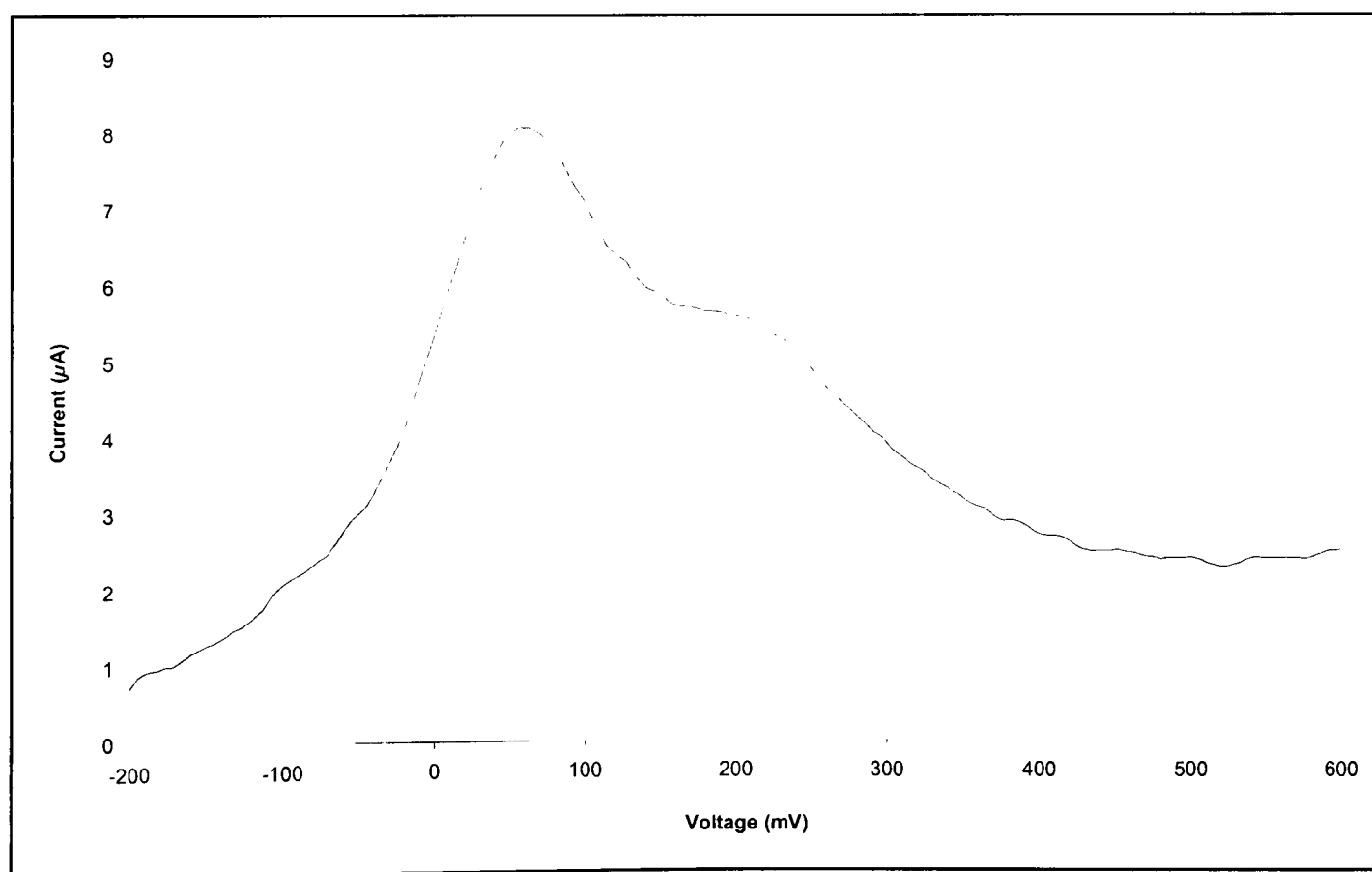


Figure 39 Square wave voltammogram of the Cu(II/III) oxidation couple of (38) frequency 5Hz, performed in DMF/CH₂Cl₂ (4:1) containing 0.1M TBABF₄ using a glassy carbon working electrode with reference to Ag/AgNO₃ at 293K ($E_{1/2}$ 0.06V, shoulder at 0.21V, errors ± 5 mV)

The presence of a shoulder on the broad copper(II/III) oxidation wave does suggest that the

copper centres are communicating with each other, although the resolution of this is poor in this experiment. This feature is clearly shown in the square wave voltammogram, (Figure 39) and in addition, the relative intensities of the two peaks are informative concerning the possible communication process between the metal centres, as the first peak is considerably larger than the second. This may suggest that the first and second oxidation processes occur at a similar potential (0.06V), and that the metals are sufficiently far apart not to greatly affect each other upon oxidation of one or two of the centres. However, the third potential (0.21V) is significantly perturbed suggesting that the presence of two adjacent positive charges makes it significantly more difficult to oxidise the third metal centre and hence a smaller peak is observed shifted anodically in comparison to the first.

9 Conclusion

A series of new dinuclear macrocycles-based on a transition metal dithiocarbamate moiety have been synthesised. Ligands were assembled by using simple organic chemistry and the final architectures constructed via metal-directed self-assembly. In addition to a range of transition metal centres, a variety of aromatic spacer groups and alkyl side chains have been deployed and found to significantly alter the nature of the bimetallic assemblies.

The structures have been characterised by ^1H and ^{13}C NMR spectroscopy, electrospray mass spectrometry, elemental analysis, UV-vis spectroscopy and X-ray crystallography. Copper(II) dithiocarbamate-based systems have also been examined through EPR and electrochemistry.

X-ray crystallographic studies have illustrated that a number of different conformations are observed in the solid state. It has been found that the nature of the ligand appears to have the biggest influence as to which conformational structure is adopted, with variation of the metal centre within the structure, in general, not altering the overall conformation of the molecule.

The structure of **(11-Ni)** has been shown by X-ray crystallography to adopt two similar

structures in the solid state; this suggests a degree of flexibility within the macrocyclic architecture. This adoption of more than one conformation by macrocyclic complexes is also shown in the solution state. Variable temperature NMR experiments of the *m*-xylyl spaced complexes **(8-M)** and **(11-M)** have indicated the presence of more than one conformation in solution.

Electrochemical studies on the copper(II)-based dithiocarbamate macrocyclic complexes, have revealed electrochemical communication between the metal centres in the dinuclear structures. Examination of the copper(II/III) oxidation waves reveal the presence of two distinct or a broad oxidation wave due to the oxidation of the first metal centre perturbing the oxidation of the second. This is greatest for the *m*-xylyl spaced macrocycles where the metal centres are closest together through space. Where the copper centres are further apart, such as **(15-Cu)**, the metals act independently. EPR studies have been undertaken on a number of the copper-based macrocycles also, revealing well-resolved spectra. The results of the EPR studies are analogous to the electrochemical studies with the spectra of the bimetallic structures also showing communication between the metal centres.

Attempted binding studies between the electron-rich macrocyclic hosts and univalent metal ions were, unfortunately, disappointing despite a precedent for cation complexation. In the case of the *m*-xylyl spaced macrocycles this may be in part due to the small cavity size created in these systems. However, the X-ray crystal structure of **(18-Cu)** clearly demonstrates the larger naphthyl spaced macrocycle generates a cavity which enable the encapsulation of suitably sized guests, as is shown by the inclusion of dichloromethane.

It has also been demonstrated that there is a significant degree of lability within dithiocarbamate bonds with first row transition metals. This has been used to generate an unsymmetrical macrocyclic complex and may be useful in allowing guests to enter/leave dithiocarbamate-based architectures.

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Chapter Three

Resorcinarene Cavitand

Dithiocarbamate Chemistry

Chapter Three: Resorcinarene Cavitand Dithiocarbamate Chemistry

Chemistry

1 Introduction

1.1 Resorcinarenes

Resorcinarenes¹ (often known as calix[4]resorcarenes²) are cup-shaped macrocyclic receptors closely related to the calix[n]arene family (Figure 1). Their synthesis was first reported by Baeyer in 1872 after the acid catalysed condensation of 1,3-dihydroxybenzene (resorcinol) with a variety of aldehydes³. It was not until much later that their tetrameric structure was initially proposed⁴ and then finally proven by X-ray crystallographic studies⁵.

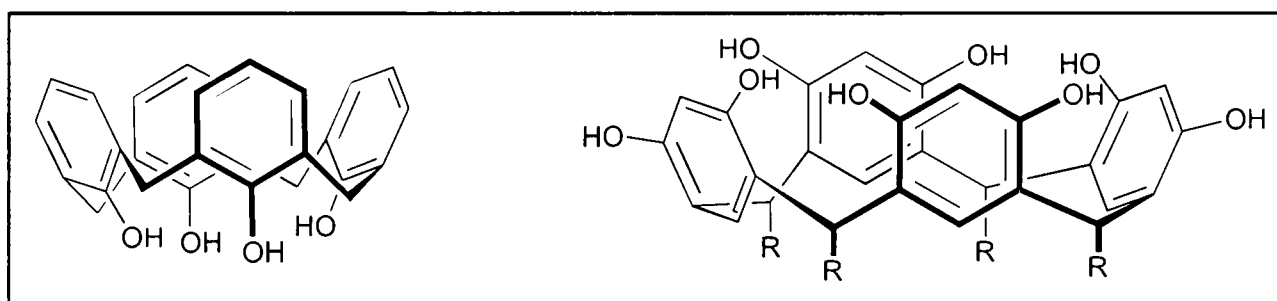


Figure 1 Calix[4]arene (left) and resorcinarene (right)

More recently, functionalisation of resorcinarenes⁶ has led to the generation of a variety of structures which have been used for a wide variety of applications ranging from the inclusion of cationic^{7,8} or polar organic guests⁹ to the formation of liquid crystals¹⁰.

1.2 Resorcinarene Cavitands

In 1982, Cram reported the synthesis of a series of resorcinarene-based organic compounds, which he christened cavitands¹¹. They are synthesised by covalent linkage of neighbouring phenolic hydroxyl groups of the parent resorcinarene to form a preorganised host with an enforced concave cavity. The linkers may be chosen to be aliphatic, aromatic or hetero-atom based and their properties dictate the dimensions of the resulting cavity¹² (Figure 2).

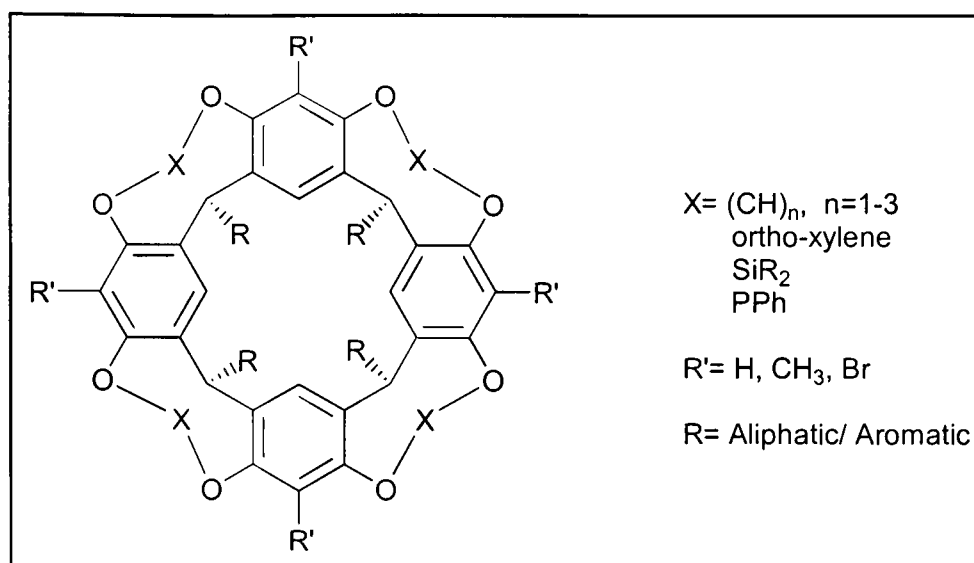


Figure 2 Resorcinarene cavitands

The highly preorganised cavitand hosts have been shown to form a number of inclusion complexes with complementary guests, such as acetonitrile, toluene and dichloromethane¹³. Organic cations, such as acetylcholine have also been observed to bind in the central cavity from the formation of favourable π -cation interactions¹⁴.

The cavitand system has also been used as a rigid framework for the development of larger, more complex systems. Reinhoudt and co-workers have synthesised crown ether derivatives using the resorcinarene cavitand system, as a “building block” to generate a cation binding site adjacent to a large hydrophobic surface¹⁵.

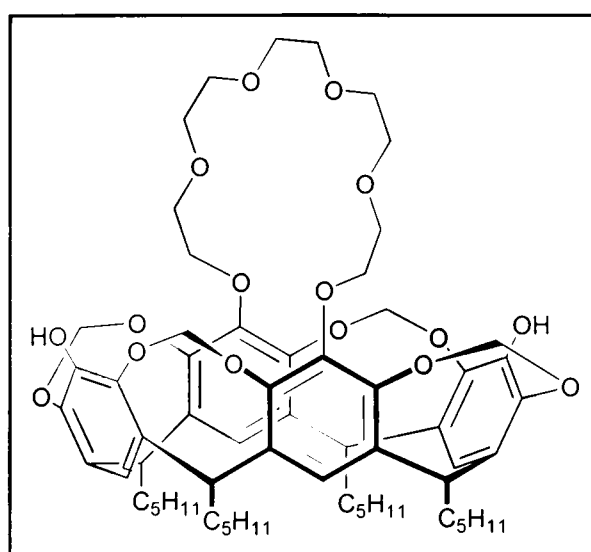


Figure 3 1,3-crown[6]cavitand

1.3 Covalently Linked Molecular Capsules

Covalent linkage of two or more cavitands has led to the formation of closed molecular containers (carcerands) which do not possess portals of significant size through which guest molecules can either enter or leave (Figure 4)¹⁶. A range of organic molecules, inorganic salts and ions have been confined within the cavities. The most impressive use, however, has been the trapping of cyclobutadiene¹⁷. This highly unstable molecule had previously only been observed at 8K in an inert gas matrix, but *in situ* formation within the host has allowed it to be studied spectroscopically.

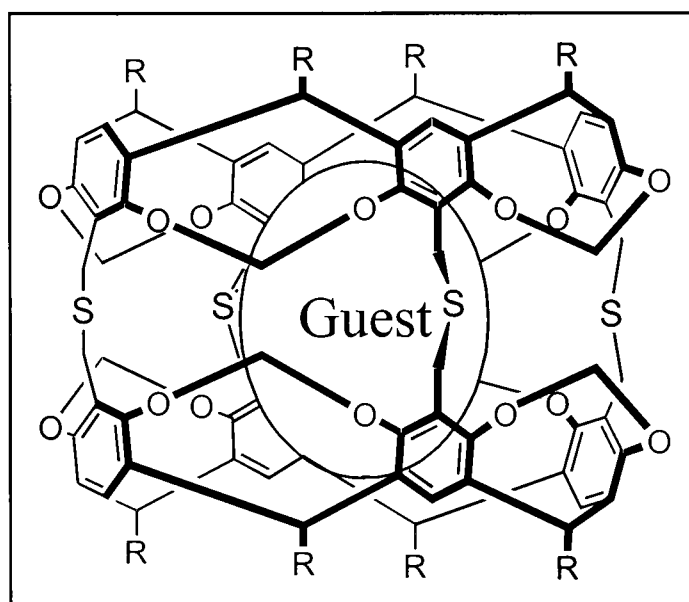


Figure 4 Carcerand receptor trapping a guest molecule

1.4 Non-Covalent Linkage of Cavitands

Molecular capsules and containers may also be generated via the use of non-covalent interactions. This approach has the additional benefit that thermodynamic equilibration reduces the synthetic effort in generating these assemblies. Functionalising the upper rim of cavitands with hydrogen bond donors/acceptors has allowed the association of two capsules forming a dimeric structure¹⁸.

For example, Furukawa and co-workers synthesised a molecular capsule where two molecules of cavitand tetracarboxylic acid and four molecules of 2-aminopyrimidine assembled in both

solution and the solid state by the formation of 16 hydrogen bonds (Figure 5)¹⁹.

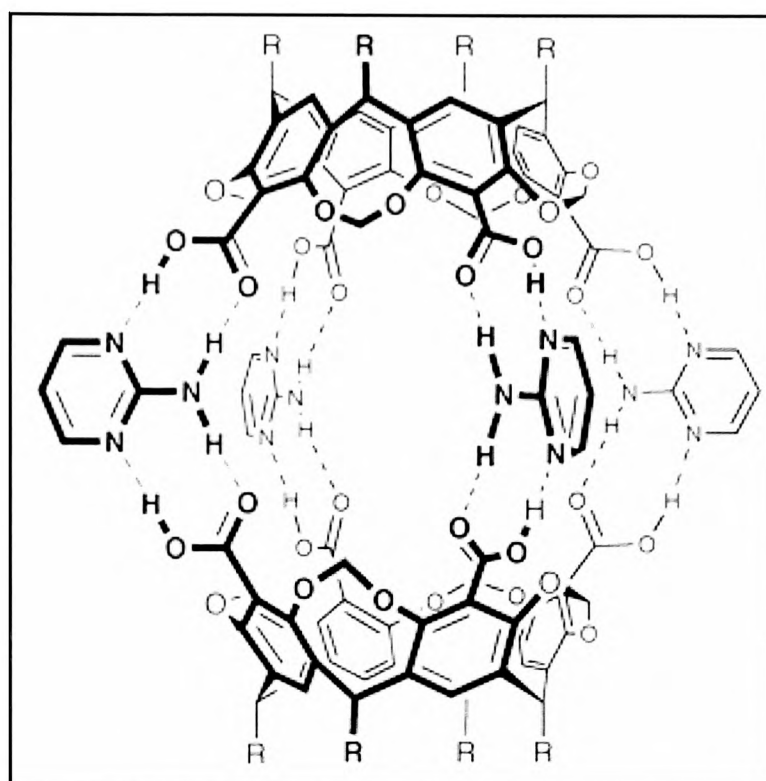


Figure 5 Molecular capsule formation via hydrogen bonding interactions ($R=C_5H_{11}$)

It is only recently, however, that resorcinarenes have been utilised in metal-directed self-assembly to generate molecular metallo-cage structures. Dalcanale and co-workers have reported the synthesis of a tetrapyridyl-resorcinarene cavitand which quantitatively formed dimeric cage structures upon addition of square planar palladium(II) (Figure 6) complexes²⁰. These complexes use *cis*-protected metal ions, by the use of either 1,3-bis-(diphenylphosphino)-propane (dppp) or ethylenediamine (en) chelating groups, to direct the assembly of the architecture.

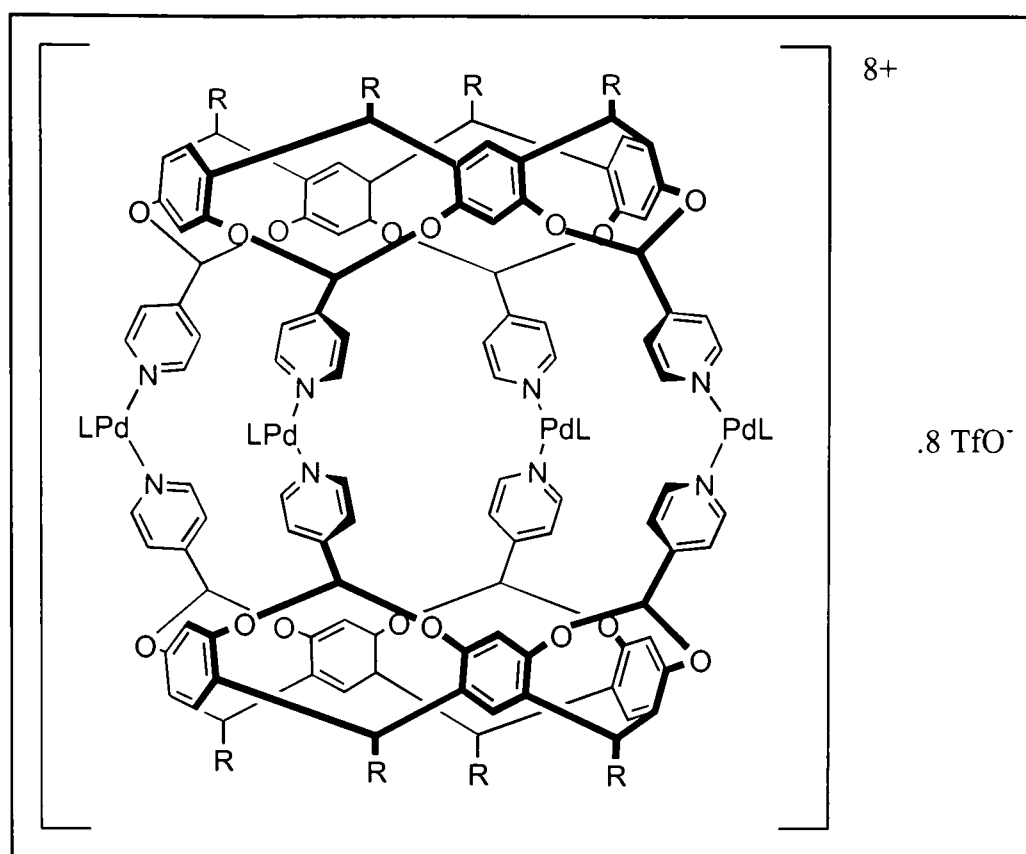


Figure 6 Tetra-pyridyl Pd(II) cavitand dimer
(L = en or dppp, R = C₁₁H₂₃ or CH₂CH₂Ph)

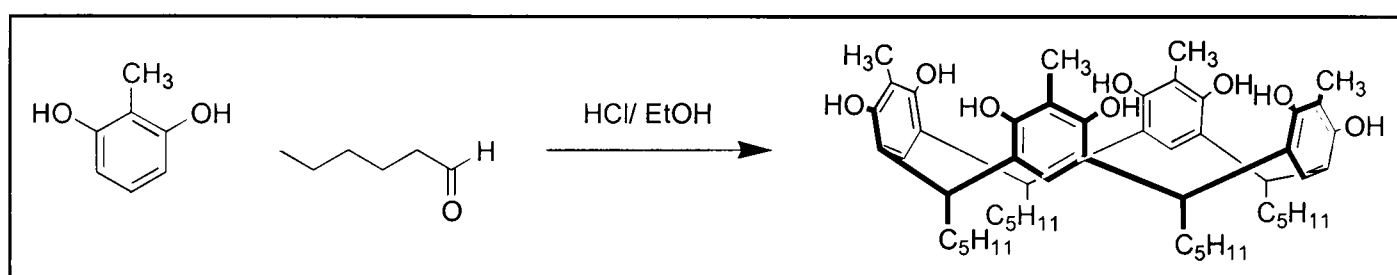
Harrison and co-workers have functionalised the upper rim of a resorcinarene cavitands with iminodiacetate moieties²¹. Cobalt(II) and iron(II) coordinated to the ligand in a distorted octahedral geometry, generating dimeric capsules²². These architectures were further shown to bind small aromatic and aliphatic guests in aqueous solution²³.

The aim of the research reported in this Chapter is to investigate resorcinarene cavitand systems functionalised with dithiocarbamate groups. Coordination with suitable metal ions has been shown to generate multinuclear molecular containers with nano-dimensional cavities^{24,25}. The synthesis of these hosts is repeated and expanded upon to produce a range of polymetallic dithiocarbamate-based complexes and their binding properties investigated with a variety of suitable guest molecules. Furthermore, the structures will be examined for their potential stabilisation and templation of nano-dimensional structures, such as gold nanoparticles (Chapter Six).

2 Synthesis and Characterisation of Resorcinarene Building Blocks

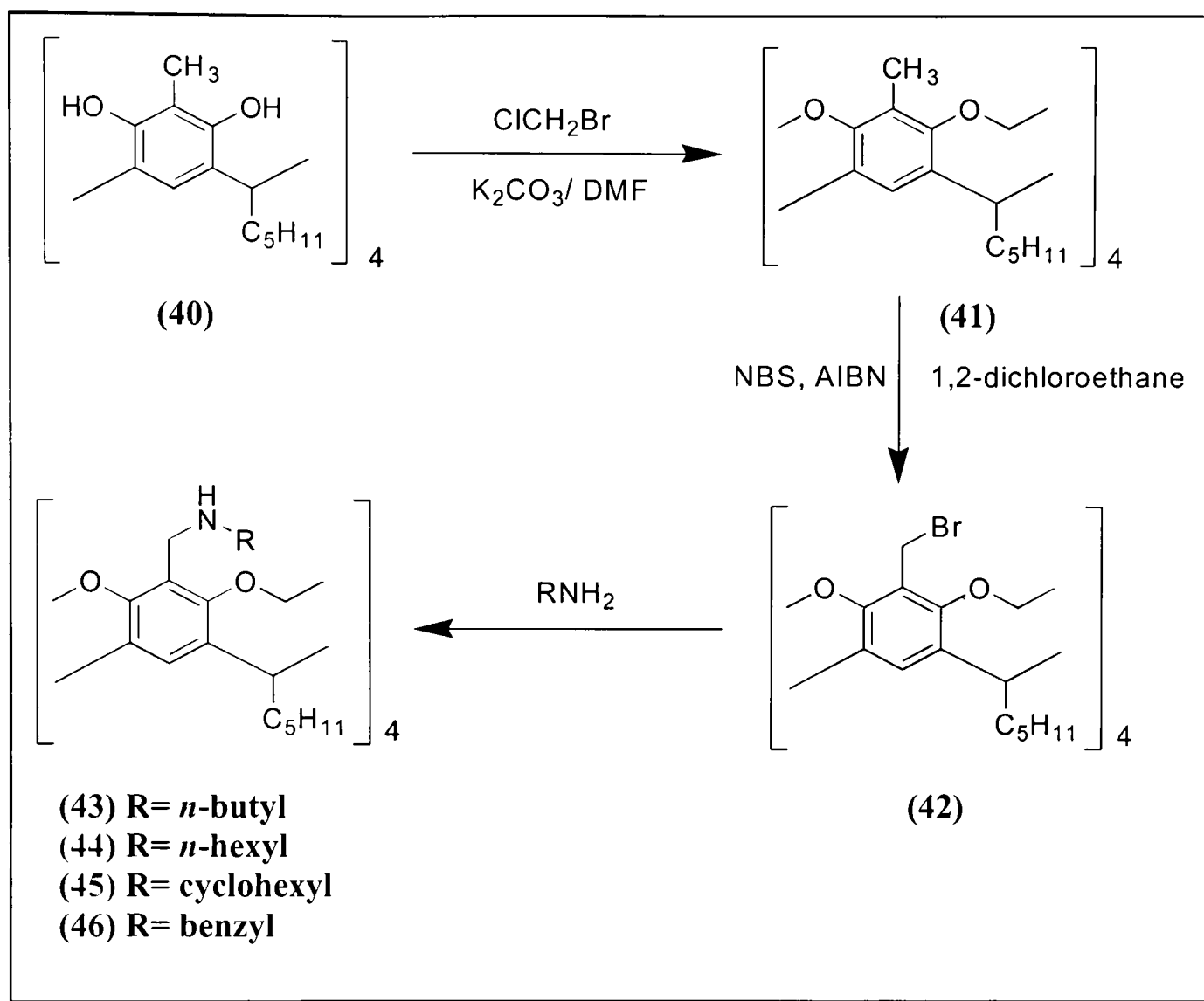
The work discussed in this section is based upon a resorcinarene prepared according to a method described by Cram and co-workers²⁶. The functionalisation of this and the ensuing synthesis and characterisation of the subsequent molecular building blocks are now described.

The one-pot, acid-catalysed aldol reaction between 2-methylresorcinol and hexanal generates a mixture of conformational isomers of the tetrameric resorcinarene (**40**). Prolonged heating in ethanol results in the exclusive precipitation of the least soluble, crown isomer (Scheme 1). The cream powder can be isolated in 85% yield and its resulting symmetrical ¹H NMR illustrates the formation of the C_{4v} conformer.



Scheme 1 Synthesis of resorcinarene (**40**)

Conversion of the resorcinarene (**40**) to the desired tetra-amines was undertaken following a modification of a reaction scheme outlined by Reinhoudt²⁷. Covalent linkage of neighbouring phenolic groups on the four aromatic rings of the resorcinarene (**40**) resulted in the formation of the resorcinarene cavitand (**41**). This was achieved, in 80% yield, by treatment of the crown isomer with excess bromochloromethane and potassium carbonate in anhydrous *N,N*-dimethylformamide (Scheme 2). The resulting ¹H NMR spectrum displays two geminally coupled doublets for the bridging methylene group (5.86 and 4.25 ppm for the outer and inner bridging protons respectively) confirming the formation of the desired preorganised structure.



Scheme 2 Preparation of resorcinarene cavitand building blocks

The tetramethylresorcinarene cavitand (41) was functionalised by bromination using *N*-bromosuccinimide (NBS) in 1,2-dichloroethane. The tetra-(bromomethyl) cavitand (42) was isolated as a pale yellow crystalline product in 50% yield, after recrystallisation from dichloromethane/ethanol.

Tetrakis-(alkylaminomethyl) cavitands were prepared by the portionwise addition of tetra-(bromomethyl) cavitand (42) to neat primary alkyl amine at room temperature. In this almost instantaneous reaction, the amine was used as the nucleophile as well as both the solvent and the base. The reaction proceeds in near quantitative yield and no overalkylation of the amino-groups were observed. Cavitands with *n*-butyl (43), *n*-hexyl (44), cyclohexyl (45) and benzyl (46) side chains were prepared via this method. All the cavitand self-assembly precursors were characterised by ^1H NMR, elemental analysis and electrospray mass spectrometry.

The tetra-amino cavitands (43) - (46) exhibit characteristic absorptions in their ^1H NMR spectra. The spectrum of (43) is displayed in Figure 7 and shows a singlet at high field corresponding to the four equivalent aromatic protons (a). The protons of the bridging OCH_2 groups are inequivalent, with the protons pointing out of the cavity appearing at significantly lower field (b) than those external to the cavity (c). This phenomenon is due to shielding effects; with the protons above the central cavity experiencing more of the π -cloud of the cavitand's aromatic rings. As these protons are magnetically inequivalent they geminally couple to one another so doublets are seen corresponding to both H_{inner} (c) and H_{outer} (b), $J = 6.9$ Hz. These protons are adjacent to the electron-rich aromatic ring; hence both doublets appear at relatively high field. It is also possible to observe the singlet corresponding to the CH_2N proton (e). Most of the other protons appear as broad resonances in the low frequency region of the spectra (g - o).

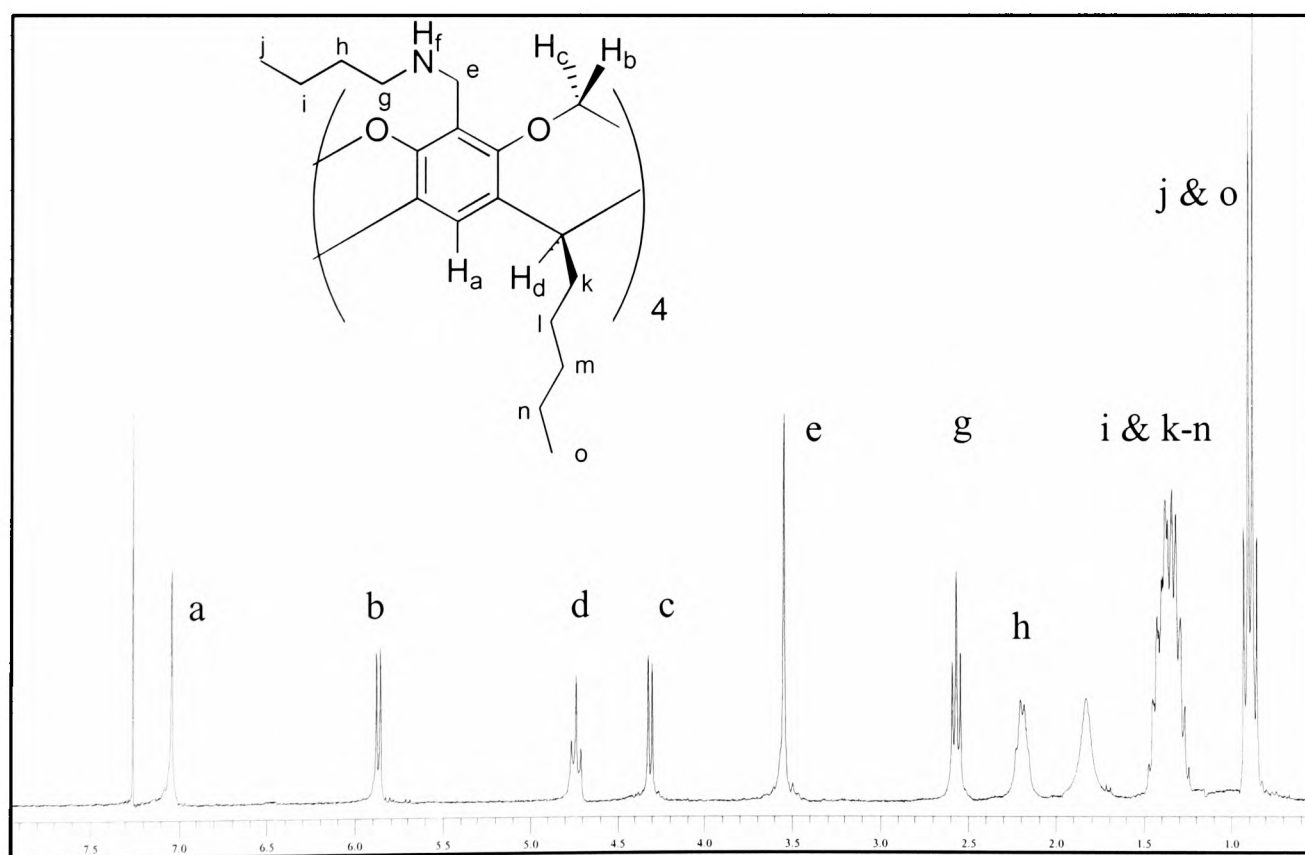


Figure 7 ^1H NMR spectrum of tetrakis-(*n*-butylaminomethyl) cavitand (43) (300MHz, CDCl_3 , 293K)

3 Metal-Dithiocarbamate Complex Formation

Previous work within this group has shown the tetrakis-(*n*-alkylaminomethyl) cavitands (**43**) and (**44**) have been able to form dithiocarbamate complexes upon addition of carbon disulphide in basic solution and subsequent treatment with transition metal salts^{24,25}. These structures have been demonstrated by X-ray crystallography to be nano-dimensional. It has been shown that addition of zinc(II) and cadmium(II) ions to the tetrakis-dithiocarbamate-functionalised cavitand yields a trimeric loop structure, containing six metal centres (Figure 8(left)). However, the analogous copper(II) complex exists as a flattened tetrahedron structure with eight copper nuclei (Figure 8(right)). It was further established that this tetrahedral arrangement was maintained upon the oxidation of the metal centres to copper(III), upon the addition of iodine.

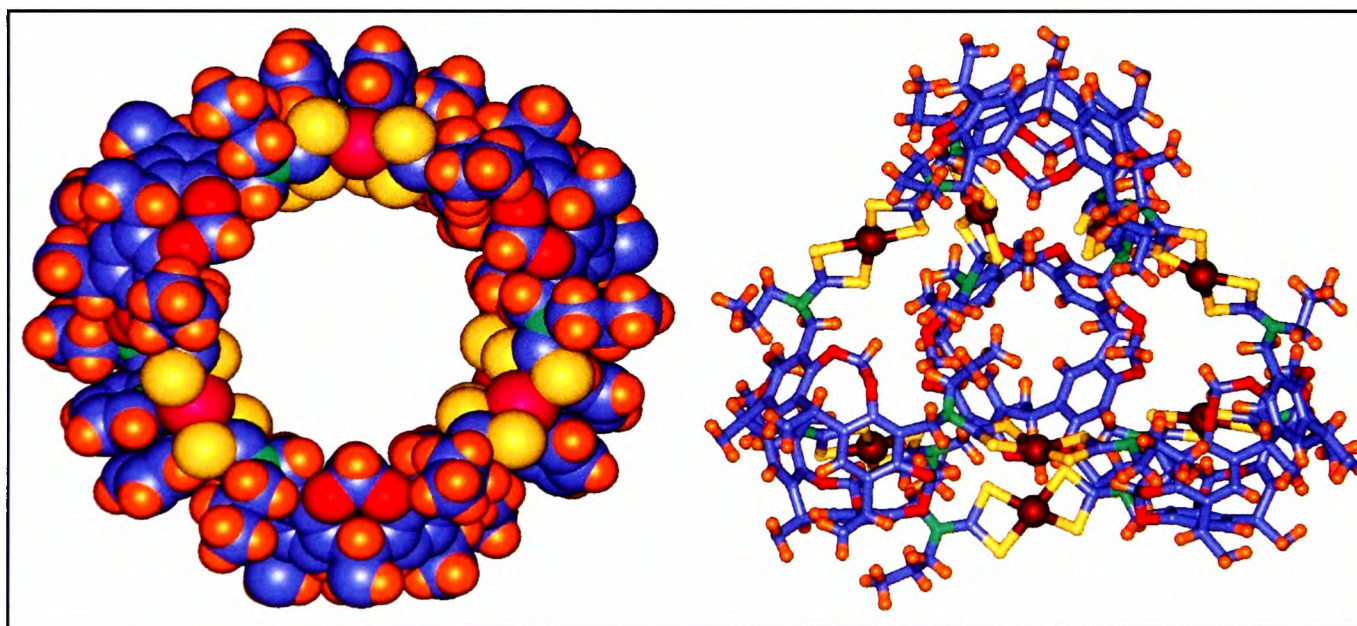


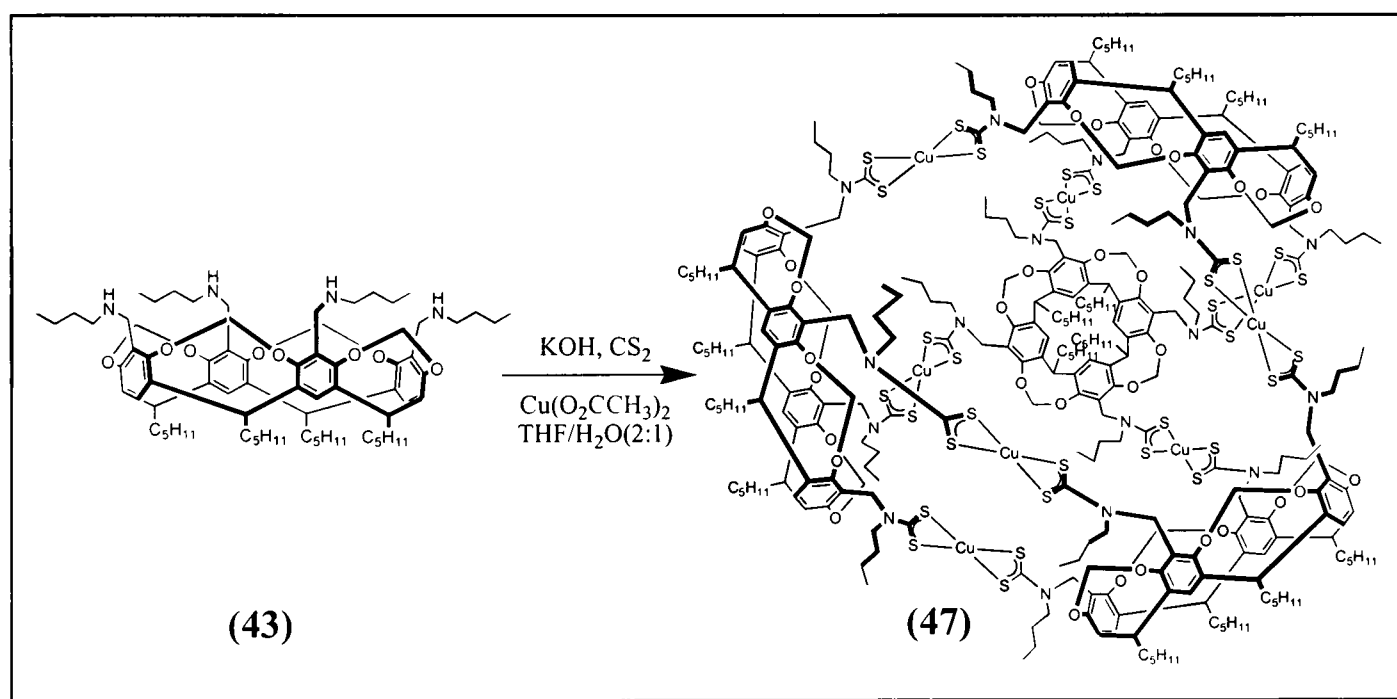
Figure 8 Zn(II) dithiocarbamate trimeric loop (left) and Cu(III) dithiocarbamate tetrameric complex (right) (Key: C - blue, H - orange, N - green, O - red, S - yellow, Zn - purple, Cu - dark red)

3.1 Synthesis of Nano-dimensional Hosts

The reactions of tetrakis-(alkylaminomethyl) cavitands (**43**) - (**46**) to form the nano-dimensional zinc(II), cadmium(II) and copper(II) dithiocarbamate complexes were performed. This allowed the further study of the structure and coordination chemistry of these complexes

as well as an examination into the variation the alkyl side chain has upon the architectures. In addition the use of these nano-dimensional structures for the stabilisation and templation of gold nanoparticles is explored in Chapter Six.

The addition of potassium hydroxide and carbon disulphide to a tetrahydrofuran/water (2:1) solution of the tetra-amine (43) generating a yellow solution characteristic of dithiocarbamate compounds. The resulting potassium dithiocarbamate salt was not isolated at this stage, instead excess copper(II) acetate was added resulting in a dark black solution. Recrystallisation of the ensuing solid generated a black crystalline solid the tetrameric copper(II) dithiocarbamate complex (47), in 50% yield.



Scheme 3 Synthesis of Cu(II) dithiocarbamate tetrameric complex (47)

The metal-directed self-assembly of copper(II) dithiocarbamate complexes was also attempted using the cyclohexyl- and benzyl-tetra-amines (45) and (46). Despite generating a black powder, which was soluble in organic solvents, mass spectrometric analysis failed to reveal the presence of any oligomeric structures. This is possibly a consequence of the bulkier side-chains either hindering the assembly process or forcing the precursor to adopt a conformation where it was unsuitable to generate a capsule.

Synthesis of the zinc(II) and cadmium(II) trimeric loops was undertaken using tetrakis-(*n*-

hexylaminomethyl) cavitand (**44**), as the resulting complexes proved to have greater solubility compared to the *n*-butyl chained structures. Addition of potassium hydroxide and carbon disulphide to a stirred tetrahydrofuran/water (2:1) solution of (**44**) and subsequent addition of zinc(II) and cadmium(II) acetate formed the complexes (**48**) and (**49**). These were purified by recrystallisation from a pyridine/water solution in 52 and 62% yields, respectively. This generates a pyramidal five-coordinate metal centre, with a pyridine donor occupying the previously vacant axial site.

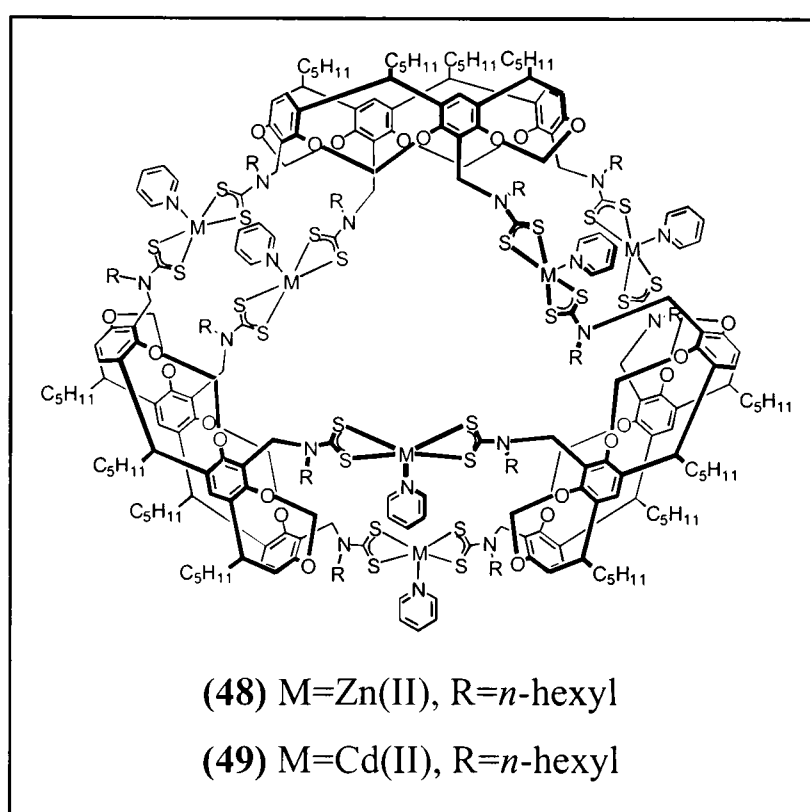


Figure 9 Zn(II) and Cd(II) trimeric loop structure

3.2 Characterisation of Complexes

It has been shown previously that although (**48**) and (**49**) display a trimeric structure in the solid state, there is little direct evidence that this is maintained in solution. Although their ^1H NMR spectra are broad, they do exhibit resonances characteristic of the presence of the resorcinarene ligands. The broad nature of the peaks is probably due to conformational mobility within the large self assembly, such as the slow rotational processes around the carbon-nitrogen bonds of the metal-dithiocarbamate units²⁸. Attempts to elucidate the

structure by both electrospray and MALDI-TOF mass spectrometry have also proved inconclusive, with only fragments observable.

3.2.1 Further Characterisation of Tetrameric Complex (47)

Unlike for the trimeric structures (48) and (49) it has been possible to demonstrate that the copper(II) dithiocarbamate-functionalised cavitand complex does maintain its tetrameric structure in solution. Electrospray and MALDI-TOF mass spectrometry, in the presence of the oxidant copper(II) triflate, have revealed adducts with triflate anions corresponding to the 4+, 5+ and 6+ states of the tetramer.

3.2.2 NMR

Due to the paramagnetic nature of the copper(II) nucleus it is not possible to obtain NMR spectra of the tetrahedral complex. However, addition of excess nitrosium tetrafluoroborate in $\text{CDCl}_3/\text{CD}_3\text{CN}$ (1:1), generated the diamagnetic copper(III) complex, allowing the spectrum to be recorded (Figure 10).

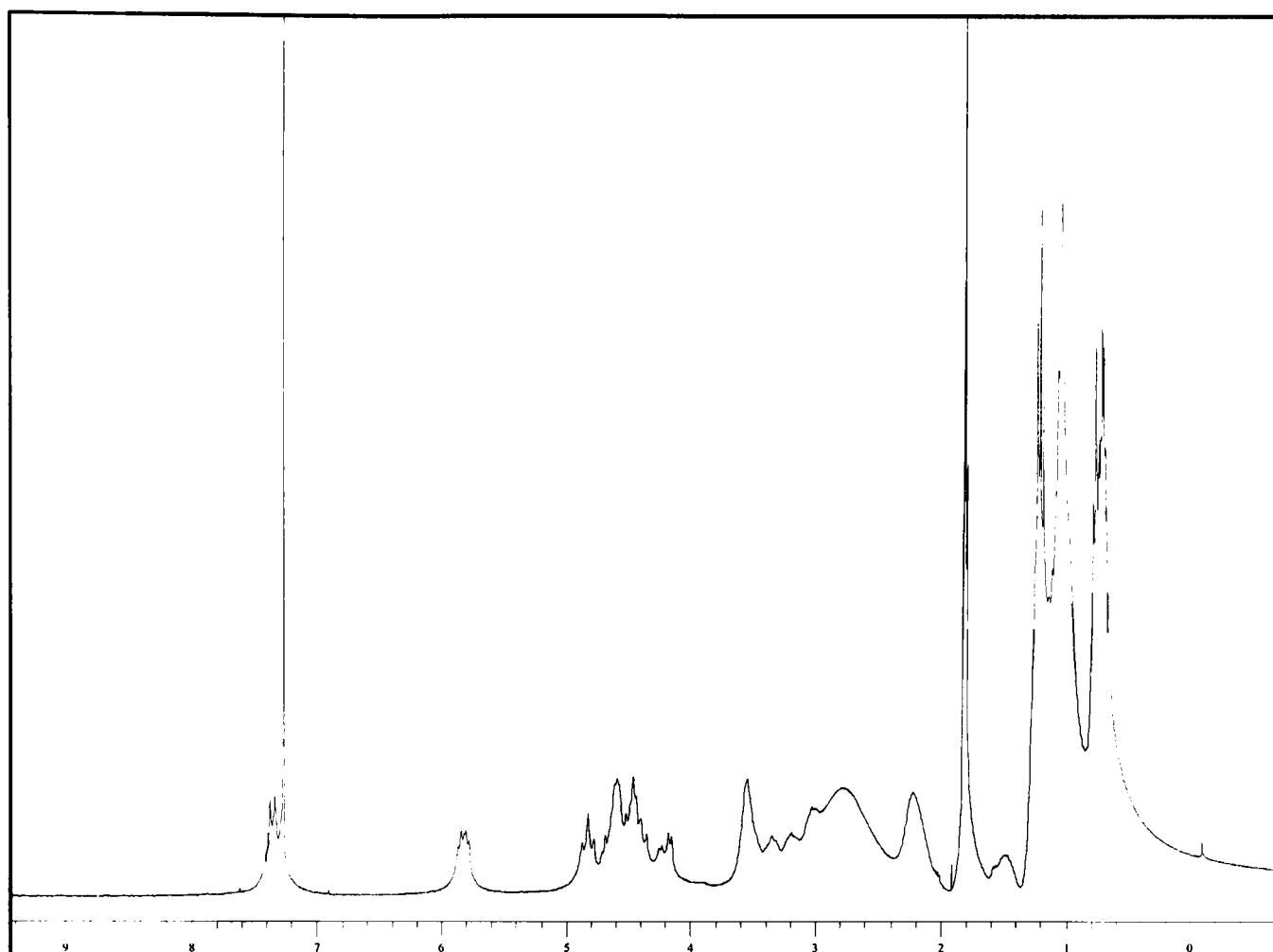


Figure 10 ^1H NMR of Cu(III) dithiocarbamate resorcinarene cavitand complex (47) in $\text{CDCl}_3/\text{CD}_3\text{CN}$ (1:1)

The spectrum displays peaks characteristic of the resorcinarene cavitand ligands, although they are once again broad in nature. The spectrum does appear more complicated than for that of the corresponding parent amine (43). For instance, the aromatic protons are observed as two broad singlets at 7.31 and 7.35 ppm and the outer bridging methylene protons are seen as a broad multiplet centred at 5.80 ppm. The lack of clarity for these signals is possibly a result of the structure of the complex, with the X-ray crystal structure of both the copper(II)²⁹ and copper(III)²⁵ dithiocarbamate-based resorcinarene complexes existing as a flattened tetrahedron in the solid state. If the same flattened tetrahedral structure was adopted in solution, then it would be expected that these two signals would appear doubled, as they would exist in two different environments. As this is the case, this is further evidence that an octanuclear structure is also adopted in solution. The remainder of the spectrum is difficult to assign due to the number of overlapping peaks, however the CH group adjacent to the

aromatic rings may be picked out as a triplet at 4.80 ppm and the alkyl chains are easily seen in the upfield region of the spectrum.

3.2.3 Electron Paramagnetic Resonance

As has been demonstrated in Chapter Two, copper(II) dithiocarbamate complexes may be studied via electron paramagnetic resonance (EPR) and give rise to high quality, well-resolved spectra. The simple mononuclear compound **(20)** was found to give a sharp four-line spectrum, due to the interactions between the $I = 3/2$ copper nucleus and the unpaired electron. In the case of the *m*-xylyl spaced macrocycles **(7-Cu)** and **(11-Cu)** a sharp seven line spectrum was observed as a result of strong electron-electron through bond coupling between the two copper centres.

An investigation into the EPR properties of the octanuclear **(47)** was undertaken in collaboration with Dr. J. Maher, University of Bristol. A spectrum of **(47)** was recorded in dichloromethane at 296K and again in dichloromethane/toluene (1:1) at 10K. The former spectrum is displayed in Figure 11.

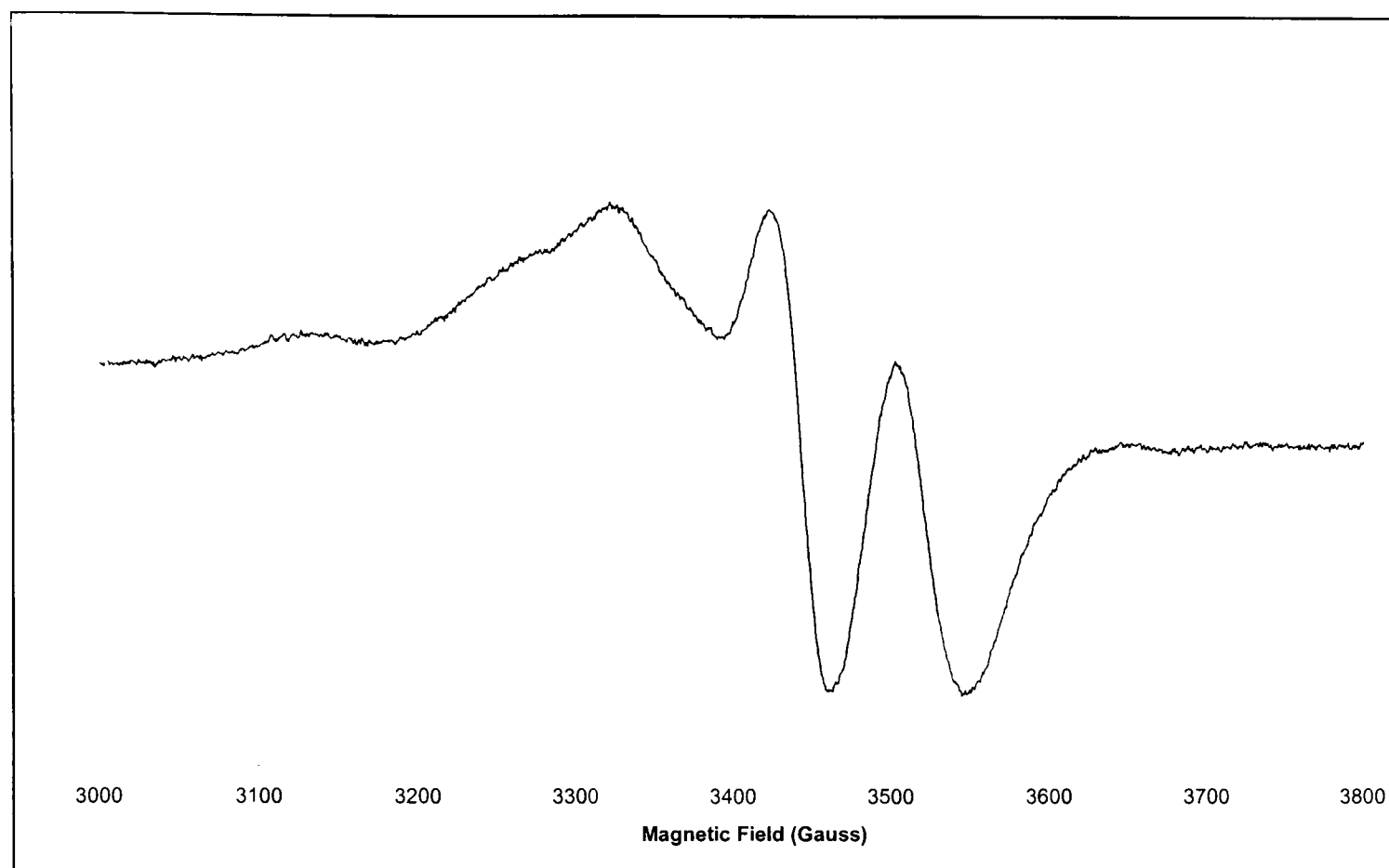


Figure 11 EPR spectrum of (47) in CH_2Cl_2 /toluene at 296K

Both spectra gave rise to broad, poorly resolved peaks, in contrast to that of the simple copper(II) bis-(*N,N'*-diethyldithiocarbamate) (**20**) (Chapter Two). However, the signal still resembles the four lines expected from a paramagnetic copper(II) species and has similar *g*- and *A*-values to previous examples (*g* = 2.047, *A* = 79G). The absence of additional peaks in the spectrum and an *A* value of 79G does suggest that the eight copper centres within the tetrahedral structure are behaving independently of each other, with any potential coupling process (as seen with shorter copper-copper through-bond distances) too long-range to be viable.

3.2.4 Electrospray Mass Spectrometry

It has been demonstrated that oxidation of the copper(II) tetramer allows its detection through mass spectrometry. This was repeated using nitrosium tetrafluoroborate as an oxidant.

A large excess of oxidant was introduced into the mass spectrometer prior to injection of a sample of (**47**), thus the dithiocarbamate complex was oxidised within the mass spectrometer.

The resulting spectrum was recorded using ambient temperatures and low cone voltages and is displayed in Figure 12.

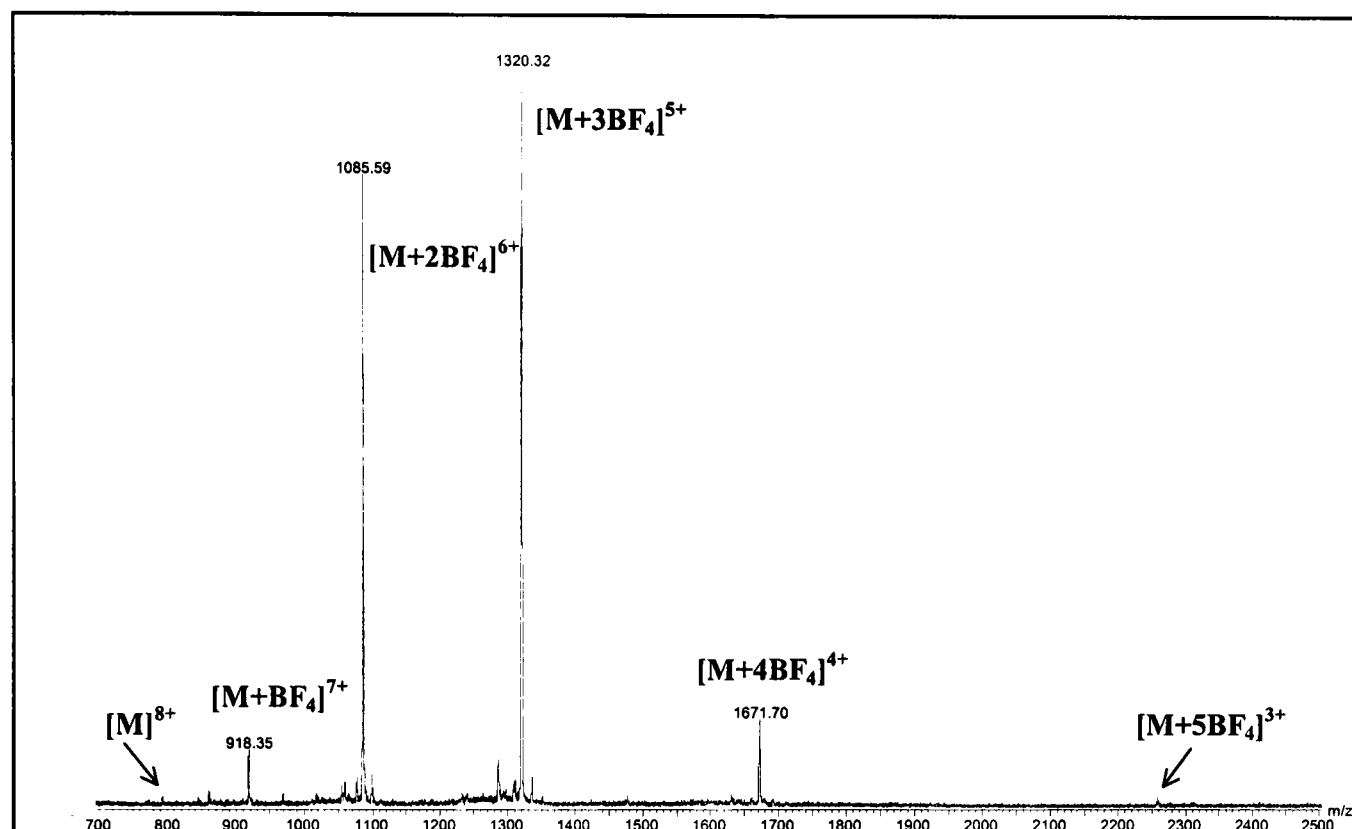


Figure 12 Electrospray mass spectrum of (47) in the presence of $NOBF_4$

The spectrum displays a series of multiply charged peaks corresponding to the formation of adducts with varying number of tetrafluoroborate anions. Since the main peaks in the spectrum represent the molecular ion-pairs of the association of two and three counteranions, it is possible that these may be inside the tetrahedral cage.

3.3 Group 10 Dithiocarbamate Complexes

It has been demonstrated in Chapter Two that the divalent Group 10 dithiocarbamate complexes of nickel, palladium and platinum can be used to assemble bimetallic macrocycles. The metal-directed self-assembly using the larger resorcinarene cavitand system was also attempted with these ions.

The tetra-dithiocarbamate derivatised cavitand was synthesised *in situ* via addition of potassium hydroxide and carbon disulphide to (43) in a stirred tetrahydrofuran/water (2:1) mixture. Nickel(II) acetate, potassium tetrachloropalladate and tetrachloroplatinate were

subsequently added, yielding green, yellow and red solids, respectively. Unfortunately, the platinum derivative was insoluble in organic solvents; however it was possible to extract the nickel and palladium complexes (**50**) and (**51**) into chlorinated solvents. These complexes (which give only one spot on a TLC plate) were purified by recrystallisation from a dichloromethane/ethanol solvent system, yielding crystalline solids. Unfortunately, single crystals of both (**50**) and (**51**) failed to diffract upon X-ray analysis, not allowing the elucidation of their structures. Elemental analysis of these solids were, however, consistent with the formation of desired nickel(II) and palladium(II) dithiocarbamate complexes with the resorcinarene functionalised ligand. The use of both electrospray and MALDI-TOF mass spectrometry, were unable to determine the structures of (**50**) and (**51**), with only fragmentation peaks visible. However, since the complexes are diamagnetic, they have been studied using NMR spectroscopy (Figures 13 and 14).

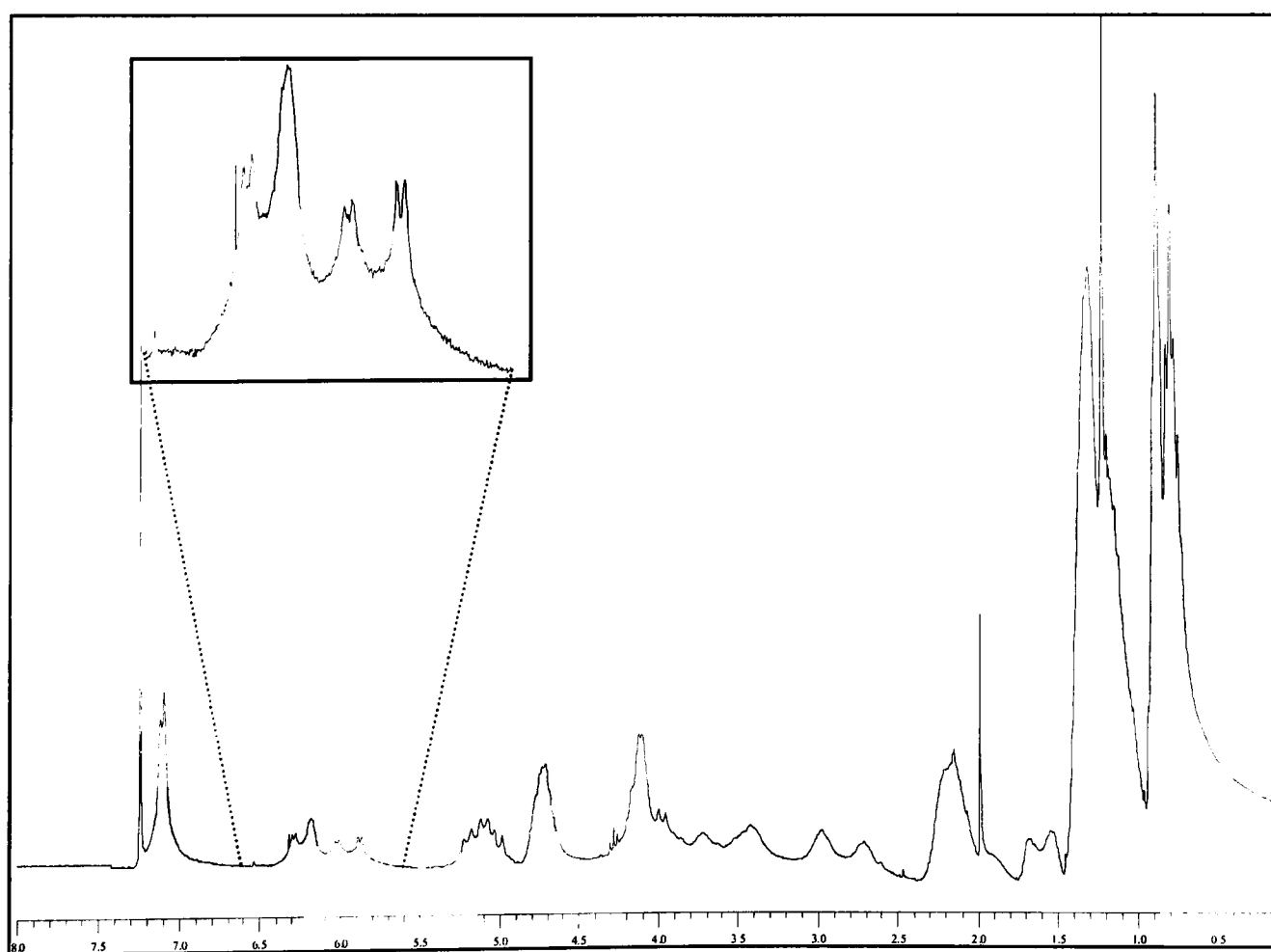


Figure 13 ^1H NMR of Ni(II) dithiocarbamate resorcinarene cavitand (R=Bu) (**50**) (300MHz, CDCl_3 , 293K) Inset: region displaying OCH_2 protons

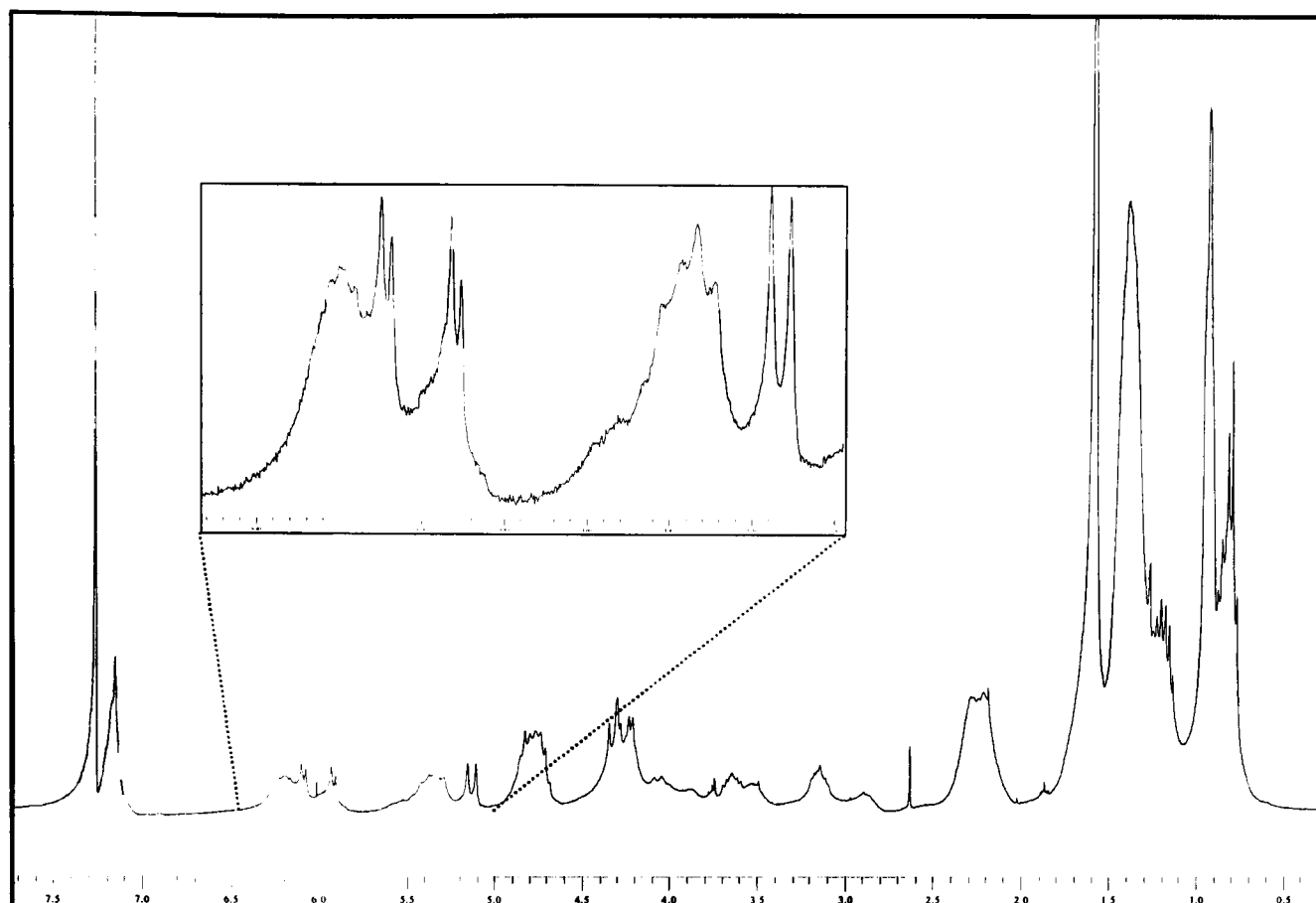


Figure 14 ¹H NMR of Pd(II) dithiocarbamate resorcinarene cavitand (R=Bu) (51) (300MHz, CDCl₃, 293K) Inset: region displaying OCH₂ protons

The resulting broad spectrum (which does not vary upon heating or cooling) displays peaks corresponding to those expected for the resorcinarene framework. Interestingly however, the OCH₂ peaks do not appear as the two doublets, which are observed in the parent resorcinarene (Figure 7), but a number of peaks (Figures 13 and 14 insets). This is possibly due to the occurrence of more than one environment of these protons within the complexes. This may imply the formation of an unsymmetrical structure, such as the flattened tetramer observed for the copper complex (47), since it would be expected that dimer or trimer formation would result in symmetrical environments for these protons. There are further factors that make it likely that the nickel(II) and palladium(II) systems adopt the same octanuclear structure as the copper(II) complex. As has been seen in Chapter Two, copper(II) dithiocarbamate complexes generally adopt the same structure in the solid state as the analogous nickel(II) and palladium(II) architectures. In addition, d⁸ gold(III) dithiocarbamate species have also been demonstrated to adopt the same square planar geometry about the central metal ion. As

discussed in Chapter Four, gold(III) dithiocarbamate resorcinarene complexes have been shown to adopt a tetrahedral geometry, both from metal-directed self-assembly of (43) in aqueous solution or from transmetallation of the corresponding copper(II) based complex (47). This suggests that the tetrahedral structure is the thermodynamically favoured structure for ions with square planar geometries. Similarly, the trimeric loop structure is only formed where there is square-based pyramidal coordination geometry about the metal ion. It is this angle generated from the metal coordination sphere which allows the necessary curve to be accommodated in the structure to create the cyclic structure. It is therefore likely, despite being unable to determine the X-ray crystal structure of the nickel(II) and palladium(II) complexes (50) and (51), by analogy, that they also adopt an octanuclear tetrahedral structure.

4 Binding Studies

4.1 Fullerene Binding By Trimeric Loop Complexes

The discovery in 1985, of buckminsterfullerene and its related fullerenes represents one of the most striking breakthroughs in chemistry in recent years, and earned the 1996 Nobel Prize in Chemistry for its discoverers³⁰. The interesting physical properties and highly symmetric cage structure of C₆₀ has resulted in rapid growth and active research in this area, ranging from superconductivity upon alkali metal doping through to biological activity³¹. There has also been significant exploration in the supramolecular chemistry of fullerenes³². For example, the binding of fullerenes by electron-rich cup-shaped hosts, such as calixarenes, CTV and modified porphyrins, have been demonstrated to form strong inclusion complexes, due to their steric and electronic complementarity^{33,34,35}. Indeed, recently C₆₀ has even been used as an effective template in the synthesis of calix[5]- and calix[6]-resorcinarenes³⁶.

It has been demonstrated, by UV-vis spectroscopy, that C₆₀ and C₇₀ form extremely strong complexes with the nano-dimensional trimeric cadmium(II) and zinc(II) structures, in toluene

and benzene³⁷. It is proposed that this strong association between host and guest is a result of the fullerene binding (in a 1:1 stoichiometry³⁸) inside the spatially complementary central cavity of the resorcinarene complex. The fullerene is held within the cavity by the formation of favourable charge transfer interactions between the electron-rich sulphur atoms of the dithiocarbamate moieties and the electron-deficient fullerene surface. This gives rise to a distinctive red-brown colour upon mixing the two components. This sulphur-fullerene interaction is suggested from molecular mechanics calculations and also through the solubility of fullerenes³⁹. As can be seen from Table 1, C₆₀ has a relatively high solubility in carbon disulphide in comparison to its solubility in other common organic solvents. It is this affinity for the electron rich-sulphur donors by the electron-deficient host that is attributed to result in its high association constants. The preorganisation of six electron-rich dithiocarbamate moieties to form a geometrically complementary host is believed to result in the strong affinity for fullerene guests.

Solvent	Solubility of C ₆₀ (mg ml ⁻¹)
Carbon disulphide	7.9
Toluene	2.8
Benzene	1.7
Carbon Tetrachloride	0.32
Hexane	0.04
Ethanol	0.01

Table 1 The solubility of C₆₀ (mg ml⁻¹) in a range of common organic solvents at 303K

4.1.1 ¹³C NMR Spectroscopy

¹³C NMR has been previously used to gauge the inclusion of fullerenes by calixarene and CTV-based hosts by measuring their induced shifts. Encapsulation by these hosts has led to

measurable upfield shifts (typically ~ 0.3 ppm) due to anisotropic shielding by the host^{40,41,42}. It has also been demonstrated that fullerenes also interact with hydrophobic cavities of the electron-rich γ -cyclodextrin (γ -CD), in a (1:2) C_{60} : γ -CD complex⁴³. These complexes are primarily stabilised through charge transfer interactions between oxygen donors of C_3 and C_4 of the glucose subunits and the electron-deficient fullerene. The induced shift of these complexes has also been measured and this has given rise to a downfield perturbation of 0.82 ppm in the ^{13}C NMR signal of C_{60} . The differing nature of these shifts is indicative of the nature of the different mode of binding between host and guest.

Due to its symmetry, C_{60} exhibits one peak in its ^{13}C NMR spectrum, which in toluene- d_8 occurs at 143.14 ppm. Addition of one equivalent of **(48)** to this NMR sample results in a red solution - characteristic of the formation of the host-guest complex. Subsequent analysis reveals a 0.58 ppm downfield perturbation of the C_{60} resonance (Figure 15). This downfield shift is consistent with the electron-deficient fullerene coordinating to the electron-rich sulphur donors of the dithiocarbamate groups. This charge transfer system results in a greater electron density residing on the fullerene when it is bound within the central cavity, leading to a downfield perturbation. This is further evidence that this is the method of coordination of the guest and not by a π - π stacking interaction with the resorcinarene subunits.

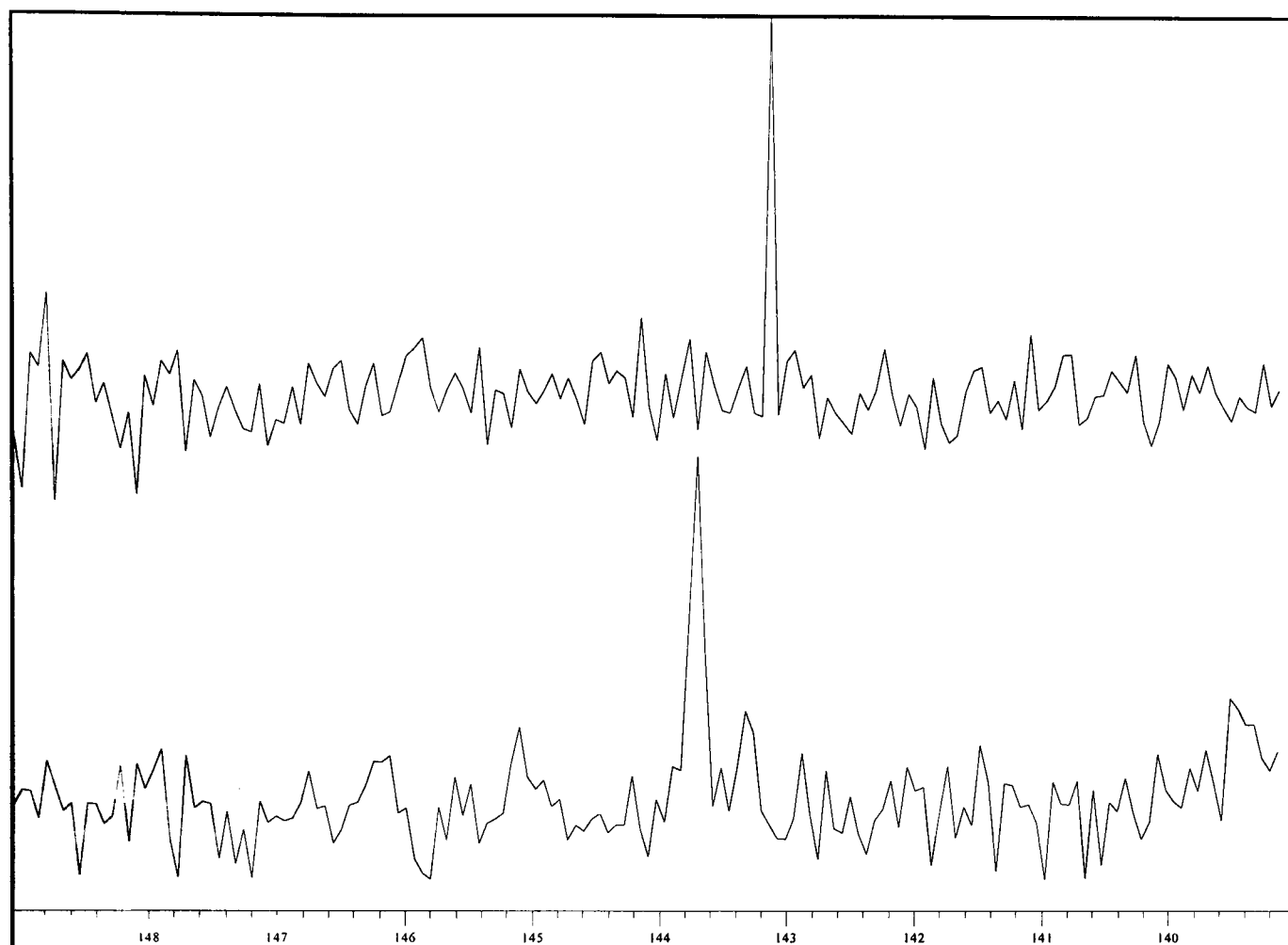


Figure 15 ^{13}C NMR spectra of C_{60} in toluene- d_8 in the presence (lower) and absence (upper) of one equivalent of Zn(II) dithiocarbamate resorcinarene complex (48)

Unfortunately, the poor solubility of C_{60} and the resorcinarene complexes did not allow the binding process to be further investigated by a titration experiment. In addition, the analogous cadmium complex (49) was also insufficiently soluble to study its binding of C_{60} via this method.

4.1.2 Electrochemical Studies

The high electron affinity of fullerenes was theoretically predicted before their solution electrochemistry was recorded⁴⁴. It was not, however, until the early 1990s that the full six one-electron reductions of C_{60} was demonstrated^{45,46,47}.

It has been possible to exploit the electrochemical properties of the fullerenes in the fabrication of sensors for host-guest chemistry. For example, D'Souza and co-workers recently synthesised a C_{60} molecule functionalised with a dibenzo[18]crown-6 unit (Figure

16)⁴⁸. Complexation of metal ion within the crown ethers cavity resulted in anodic shifts in the C_{60} redox waves, as the presence of the electron-withdrawing guest made the reduction of the fullerene easier. The first two reduction waves of the complex were investigated and it was found that, in general, the magnitudes of the induced shifts of the second reduction wave were greater than the first, with the second reduction wave of the potassium complex giving the largest (38mV) shift.

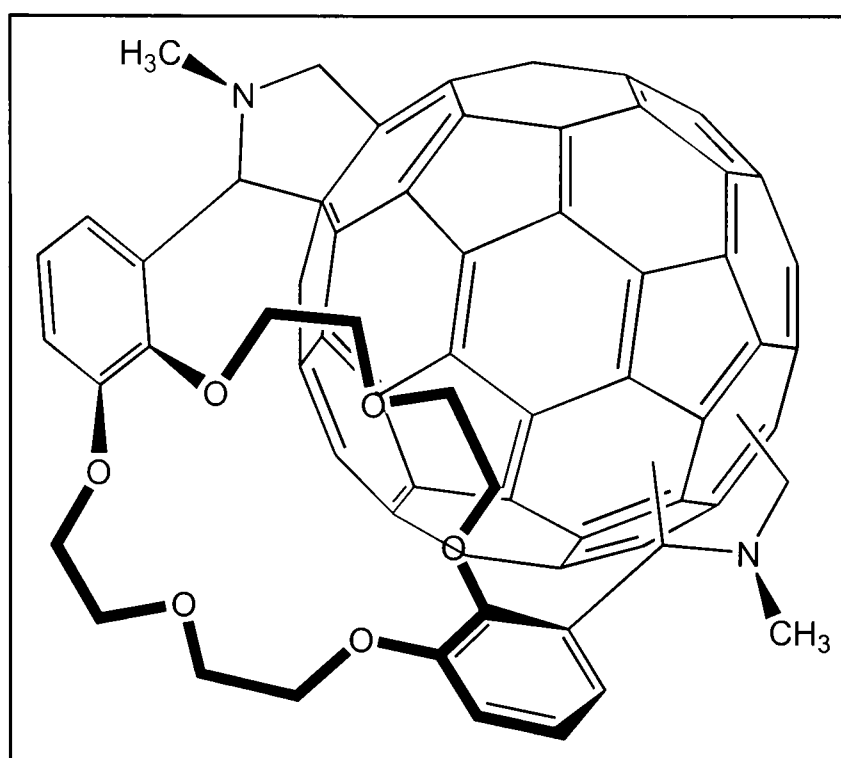


Figure 16 Bis-functionalised fullerene-dibenzo[18]crown-6 conjugate

An investigation was undertaken as to whether the interaction between **(48)** and C_{60} could be probed through the study of the electrochemical properties of the fullerene. The cyclic and square wave voltammetry of the first three reduction waves of C_{60} were recorded in a 0.1M tetra-*n*-butylammonium tetrafluoroborate toluene/acetonitrile (85:15) solution. One equivalent of **(48)** was then added to the purple solution, which turned orange: characteristic of host-guest complexation. The resulting cyclic voltammogram is shown in Figure 17 and the electrochemical data displayed in Table 2.

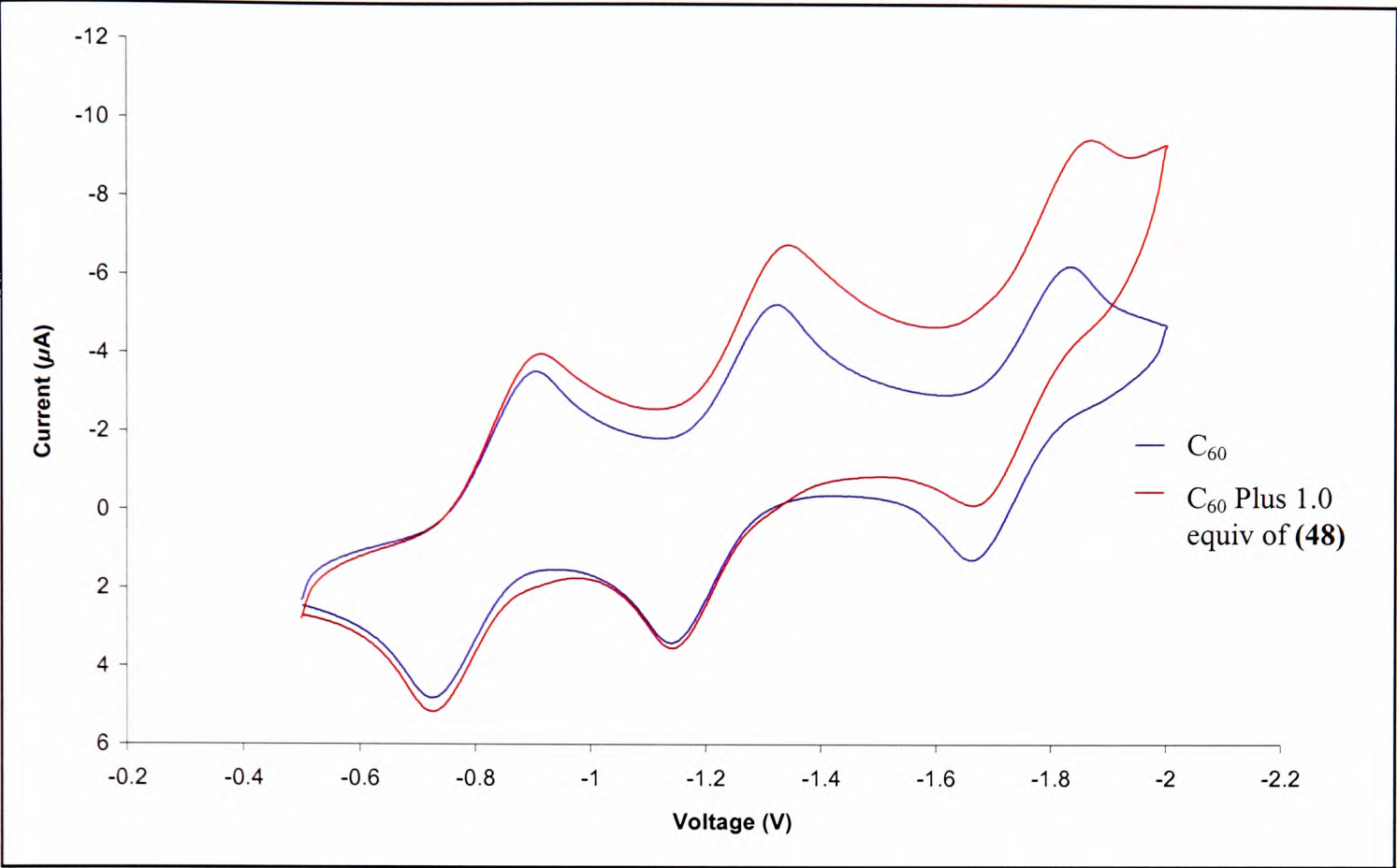


Figure 17 Cyclic voltammogram of C₆₀ in the presence and absence of the trimeric Zn(II) dithiocarbamate resorcinarene complex (48) (85:15 toluene:MeCN containing 0.1M TBABF₄) , working electrode glassy carbon scan rate 100 mVs⁻¹ {Ag/Ag⁺ reference electrode}

		Reduction 1 (V)	Reduction 2 (V)	Reduction 3 (V)
C ₆₀	E _½	-0.83	-1.24	-1.74
	E _{pc}	-0.90	-1.32	-1.83
	E _{pa}	-0.73	-1.14	-1.66
C ₆₀ Plus (48)	E _½	-0.83	-1.25	-1.76
	E _{pc}	-0.91	-1.34	-1.87
	E _{pa}	-0.73	-1.14	-1.66

Table 2 Electrochemical data for the first three reduction waves of C₆₀ in the presence and absence of Zn(II) dithiocarbamate complex (48) (Errors estimated at ±5mV)

Addition of (48) does not result in a discernable change in the first reduction wave of C₆₀. It does, however, lead to a 10 and 20mV cathodic shift for the second and third waves,

respectively. This illustrates, as expected, that of the reduction of the fullerene becomes more difficult when it is bound inside the electron-rich cavity of **(48)**. The fact that the reductions also become increasingly more difficult with each subsequent electron transferred, shows the decreasing affinity between the electron-rich host and the increasingly negatively-charged fulleride anions.

4.2 Fullerene Binding by Tetrameric Copper(II) Complexes

The copper(II) dithiocarbamate tetrameric resorcinarene complex **(47)**, possesses large internal dimensions (approximately 20 Å across) potentially big enough for the inclusion of a large guest species. However, entrance to this cavity is restricted, since its portals are too small (diameter ~8 Å) to easily allow a large guest molecule to pass through them into the centre. It may, however, be possible to utilise the lability of the copper(II) dithiocarbamate bond (as previously demonstrated in Chapter Two) to enable the encapsulation of suitably large guests, such as C₆₀, within the internal cavity of the nano-dimensional host. Here, rapid assembly/disassembly of the labile architecture increases the portal size which then allows the inclusion of the large guest species.

4.2.1 ¹³C NMR

A 1:1 mixture of C₆₀ and the copper(II) tetrameric host **(47)** was prepared and its ¹³C NMR recorded. Solubility determined that a 2:1 toluene-d₈/chloroform-d solution be used. In the absence of any host, C₆₀ exhibits one peak in its spectrum, at 143.19 ppm. One equivalent of **(47)** was then added to the solution and the spectrum was re-recorded five days later. After this time, the peak was observed to be shifted upfield to 143.09 ppm. This is in contrast to **(48)** which observed a much larger downfield shift upon binding C₆₀. However, the difference in the shifts can be attributed to the variation in coordination of the guest. In the case of the

zinc(II) based system coordination occurs via the formation of a charge transfer complex with the electron-rich sulphur donors. No such interactions are observed for the binding of the copper(II) analogue and so the binding process is predominantly through hydrophobic interactions and π - π stacking with the aromatic groups of the resorcinarene subunits. The upfield shift is therefore consistent with the fullerene being encapsulated by the host and experiencing anisotropic shielding from the aromatic groups of the resorcinarene moieties.

4.2.2 Electrospray Mass Spectrometry

The *in situ* oxidation of the copper(II) dithiocarbamate resorcinarene tetrameric complex (**47**) with nitrosium tetrafluoroborate, has been shown to enable the generation of high quality mass spectra of the oxidised copper(III) structure. An investigation into whether this technique may also indicate potential guest binding was undertaken.

An equimolar 1 μ M solution of C₆₀ and the copper(II) dithiocarbamate tetramer (**47**) was prepared in acetonitrile/dichloromethane/toluene (18:1:1). 10 μ L of this was injected into the electrospray mass spectrometer at regular intervals, following the injection of a 1 mM solution of the oxidant nitrosium tetrafluoroborate. Over time, peaks began to emerge for the presence of C₆₀ adducts with the tetrameric host [T.C₆₀]. Interestingly, only peaks for a 1:1 complex were observed, suggesting the association may be occurring within the central cavity, as opposed to externally where the formation of multiple adducts would be expected and without any time dependence. Since these peaks grew over time, it is likely that their growth represent the encapsulation of C₆₀ within the nano-dimensional framework. This would mean that inclusion of the electron-deficient guest was allowed, over time, into the electron-rich cavity by the lability of the copper(II) dithiocarbamate bonds.

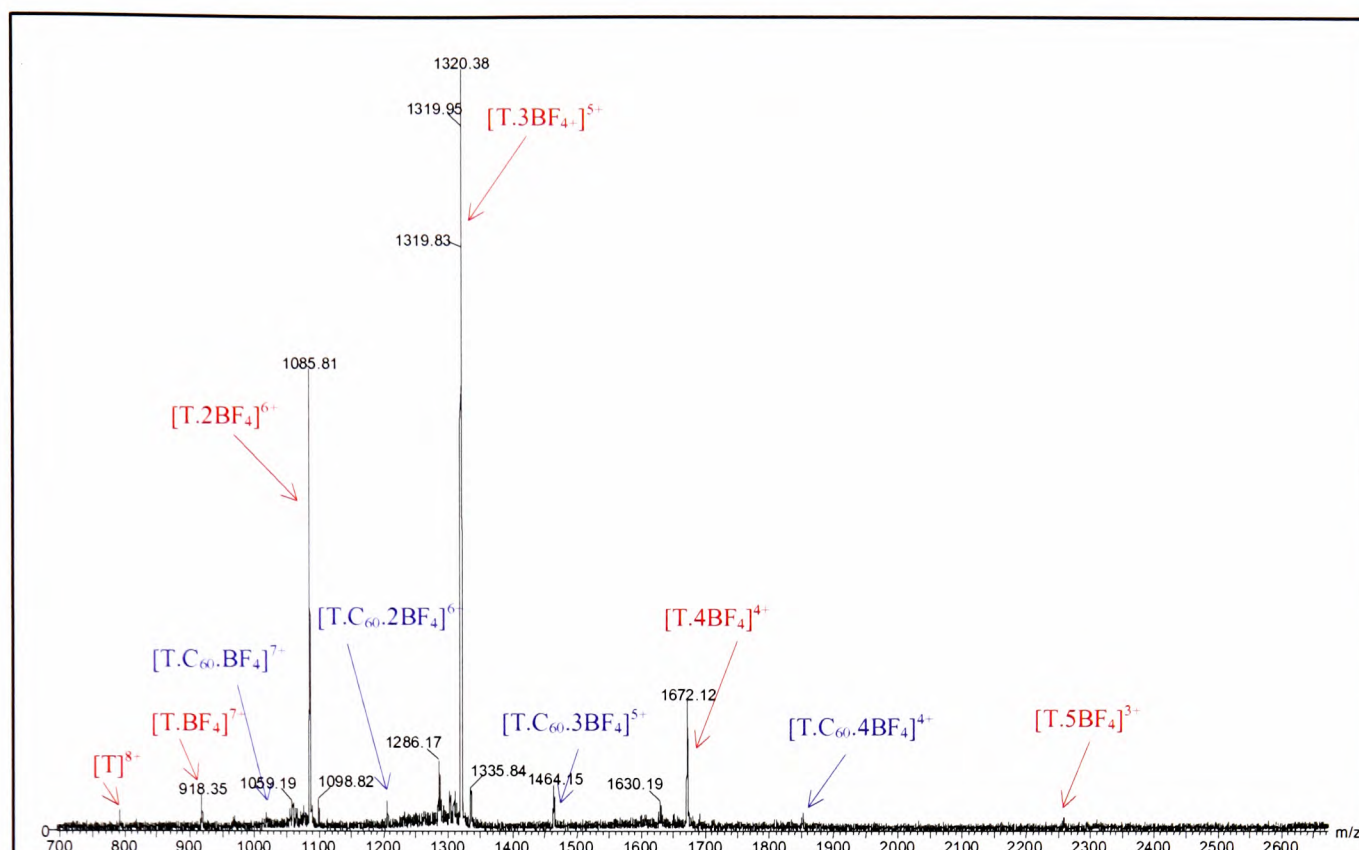


Figure 18 Electrospray mass spectrum of 1:1 solution of Cu(II) tetramer (47) and C₆₀ after 10 minutes

After only 10 minutes small peaks could be observed for adducts with C₆₀ (Figure 18). These continued to become greater in intensity and after 24 hours were significantly larger (Figure 19). After this time the peaks did not continue to grow, possibly suggesting that the system had reached equilibrium. Addition of ten equivalents of C₆₀ to the tetrameric host, gave rise to a similar spectrum, after one hour, to that observed with just one equivalent after 24 hours, suggesting the equilibrium had been shifted.

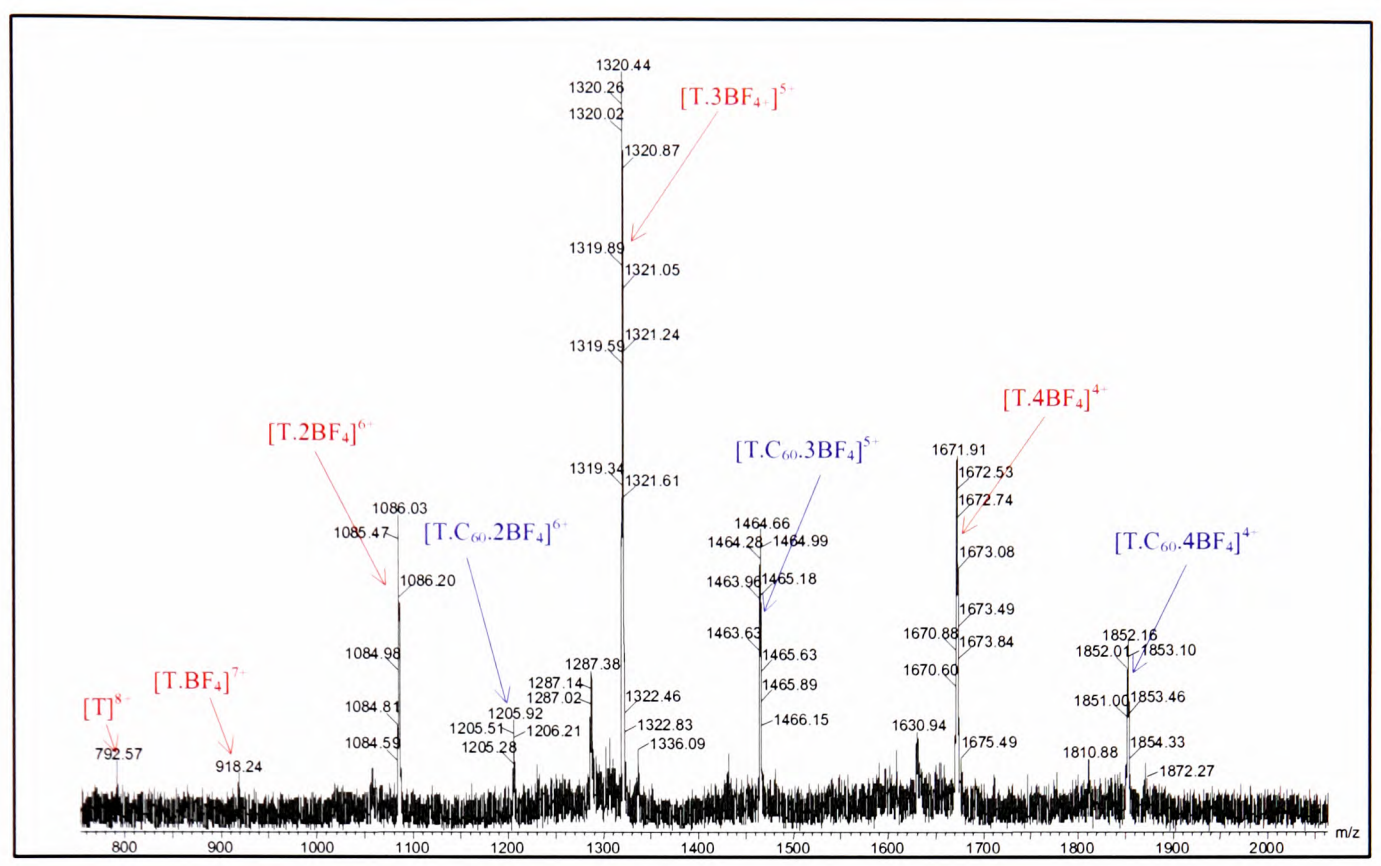


Figure 19 Electrospray mass spectrum of 1:1 solution of Cu(II) Tetramer (47) and C₆₀ after 24 hours

4.2.3 Electrochemistry

It has previously been demonstrated that the copper resorcinarene dithiocarbamate complex (47) displays one quasi-reversible copper(II/III) oxidation wave. This is perhaps somewhat surprising considering the number of different metal ions and environments - although it does suggest that the copper centres are electronically independent of each other.

The cyclic and square wave voltammograms of (47) were re-recorded in a 0.1M tetra-*n*-butylammonium tetrafluoroborate dichloromethane/toluene/acetonitrile (9:9:2) solution. The resulting cyclic voltammogram is displayed in Figure 20.

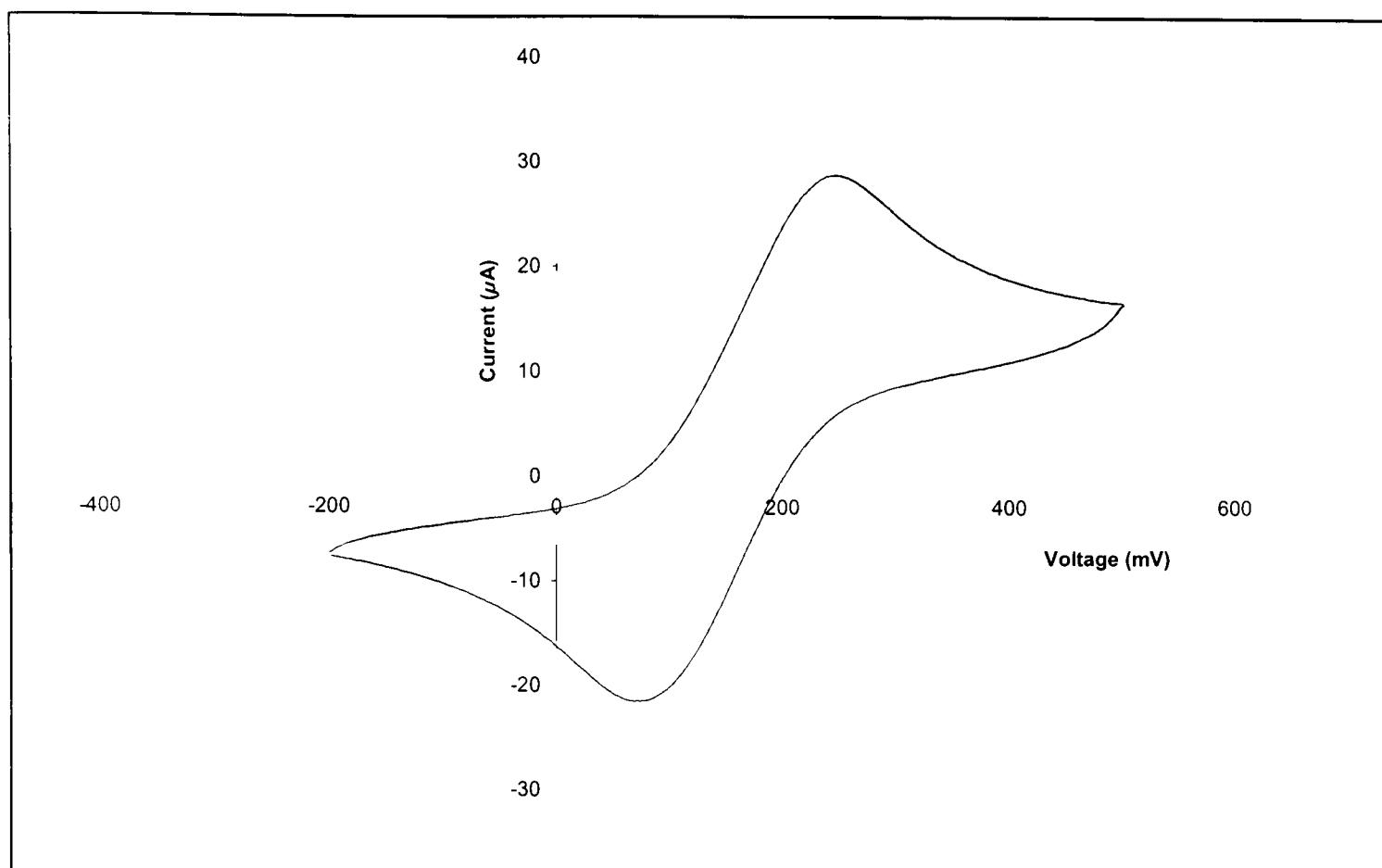


Figure 20 Cyclic voltammogram of Cu(II/III) oxidation wave of tetrameric complex (47) (9:9:2 CH_2Cl_2 /toluene/MeCN containing 0.1M TBABF₄) working electrode glassy carbon, reference electrode Ag/AgNO₃, scan rate 100 mVs⁻¹

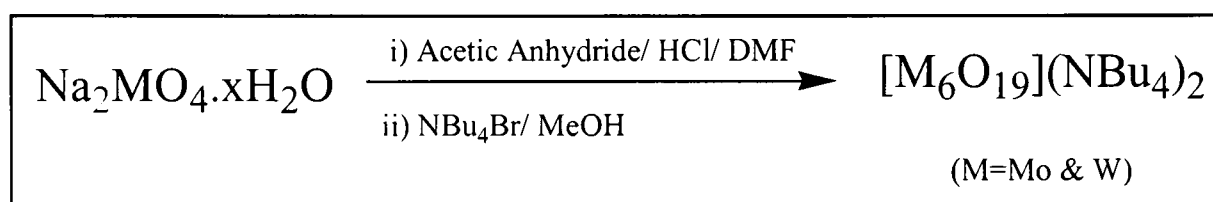
As can be seen, this generated a single electrochemical wave ($E_{\text{ox}} = 0.25\text{V}$, $E_{\text{red}} = 0.07\text{V}$, $E_{1/2} = 0.16\text{V}$) corresponding to the copper(II/III) oxidation. One equivalent of C₆₀ was added to this solution and its electrochemical properties were investigated at regular intervals. Unfortunately, even after 24 hours, the presence of the fullerene did not perturb the copper(II/III) oxidation wave. Due to the low solubility of C₆₀ it was not possible to examine the effect of adding excess of the fullerene to the solution.

4.3 Polyoxometallate Binding

Polyoxometallates are large spherical structures based upon the linking of MO₆ octahedra, which have proved very versatile in the fields of catalysis, medicine and material science⁴⁹. The most common structure, the Lindqvist structure [M₆O₁₉]ⁿ⁻, is formed by the edge linking of six MO₆ subunits resulting in an octahedral nano-dimensional metal oxide cluster. Recently, anionic polyoxometallates were shown to strongly interact with planar aromatic

moieties appended with cationic side-arms predominantly through electrostatic attractions⁵⁰. Due to the structural similarity between the planar aromatic groups and the resorcinarene frameworks, it was investigated whether polyoxometallates would interact within the large aromatic-rich cavities of charged resorcinarene dithiocarbamate complexes. This was achieved through the use of electrospray mass spectrometry.

The tetra-*n*-butylammonium (TBA) salts of the dianionic molybdenum and tungsten Lindqvist-type polyoxometallates were prepared through literature procedures (Scheme 4)^{51,52}. Unfortunately, due to the poor solubility of the tungstate cluster, complexation studies could not be undertaken with this species.



Scheme 4 Synthesis of polyoxometallates

A 1 μM solution of the copper(II) dithiocarbamate tetramer (**47**) and ten equivalents of $(\text{TBA})_2[\text{Mo}_6\text{O}_{19}]$ in acetonitrile/dichloromethane (99:1) was prepared and enough nitrosium tetrafluoroborate added to generate a green solution. This ensured the oxidation to the corresponding copper(III) based dithiocarbamate complex. The solution was subsequently injected in the electrospray mass spectrometer and the resulting spectrum is displayed in Figure 21.

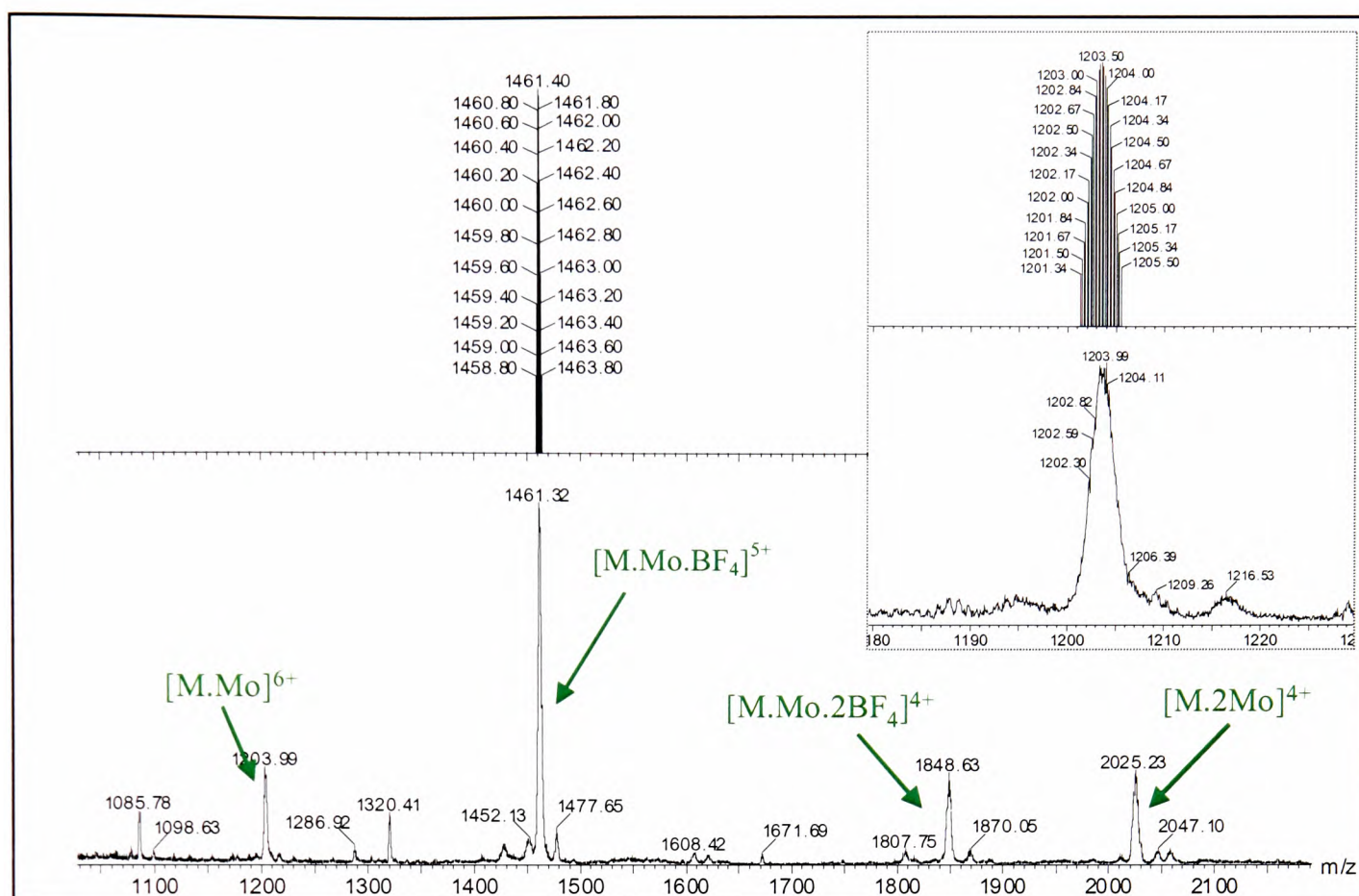


Figure 21 Electrospray mass spectrum of Cu(III) resorcinarene dithiocarbamate complex (47) in the presence of Mo₆O₁₉²⁻ (Mo) {Inset: Isotope model for 1:1 complex, 6+ peak, upper isotope model for 1:1 complex.BF₄, 5+ peak}

Observation of the resulting electrospray mass spectrum revealed peaks corresponding to the formation of adducts with both polyoxometallate and tetrafluoroborate. It is possible that this is a consequence of a molybdate anion associating within the central cavity of the complex, via a combination of electrostatic and favourable interactions with the aromatic groups. However, a peak was also seen for combination of two molybdate anions with the tetramer, suggesting that this association may also be occurring external to the central cavity, as it is unlikely that there is sufficient room to accommodate two polyoxometallates internally. Unfortunately, due to solubility problems it was not possible to investigate the electrochemical properties of (47) in the presence of polyoxometallate anions.

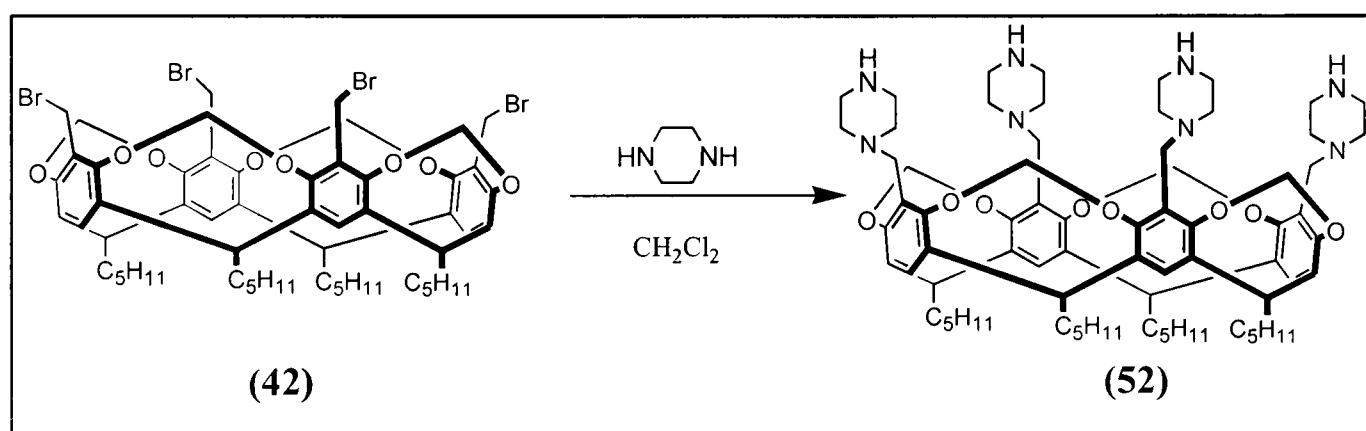
5 Flexible Resorcinarenes

Since the formation of dithiocarbamate complexes of the rigid aminomethyl-methylene-spaced cavitands generated structures of high nuclearity, investigation of cavitand ligands

with increased flexibility was undertaken to see if they would create different, possibly lower symmetry, architectures. Ligands with a greater degree of flexibility were therefore designed to observe the effect upon the self-assembly process.

5.1 Piperazine-Based Resorcinarenes

Addition of tetrakis-(bromomethyl)resorcinarene (**42**) to a dichloromethane solution of excess piperazine, generated the tetrapiperazine substituted cavitand (**52**) (Scheme 5). This was purified through removal of the excess amine by sublimation under reduced pressure to produce a white solid in 84% yield. The product was fully characterised by NMR, mass spectrometry and elemental analysis.



Scheme 5 Synthesis of piperazine-appended resorcinarene subunits

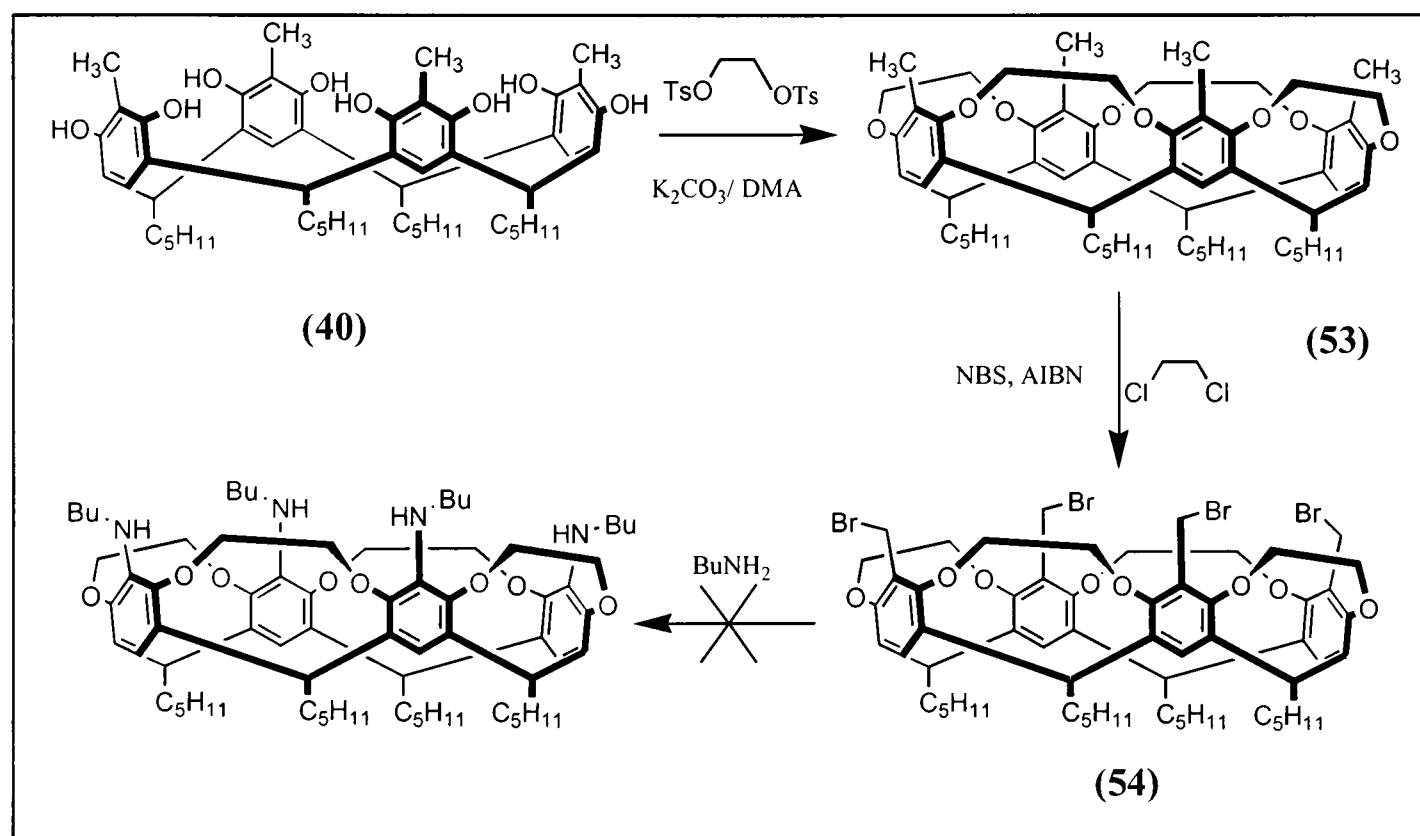
Dithiocarbamate salt formation occurred via addition of potassium hydroxide and carbon disulphide in a tetrahydrofuran/water (2:1) solution. Two equivalents of copper(II), nickel(II) and zinc(II) acetate salts were subsequently added, and stirred for 18 hours. After this time the resultant brown, green and off-white solids were collected.

Unfortunately, all of the resultant dithiocarbamate complexes proved to be insoluble, and are presumably polymeric solids. This is possibly a result of removing the solubilising alkyl chains that previous amines have possessed, although the less-preorganised nature of the ligand and the presence of a tertiary amine group cannot be disregarded as factors for disrupting the self-assembly process in the formation of discrete nano-dimensional

complexes⁵³.

5.2 Ethylene-Spaced Resorcinarenes

Cram and co-workers have synthesised a range of more flexible resorcinarenes using different spacers to link the phenolic oxygen atoms¹³. An ethylene-spaced cavitand (**53**) was synthesised using Cram's method (Scheme 6), although the incorporation of longer spacer groups resulted in much reduced yields (only 16% compared to 76% for the methylene-spaced analogue (**41**)). The ethylene-spaced cavitand (**53**) was used as a building block for the development of dithiocarbamate-derivatised flexible building blocks.



Scheme 6 Synthesis of ethylene-spaced resorcinarene subunits

The benzylic position was functionalised by bromination. This was achieved via addition of *N*-bromosuccinimide in 1,2-dichloroethane and yielded a crystalline solid after recrystallisation of the crude product from dichloromethane/ethanol. Unfortunately, addition of **(54)** to a large excess of primary amine did not produce the desired tetra-aminated product. Elemental analysis revealed a significantly reduced proportion of nitrogen than was expected and electrospray mass spectrometry showed the formation of $[\text{M}-\text{NHBu}]^+$ and $[\text{M}-2\text{NHBu}]^+$

peaks, with no observation of the $[M+H]^+$ peak. This suggests that the greater degree of flexibility in the cavitand system allows intramolecular amination that is not permitted in the more rigid methylene-spaced system.

6 Conclusion

It has been demonstrated that dithiocarbamate-derivatised resorcinarene cavitands can form nano-dimensional architectures via transition metal-directed self-assembly. These structures have been characterised by a variety of spectroscopic techniques, including NMR, mass spectrometry and electrochemistry. Synthesis of nickel(II) and palladium(II) derivatives have been undertaken, with both structures believed to adopt octanuclear tetrahedral architectures. Unfortunately, attempts to generate lower nuclearity complexes through the development of more flexible and bulky ligands have proved unsuccessful due to a variety of solubility and conformational problems.

The binding of nano-sized guests, such as C_{60} , has been investigated. The zinc(II) trimeric complex (**48**) has been shown via ^{13}C NMR and electrochemical studies to strongly interact with buckminsterfullerene, displaying significant perturbations upon binding. The copper(II) dithiocarbamate resorcinarene complex (**47**) was also investigated for its affinity for binding C_{60} and polyoxometallates using ^{13}C NMR and electrospray mass spectrometry. The latter suggests that the labile copper-dithiocarbamate bond allows the encapsulation of fullerenes over time within the sterically and electronically complementary central cavity of the host.

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Chapter Four

Gold(III) Dithiocarbamate

Chemistry

Chapter Four: Gold(III) Dithiocarbamate Chemistry

1 Introduction

It has been demonstrated in Chapter Two, that the dithiocarbamate ligand can be used in metal-directed self-assembly to synthesise dinuclear macrocyclic complexes of copper(II), nickel(II), palladium(II) and platinum(II). It has previously been noted that the dithiocarbamate ligand, through effective charge delocalisation, is able to stabilise high oxidation state metal complexes¹. One such example of this is the gold(III) dithiocarbamate system where such complexes², also adopt a four coordinate, square planar geometry about the central metal³. Consequently, gold(III) bis-dithiocarbamate complexes are positively charged (Figure 1).

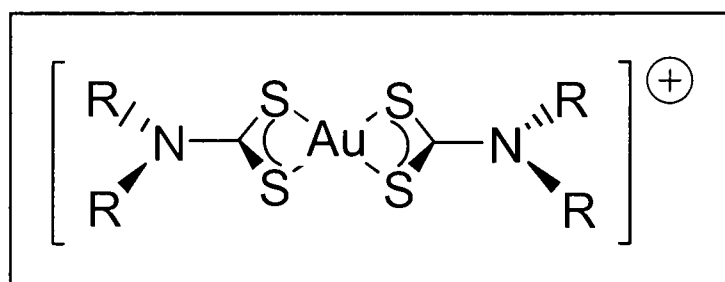


Figure 1 Au(III) bis-dithiocarbamate complex

The synthesis of the analogous tris-dithiocarbamate complexes has also been reported⁴. X-ray crystallographic studies have shown that these neutral systems also exist in a square planar coordination geometry about the central metal (Figure 2). This feature is indicative of the large ligand field stabilisation energies that third row transition metals exhibit. The square planar coordination is achieved, in this case, by the dithiocarbamate ligand acting as both a monodentate and a bidentate ligand. The central gold atom is coordinated to both the sulphur atoms of one ligand and just one of the sulphur donors of the other two⁵. Complexes of this type, however, are rare due to their limited stability, especially in solution.

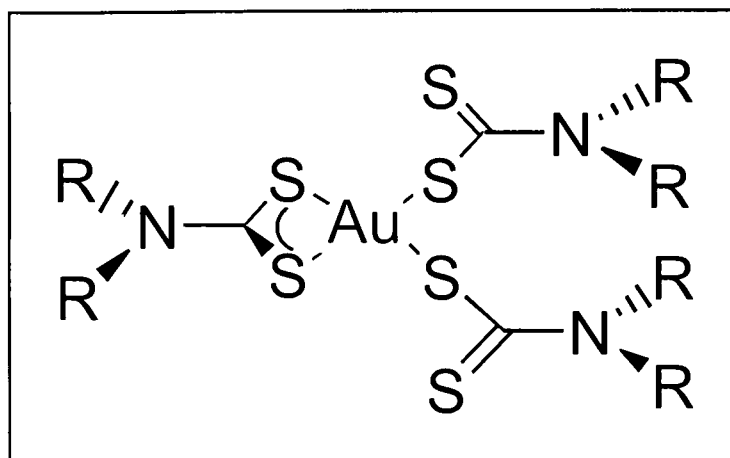
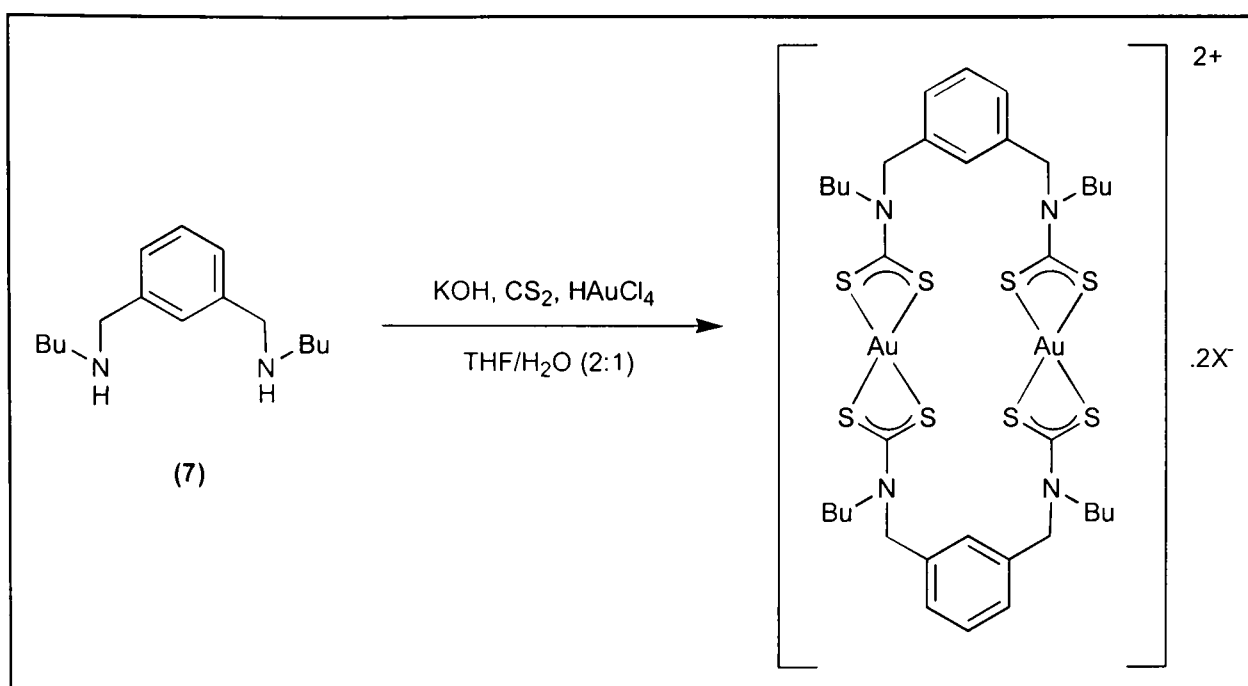


Figure 2 Au(III) tris-dithiocarbamate complex

An investigation as to whether the positively-charged gold(III) bis-dithiocarbamate subunit could be incorporated into macrocyclic systems was undertaken. The synthesis of such electron-deficient systems may result in potential hosts for suitable electron-rich guest species.

2 Gold(III) Dithiocarbamate-based Macrocyclic Synthesis

In an attempt to synthesise dinuclear gold(III) dithiocarbamate-based macrocyclic complexes, a metal-directed self-assembly reaction was attempted with the *m*-xylyl spaced bis-amine (**7**). This was initially attempted using an analogous one-pot method to that used for macrocyclic synthesis described in Chapter Two. Addition of potassium hydroxide, carbon disulphide and hydrogen tetrachloroaurate to (**7**) in tetrahydrofuran/water (2:1) resulted in the formation of a golden brown solution (Scheme 1).



Scheme 1 Initial synthesis of dinuclear Au(III) dithiocarbamate macrocyclic complex

Analysis of the resulting solution by electrospray mass spectrometry revealed the formation of the desired dicationic macrocyclic complex. However, numerous gold(I) species were also present in the solution, which proved impossible to separate from the desired macrocyclic product. One of these major impurities was shown by a peak in the electrospray mass spectrum at an m/z value of 1386.8. This corresponded to the trinuclear gold(III)-gold(I) mixed-valence product, as illustrated in Figure 3.

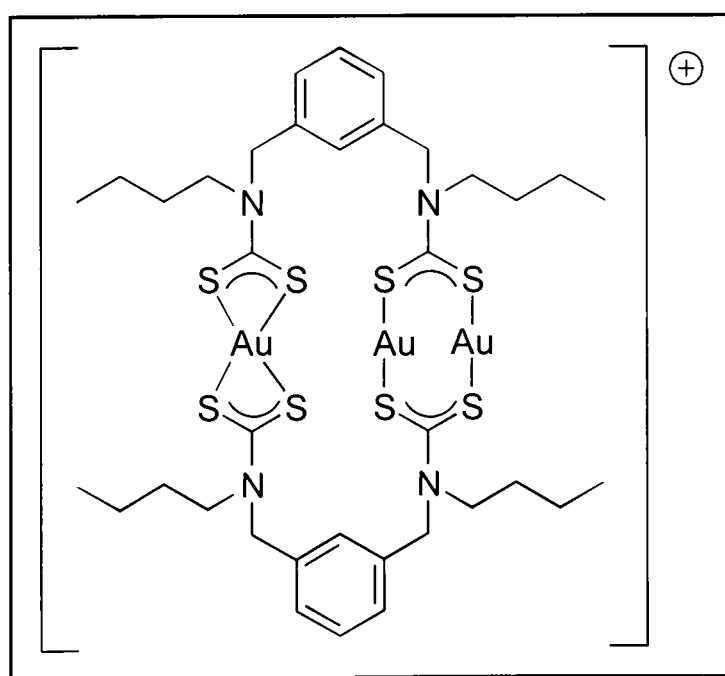


Figure 3 Trinuclear mixed-valence Au macrocyclic product

The reduction of gold(III) species in aqueous solvents has been noted previously⁶, due to tendency of the gold centre to undergo hydrolysis and subsequent reductive elimination reactions. As a result of this, gold(III) is problematic to work with and its coordination chemistry is relatively scarce in the literature. It is also noteworthy that thiol ligands are incapable of stabilising the gold(III) oxidation state^{7,8}. Addition of thiols to aqueous solutions of tetrachloroaurate salts results in the reduction of gold(III) to gold(I), in forming gold(I) monothiolate complexes (Scheme 2). This is in contrast to the dithiocarbamate ligand which is known to preferentially stabilise the higher gold(III) oxidation state, over gold(I), in mononuclear complexes. It is possible, however, that the presence of an adjacent positively-charged centre, decreases the affinity of the dithiocarbamate ligand to stabilise the higher oxidation state, hence mixed-valence complexes are observed.



Scheme 2 Reduction of tetrachloroaurate salts by thiols

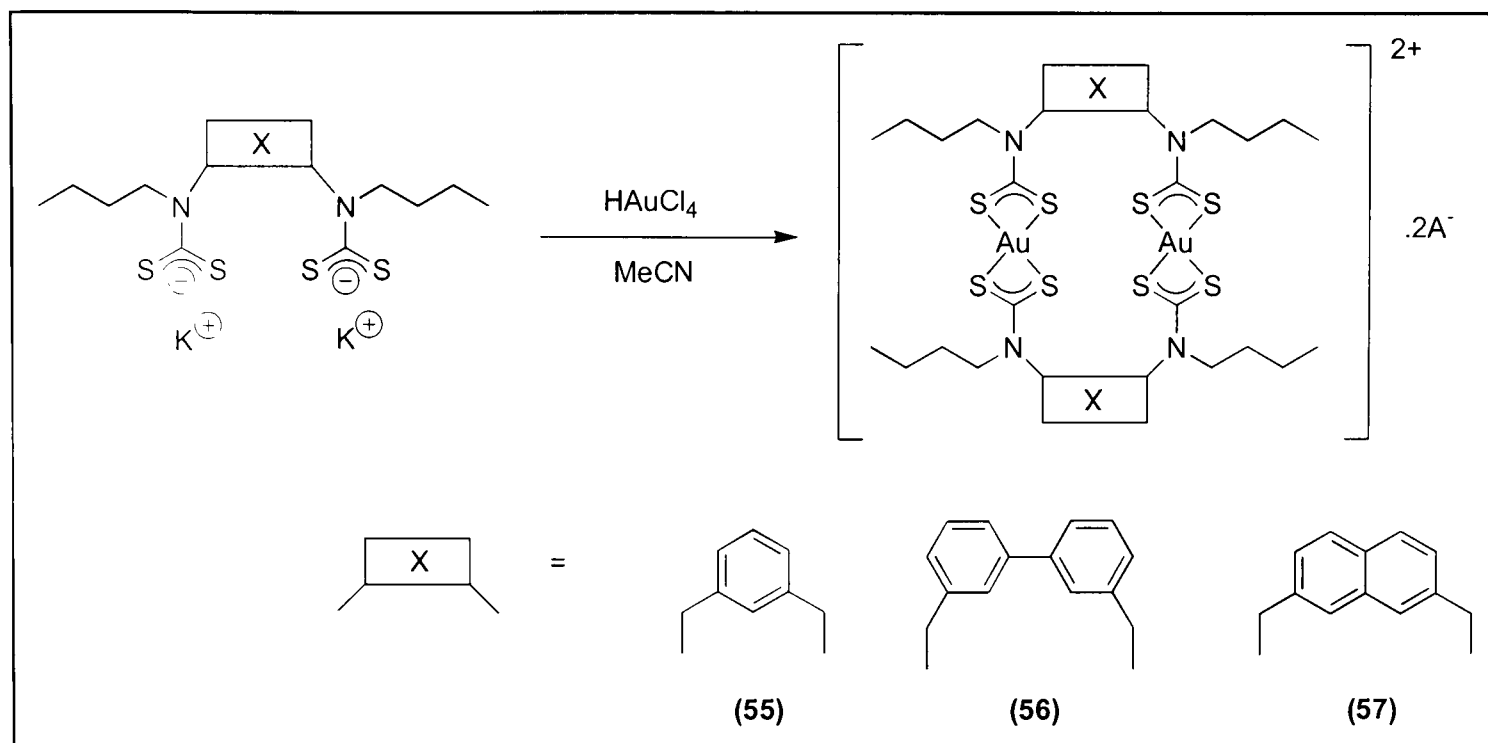
It was therefore apparent that an alternative synthetic approach was required to generate gold(III) dithiocarbamate-based macrocyclic systems.

2.1 Direct Reactions

Since it was not possible to synthesise gold(III) macrocyclic complexes from reactions in aqueous solvent systems, it was decided to perform these reactions in anhydrous polar solvents. In order to achieve this, it was necessary to first isolate the potassium bis-dithiocarbamate salt of the desired ligand and subsequently react this with a gold(III) salt (Scheme 3).

Three gold(III) dithiocarbamate macrocyclic complexes were isolated via the reaction of the appropriate potassium bis-dithiocarbamate salt with two equivalents of hydrogen

tetrachloroaurate in acetonitrile. Precipitation of the desired products from the golden solution was achieved by the addition of diethyl ether, affording orange solids.



Scheme 3 Synthesis of dinuclear Au(III) dithiocarbamate complexes

These solids were characterised by ^1H NMR and electrospray mass spectrometry. The ^1H NMR of (55) and its subsequent spectral assignment are displayed in Figure 4.

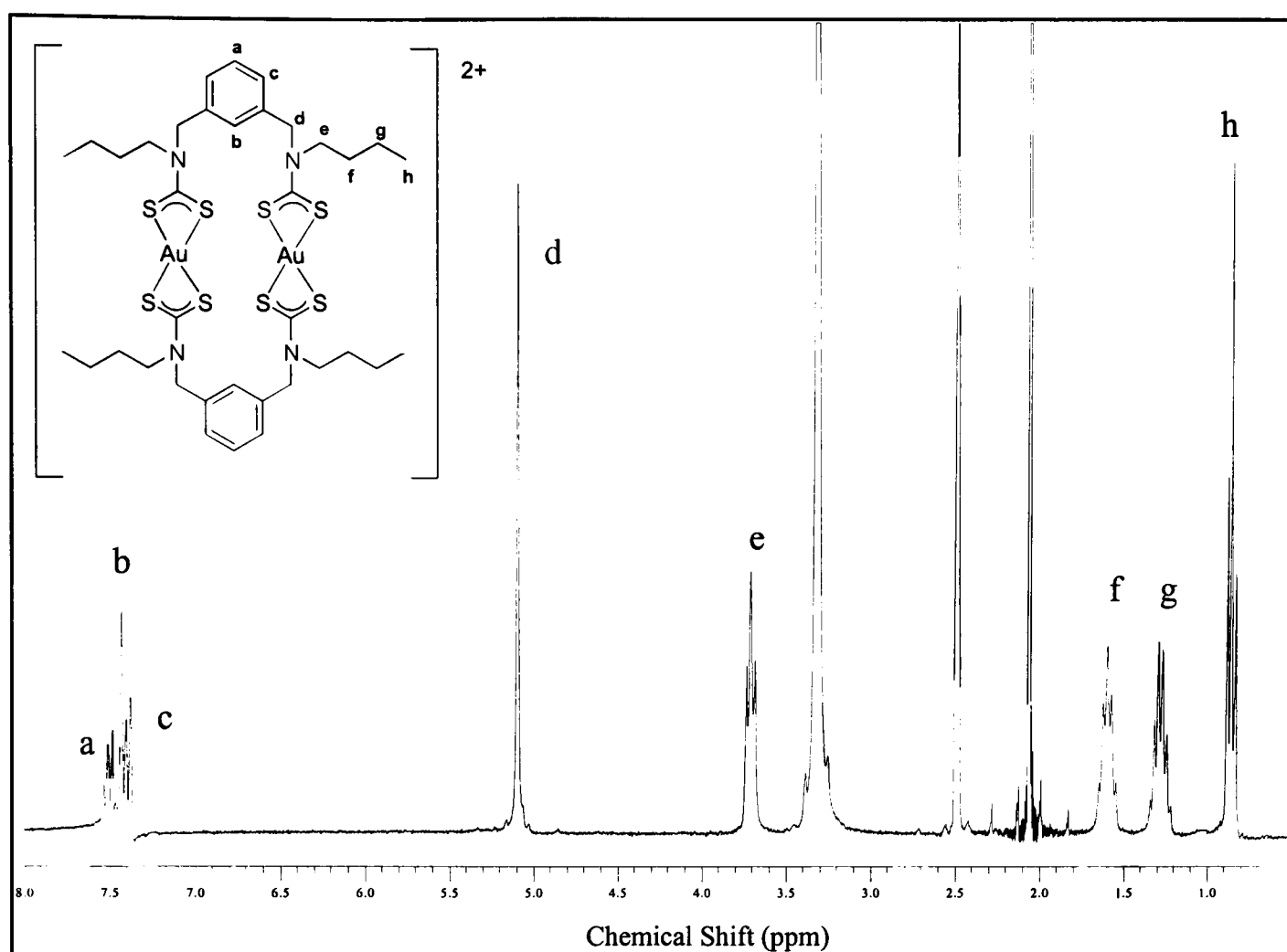


Figure 4 ^1H NMR spectrum of Au(III) dithiocarbamate-based *m*-xylyl-spaced macrocyclic complex (300MHz, DMSO- d_6 /CD $_3$ CN (1:1), 293K)

As can be seen, the complex gives a very sharp ^1H NMR spectrum, with well-resolved peaks. The proton pointing into the central electron-deficient cavity (b) is observed as a singlet at 7.23 ppm. Electrospray mass spectrometry revealed that the peak corresponding to the dicationic $[\text{M}]^{2+}$ macrocyclic complex dominated the spectrum.

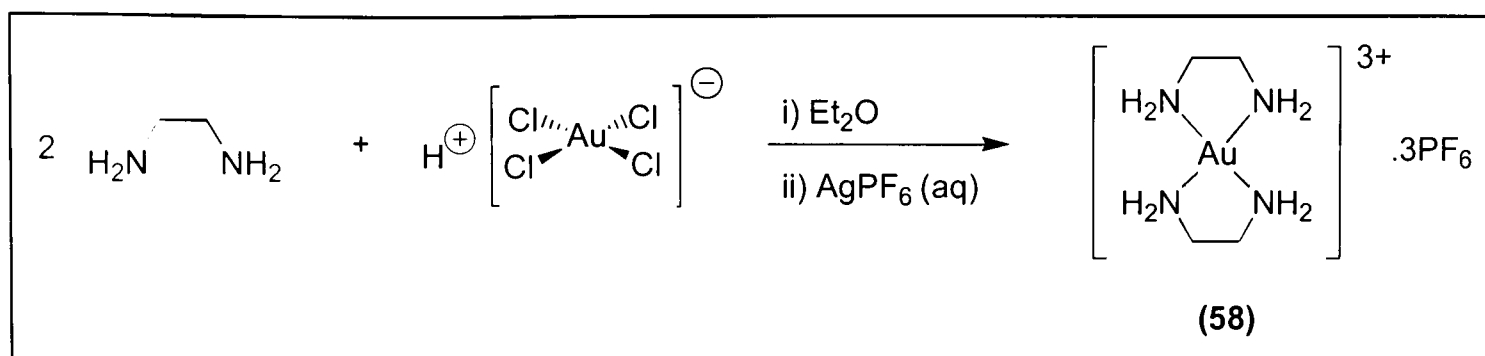
Unfortunately, elemental analysis on these compounds was not entirely satisfactory. This was due to the variable nature of the accompanying counteranion to the dinuclear macrocyclic complex. In general, the analysis was consistent with the formation of a dichloride salt. However, the fact that the proportion of carbon was often too low and that of gold higher than expected suggested the presence of a small proportion of either AuCl_4^- or AuCl_2^- counteranions within the sample, in addition to chloride. The presence of these gold-based counteranions within gold(III) complexes has previously been noted⁶. This feature limits the solubility of the resultant complexes and their resultant purification has also proved

problematic.

Attempts were made to purify the macrocycles both by ion-exchange chromatography and precipitation through the addition of silver(I) salts. Unfortunately, neither of these methods proved successful. Surprisingly, the use of ion-exchange columns did not result in a significant change in the elemental analysis of the complexes, possibly suggesting that a strong ion-pair is formed that is difficult to separate. The addition of silver(I) hexafluorophosphate to a solution of the gold(III) dithiocarbamate-based macrocycles, was designed to precipitate silver chloride and leave the gold macrocycle with the non-coordinating hexafluorophosphate salt. Unfortunately, the addition of the silver salt led to the formation of an insoluble solid. This is possibly a result of the silver ions competing for the dithiocarbamate ligand via a transmetallation reaction.

2.2 Alternative Gold Starting Materials

In an attempt to eliminate the problem of the counteranion in gold(III) dithiocarbamate complexes, generation of these structures was attempted using a gold material with a non-coordinating counteranion. With this aim, gold(III) bis-(ethylenediamine) trichloride ($\text{Au(en)}_2\text{Cl}_3$) was synthesised according to a literature preparation through the combination of ethylenediamine (en) and hydrogen tetrachloroaurate⁹. This was subsequently treated with silver hexafluorophosphate to generate **(58)** $\text{Au(en)}_2(\text{PF}_6)_3$ in an overall yield of 80% (Scheme 4). ^1H NMR spectroscopy revealed that the resonances of the ethylenediamine protons had been shifted downfield by 0.50 ppm due to the electron-withdrawing nature of the coordinated metal centre. ^{31}P and ^{19}F NMR spectroscopy, in addition to negative-mode electrospray mass spectrometry, confirmed the presence of the hexafluorophosphate counteranion, and elemental analysis was consistent with the formation of the desired complex.



Scheme 4 Formation of Au(III) bis-(ethylenediamine) tris-hexafluorophosphate (58)

The reaction between the ethylenediamine gold(III) salt (58) and potassium bis-dithiocarbamate salts was attempted in acetonitrile solution. This generated a very dark, poorly soluble brown solid, which gave a broad, uninformative ^1H NMR spectrum. Analysis of the electrospray mass spectrum indicated that numerous gold(I) species were present. It is therefore likely that the presence of ethylenediamine, as a by-product of the reaction, acts as a reducing agent for the gold(III) centres, resulting in the formation of a mixture of numerous gold(I) and gold(III) complexes. It is likely that this reduction occurs via a similar mechanism to that of the reduction of tetrachloroaurate salts by thiol ligands, as previously seen (Scheme 2).

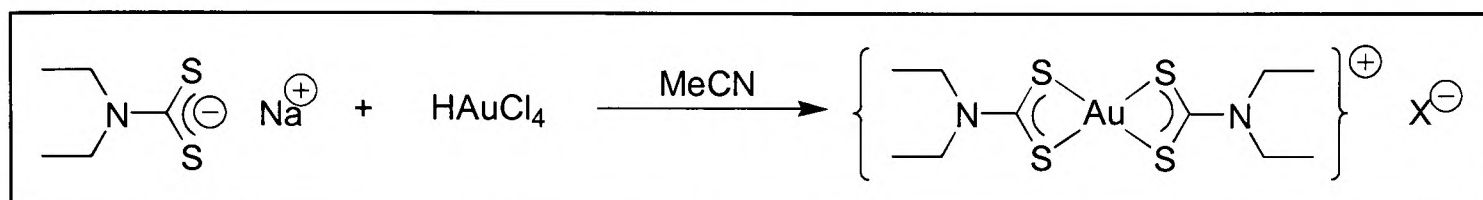
2.3 X-Ray Crystallography

As described in the previous sections, a number of dinuclear macrocyclic gold(III) dithiocarbamate-based complexes have been produced. Whilst both ^1H NMR spectroscopy and electrospray mass spectrometry have provided evidence for the formation of the desired cyclic cationic structure, elemental analysis suggests the accompanying counteranions are a mixture of chloride and gold-based species.

In an attempt to deduce the precise nature of the counteranions resulting from the gold(III) dithiocarbamate-based macrocyclic synthesis, a series of crystallisations of simple acyclic gold(III) dithiocarbamate complexes were set up. This was in order to investigate the effect of the synthetic procedure had upon the accompanying anion. The resultant structures were

solved by Dr. A. Cowley, University of Oxford.

Initially, the reaction of hydrogen tetrachloroaurate with sodium *N,N'*-diethyldithiocarbamate in acetonitrile, was investigated (Scheme 5). This generated a golden coloured solution which was filtered and subsequently layered with diethyl ether, giving rise to the formation of an orange single crystal (**59**).



Scheme 5 Synthesis of Au(III) bis-(*N,N'*-diethyldithiocarbamate) complex

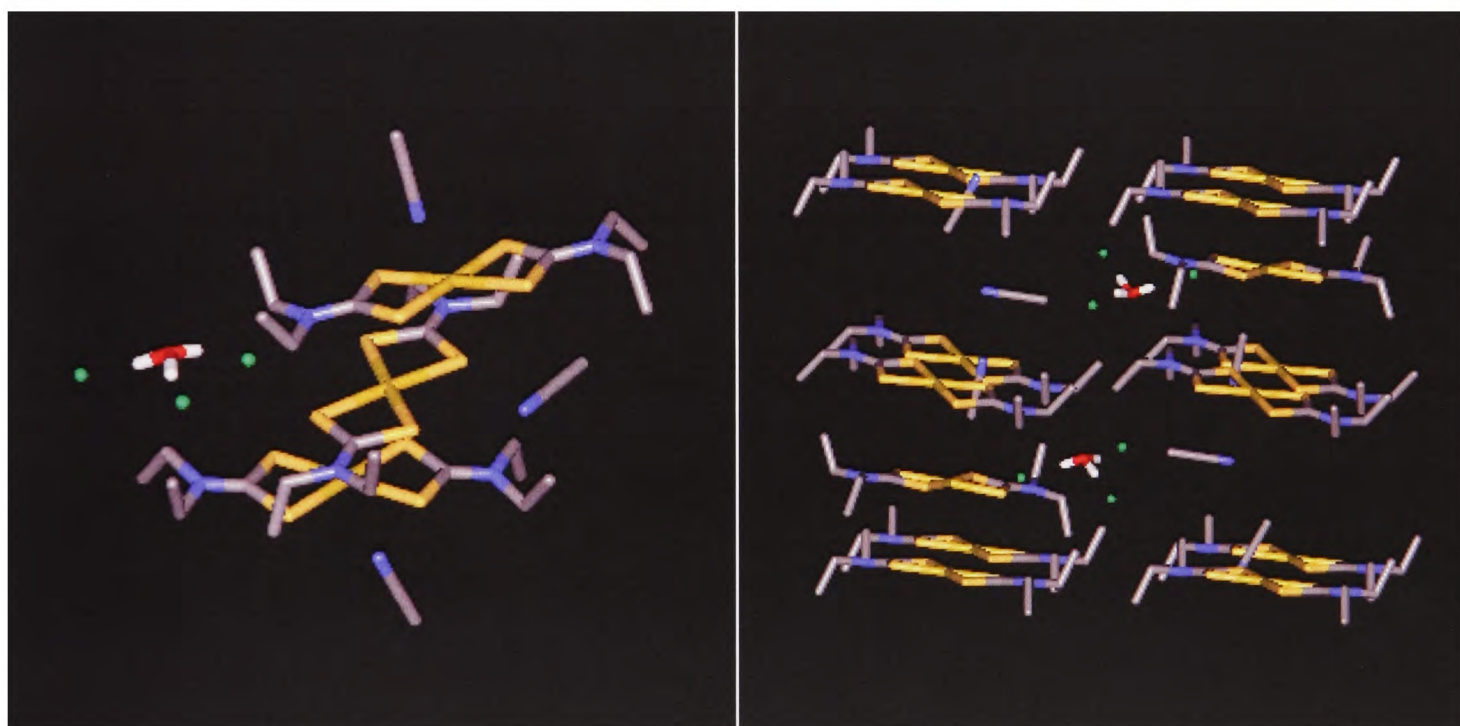


Figure 5 X-ray crystal structure of $(\text{Au}(\text{dtc})_2)_2 \cdot 3\text{Cl} \cdot \text{H}_3\text{O} \cdot 3\text{MeCN}$ (**59**) Right: packing structure demonstrating hydroxonium-chloride in channels (non-polar hydrogen atoms omitted for clarity, Key: C – grey, H – white, N – blue, S – yellow, O – red, Cl – green, Au – gold)

The resulting structure (Figure 5) shows a square planar gold(III) ion, coordinated to two dithiocarbamate ligands. There are three crystallographically-distinct $\{\text{Au}(\text{dtc})_2\}^+$ cations, three chloride ions, a single cation (believed to be H_3O^+) and three acetonitrile molecules within the unit cell. In order for the electrostatic charges to balance within the crystal structure, a unipositive cation must also be present. Of the possible ions, the best fit to the observed intensity data was obtained when the electron density between the chloride anions

was modelled as being the oxygen atom of a hydroxonium cation. This assignment was confirmed by location of three nearby peaks in a further difference Fourier map with pyramidal geometry, and by observation of three relatively short oxygen-chloride contacts (2.89Å) indicative of hydrogen bonding. The presence of hydroxonium is likely to be a result of using the highly acidic hydrogen tetrachloroaurate as a starting material. The packing diagram of the crystal structure shows how the chloride anions hydrogen bond to the hydroxonium cations in channels between the stacks of the $\{\text{Au}(\text{dtc})_2\}^+$ subunits (Figure 5(right)). Important crystallographic parameters are highlighted in Table 1.

(59)	
$d(\text{Au-S}_{\text{inter}})$ Å	2.33, 2.34
$d(\text{N-C}(\text{S}_2))$ Å	1.31
$d(\text{Au-S}_{\text{intra}})$ Å	3.53, 3.78
$\theta(\text{S-Au-S}_{\text{adj}})^\circ$	75.2, 75.3

Table 1 Selected crystallographic parameters for (59)

The expected dimeric structure is consistent with previously published gold(III) dithiocarbamate structures¹⁰. The central gold(III) ion is coordinated in a distorted square planar geometry, as a result of the restricting chelating angle of the dithiocarbamate ligands. The $\{\text{Au}(\text{dtc})_2\}^+$ units are stacked along the crystallographic *c*-axis, and are slightly tilted with respect to each other. One of the gold atoms has two relatively short axial interactions with the sulphur atoms of neighbouring complexes (intramolecular axial gold-sulphur distances are 3.54 and 3.78Å) whereas the other gold atoms have rather longer axial interactions with two pairs of sulphur atoms (approximately 4Å).

As was also seen in the dithiocarbamate complexes described in Chapter Two, the length of the nitrogen-carbon bond of the dithiocarbamate linkage is considerably less than would be

expected for a typical single carbon-nitrogen bond (1.47Å) and closer to that of a carbon-nitrogen double bond (1.28Å)¹¹. This demonstrates the significant double bond character between the two atoms due to the effective delocalisation of charge about the dithiocarbamate group and subsequent high covalent character of the metal-sulphur bonds. The fact that the nitrogen-carbon bond in **(59)** is 1.31Å indicates that a high degree of covalency is also seen within the gold-sulphur bonds, typical of a third row transition metal complex.

2.4 Non-Coordinating Counteranions

As has been demonstrated, it is possible to generate halide complexes of gold(III) *N,N'*-dialkyldithiocarbamates, and similar complexes with accompanying gold-based anions have also been reported in the literature¹². Ideally, however, the use of a non-coordinating counteranion would be beneficial, and this would allow further investigation of the potential binding properties of these hosts. To this end, the preparation of gold(III) bis-(*N,N'*-diethyldithiocarbamate) cation, with two different non-coordinating counteranions, was undertaken, using the following methods

Initially, tetraphenylborate was used as a non-coordinating anion for the gold(III) bis-(*N,N'*-diethyldithiocarbamate) cation. This was achieved through the addition of one equivalent of sodium tetraphenylborate (dissolved in ethanol) to a chloroform solution of the gold(III) bis-(*N,N'*-diethyldithiocarbamate cation), resulting in a yellow precipitate **(60)**¹³. This was collected by filtration and crystallised from hot chloroform, to yield orange/yellow needles. The product can be identified by ¹H NMR spectroscopy in DMSO-d₆, showing a 1:1 ratio of {Au(dtc)₂}⁺ cation:tetraphenylborate anion. Elemental analysis is consistent with the formation of {Au(dtc)₂}BPh₄.2CHCl₃.H₂O.

A single crystal of **(60)**, suitable for X-ray structural analysis, was prepared. This was achieved via the vapour diffusion of isopropyl ether into a 1,2-dichloroethane solution of the

crude product.

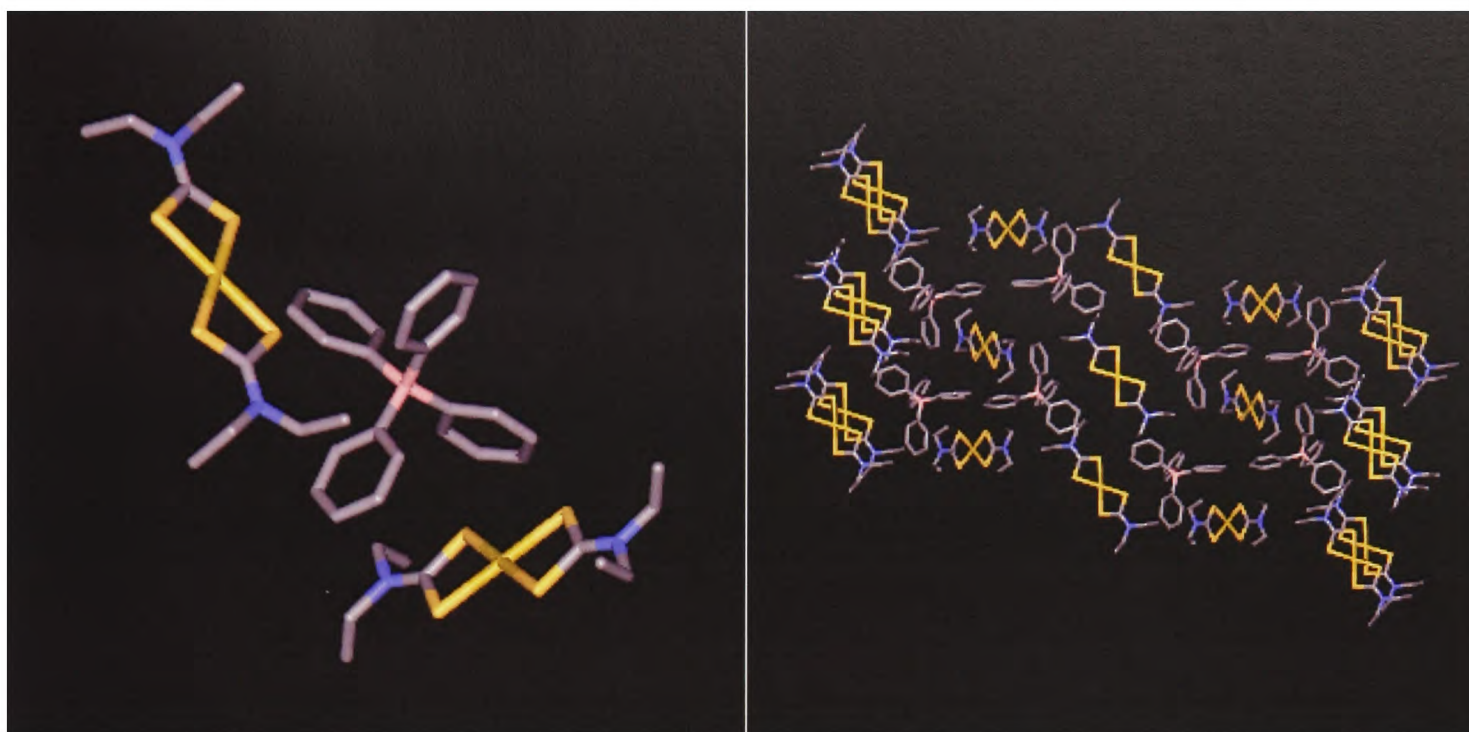


Figure 6 X-ray crystal structure of $\text{Au(dtc)}_2\text{BPh}_4$ (**60**) Right: packing diagram (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, B – pink, Au – gold)

The structure (Figure 6) contains two distinctive $\{\text{Au(dtc)}_2\}^+$ cationic units about a central tetraphenylborate anion. The tetraphenylborate anion arranges itself in ribbons within the crystal cell (Figure 6(right)), with the anion being too large and bulky to allow intermolecular gold-sulphur interactions, as previously seen in (**59**).

Similarly, a sample of gold(III) bis-(*N,N'*-diethyldithiocarbamate) hexafluorophosphate was also prepared. This was synthesised via the addition of a methanolic solution of ammonium hexafluorophosphate to a methanol solution of the prepared gold(III) bis-(*N,N'*-diethyldithiocarbamate) cation. This resulted in the precipitation of a yellow solid (**61**) which was collected and recrystallised from methanol/diethyl ether. The determined X-ray crystal structure is displayed in Figure 7, and selected crystallographic parameters for both (**60**) and (**61**) are reported in Table 2.

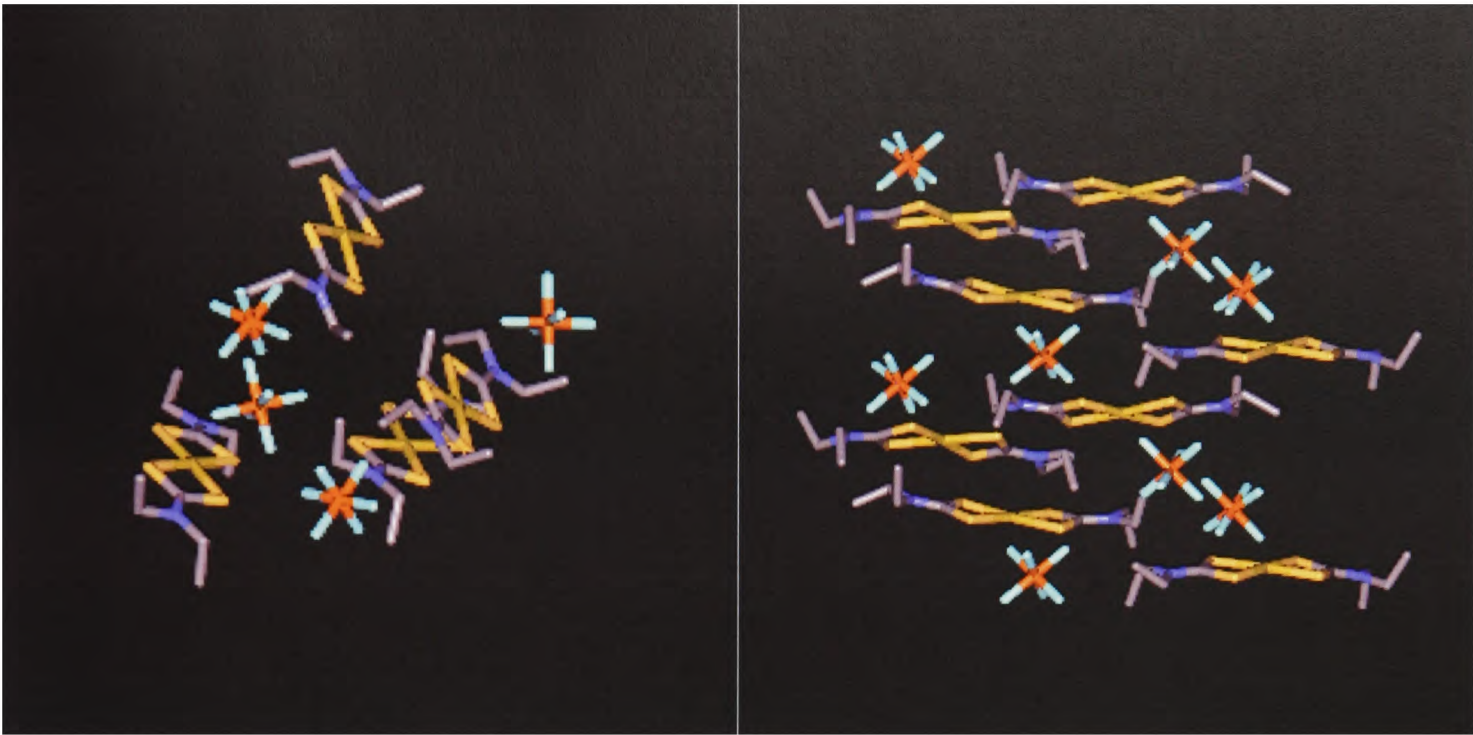


Figure 7 X-ray crystal structure of Au(dtc)₂PF₆ (61) Right: packing structure (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, P - orange, F – light blue, Au – gold)

	(60)	(61)
d(Au-S _{inter}) Å	a) 2.33, 2.34, b) 2.33	2.33, 2.33, 2.33, 2.34
d(N-C(S ₂)) Å	a) 1.30, b) 1.31	1.28, 1.31
θ(S-Au-S _{adj}) ^o	a) 75.5, b) 75.4	75.5, 75.7

Table 2 Selected crystallographic parameters for (60) and (61)

The structure of (61) shows the formation of the desired complex, with the unit cell of the structure containing four distinctive gold(III) complexes and hexafluorophosphate anions. The gold(III) complex lies on a site with no crystallographic symmetry, but has a local mirror plane relating the two dithiocarbamate ligands. The coordination geometry around the gold atom closely approximates planarity (root mean square deviation of the gold and coordinated sulphur atoms from their best plane is 0.02Å). Unlike the structure of (59), however, there are no intermolecular interactions between either the {Au(dtc)₂}⁺ subunits or between anion and

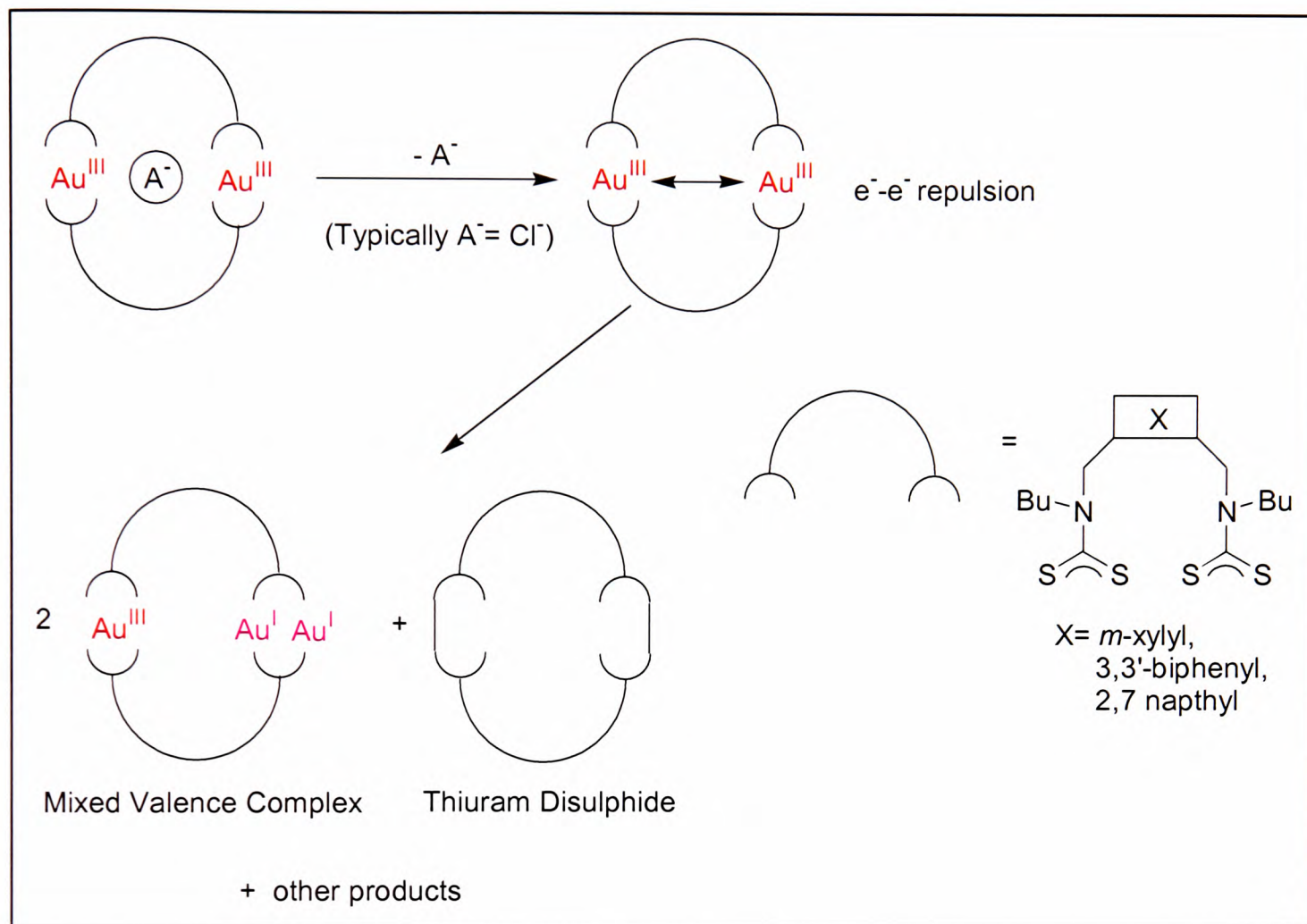
cation. This feature is the same for both **(60)** and **(61)**, indicating the effect of having larger, non-coordinating counteranions.

A further point of interest about the crystal structure of **(61)** is that despite the non-chiral nature of the component ions, the crystal is in fact chiral. Refinement of the Flack enantiopole parameter gives a value of approximately zero, indicating the crystal consists of a single enantiomer¹⁴.

Given the success of generating simple mononuclear gold(III) dithiocarbamate salts with non-coordinating counteranions, attempts were made to generate dinuclear complexes using this methodology. Samples of **(55)**, **(56)** and **(57)** were dissolved in ethanol or acetonitrile and two equivalents of sodium tetraphenylborate added. In addition a methanolic solution of **(55)** was combined with two equivalents of ammonium hexafluorophosphate. Unfortunately, in all of these cases addition of the non-coordinating anion lead to the precipitation of a poorly soluble dark brown/black solid, not the expected golden solid. Analysis by electrospray mass spectrometry revealed that the gold(III) centres had been partially reduced to gold(I), leaving a mixture of mixed-valence complexes. Elemental analyses proved unsatisfactory, which is in agreement with the conclusion that side-products were also being generated.

It is somewhat surprising that this method fails to exchange the counteranions, given the success of **(60)** and **(61)**. It is therefore likely that the presence of a coordinating counteranion is required to stabilise the dinuclear gold(III) dithiocarbamate complexes. This is likely to be due to a stabilisation of the complexes by the formation of a cascade complex between the two proximal gold(III) centres. In the absence of this, the adjacent positively-charged centre perturbs the oxidation potential of the second gold centre such that it is no longer able to stabilise the higher oxidation state and the centre is reduced. A proposed mechanism for this decomposition is highlighted in Scheme 6. This suggests the gold centres may be reduced to

the gold(I) oxidation state through the oxidation of liberated dithiocarbamate ligands to thiuram disulphide compounds ($R_2NCS_2S_2CNR_2$).



Scheme 6 Proposed decomposition of dinuclear Au(III) dithiocarbamate complexes upon the removal of coordinating counteranions

3 Gold(I) Dithiocarbamate Chemistry

In addition to stabilising gold(III) oxidation state, the dithiocarbamate ligand has also been shown to be effective in stabilising the gold(I) state¹⁵. Gold(I) dithiocarbamate complexes (in contrast to the analogous cage and cluster complexes of copper(I) and silver(I)¹⁶) have been shown to exist as a dimeric structure with short gold-gold contacts. The intermolecular gold-gold distances are shorter than those observed in the bulk metal, and significant intramolecular aurophilic interactions have also been seen¹⁷.

The attempted synthesis of gold(I) dithiocarbamate-based macrocycles by the use of simple aromatic spacer groups was undertaken. Such structures are interesting as they may allow the

detection of potential guest species by the study of the luminescent properties of the gold(I) dithiocarbamate linkage¹⁸. In addition, such macrocycles also may be able to be oxidised to the related gold(III) complexes, a process which may “turn on” their anion binding potential (Figure 8).

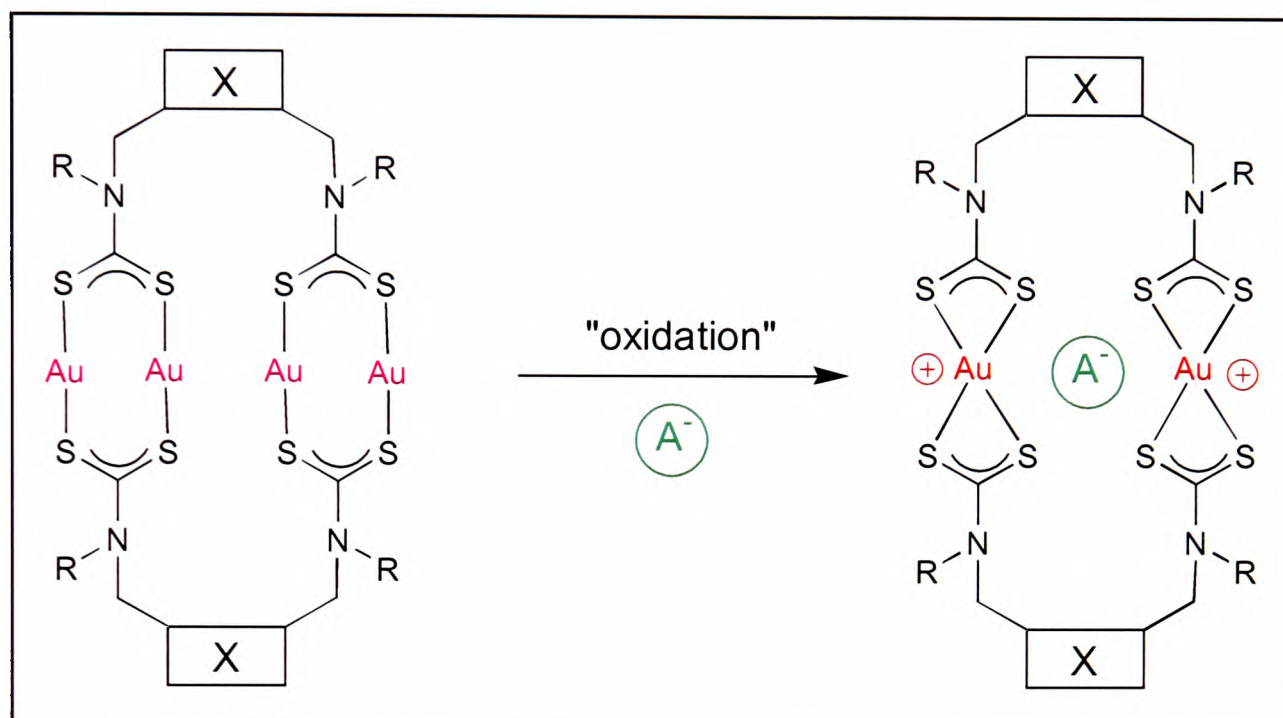
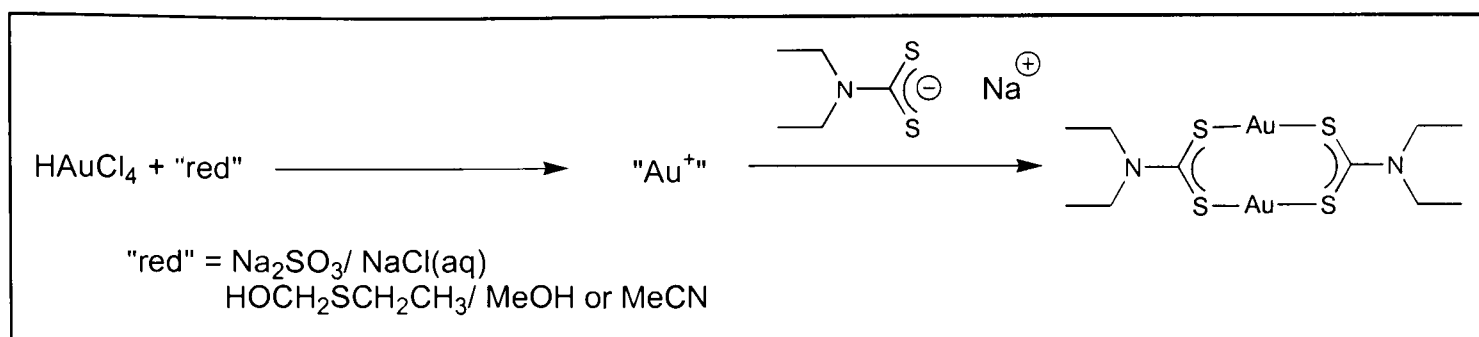


Figure 8 Potential to "turn on" anion binding via the oxidation of Au(I) dithiocarbamate macrocyclic complexes

Initially, a sample of gold(I) *N,N'*-diethyldithiocarbamate was prepared through modification of a literature procedure¹⁹. Hydrogen tetrachloroaurate was dissolved in an ice-cold saturated sodium chloride solution²⁰ and reduced to gold(I) with sodium sulphite²¹. This changed the solution from a yellow colour to colourless. Addition of sodium *N,N'*-diethyldithiocarbamate afforded a fine yellow precipitate, which was recrystallised from hot dimethylsulphoxide to yield orange needles (Scheme 7). Elemental analysis results were consistent with the formation of the desired product, although its poor solubility prevented the study of its NMR properties.



Scheme 7 Synthesis of Au(I) dithiocarbamate complexes

An analogous procedure was used to prepare a tetranuclear gold(I) dithiocarbamate-based macrocycle. Unfortunately, addition of the *m*-xylyl spaced bis-dithiocarbamate salt to the gold(I) solution resulted in the formation of a poorly soluble black solid. Analysis of this by electrospray mass spectrometry revealed the formation of a mixture of mixed-valence complexes containing both gold(I) and gold(III) centres. Experiments using larger aromatic spacer groups were also attempted, but these too resulted in poorly soluble mixed-valence complexes. Similar experiments were attempted using the alternative reducing agent ethyl(2-hydroxyethyl)sulphide²² in methanolic solutions, but these also failed to generate the desired tetranuclear gold(I) dithiocarbamate complexes.

Unfortunately, it has not proved possible to generate macrocyclic complexes spaced by two gold(I) dithiocarbamate bridges. This is in some part due to the very poor solubility of these complexes, but it also has been shown to be difficult to maintain the gold in a reduced oxidation state. This is due to the greater affinity of the dithiocarbamate ligand for higher oxidation states.

4 Transmetallation

It has been demonstrated, within this Chapter, that gold(III) can form a number of stable complexes with the dithiocarbamate ligand. This is a result of the high affinity of gold for sulphur-based ligands and the effective stabilisation of the positive charge due to delocalisation across the dithiocarbamate ligand.

It has also been shown in Chapters Two and Three that a range of multinuclear first row transition metal dithiocarbamate complexes may be formed with a range of ligands. Such structures were shown to interact with a variety of cationic, anionic²³ and neutral guest species. An examination as to whether the tetrachloroaurate anion would be a suitable guest especially for dinuclear copper(II) dithiocarbamate macrocyclic complexes was undertaken. Initially, the stability of the anion in the presence of the copper(II) dithiocarbamate complex **(20)** was studied. One equivalent of hydrogen tetrachloroaurate, dissolved in acetonitrile, was added to a dichloromethane solution of **(20)**. Unexpectedly, the dark brown solution rapidly turned golden yellow, indicative that a chemical reaction had occurred. The solution was analysed by electrospray mass spectrometry and this revealed that after the addition of the tetrachloroaurate salt, the peak corresponding to the copper(II) dithiocarbamate complex **(20)** (m/z 358.9) was no longer present and a new peak relating to the formation of a gold(III) dithiocarbamate complex had formed (m/z 492.9) (Figure 9). The copper(II) centre had therefore been displaced in the dithiocarbamate complex by the gold(III) cation. This is likely to be a thermodynamic phenomenon; due to the higher affinity gold has for the sulphur donors in comparison to copper. In addition, the greater LFSE exhibited by third row transition metals in comparison to first row metals leads to an enthalpic gain upon metal exchange.

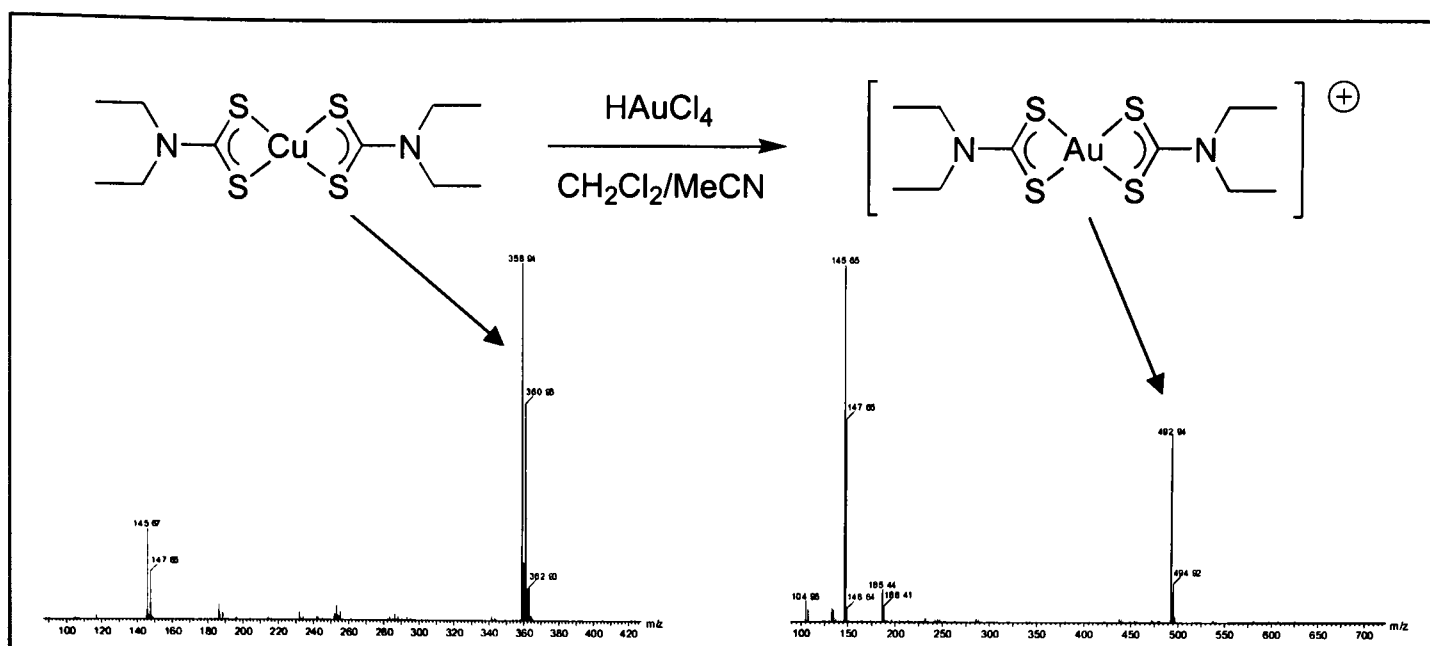
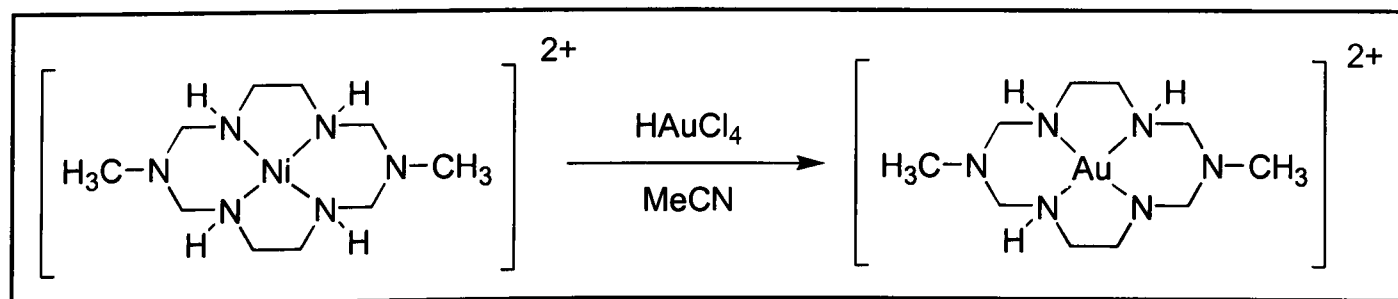


Figure 9 Electrospray mass spectra of a solution of Cu(II) bis-(*N,N'*-diethyldithiocarbamate) (**20**) before and after the addition of H[AuCl₄]

In addition, the same reaction was performed using nickel(II) bis-(*N,N'*-diethyldithiocarbamate) (**21**) and zinc(II) bis-(*N,N'*-diethyldithiocarbamate)²⁴. Both reactions also generated the same gold(III) bis-(*N,N'*-diethyldithiocarbamate) cationic complex.

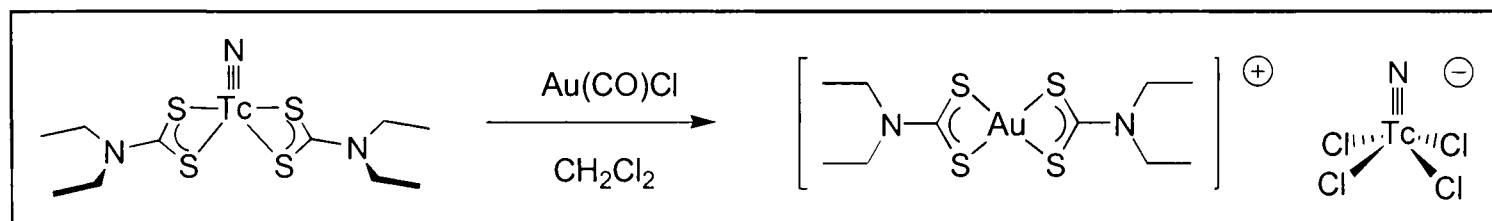
The exchange of metal centres in macrocyclic coordination complexes with gold(III) has rarely been recorded in the literature. There has been a report of gold(III) substituting for a nickel(II) centre which is coordinated in an azamacrocyclic complex (Scheme 8)²⁵. Here, it is believed that initial coordination of the tetrachloroaurate anion to a nitrogen donor atom of the macrocycle is the rate determining step in this transformation. Although in this case one metal centre is exchanged for another, the integrity of the macrocycle is not compromised by this interconversion.



Scheme 8 Transmetalation of a Ni(II) azamacrocyclic complex with Au(III)

There has only been one example of metal exchange of dithiocarbamate complexes with gold reported²⁶. This involved the addition of the gold(I) species, gold(carbonyl)chloride to

technetium nitride dithiocarbamate (Scheme 9). This generated the gold(III) bis-(*N,N'*-dithiocarbamate) cation, with the solvent, dichloromethane, acting as both an oxidising agent and chloride source.



Scheme 9 Formation of Au(III) dithiocarbamate complex through transmetallation of technetium nitrido dithiocarbamate complex

Considering the difficulties encountered in synthesising dinuclear gold(III) dithiocarbamate complexes of sufficient purity, it was decided to investigate the generation of gold(III) dithiocarbamate complexes via a transmetallation reaction.

4.1 Transmetallation Recrystallisations

It has previously been noted that gold(III) coordination complexes are often difficult to work with due to the problem of their counteranion⁶. It is common for these species to precipitate with AuCl₄⁻, AuCl₂⁻ or a mixed AuCl₄⁻/AuCl₂⁻ salt, which often prove difficult to characterise due to their limited solubility.

To determine the identity of the counteranion in these potentially useful transmetallation reactions, a series of crystallisations were undertaken. These studies generated the gold(III) *N,N'*-diethyldithiocarbamate cation {Au(dtc)₂}⁺ from both a number of solvent systems and range of starting materials. The resulting structures were solved by Dr A. Cowley at the Chemical Crystallography Laboratory, Oxford. The results of these experiments are now discussed, and reinforce the complexity of the counteranion towards the gold(III) cation.

4.1.1 Copper-Based Counteranions

Initially, the metathesis reaction between copper(II) bis-(*N,N'*-diethyldithiocarbamate) (**20**)

and hydrogen tetrachloroaurate was studied. This reaction was performed in a dichloromethane/acetonitrile (1:1) solvent system, which was subsequently layered with diethyl ether to effect crystallisation. This afforded single black crystals of (62), suitable for X-ray analysis.

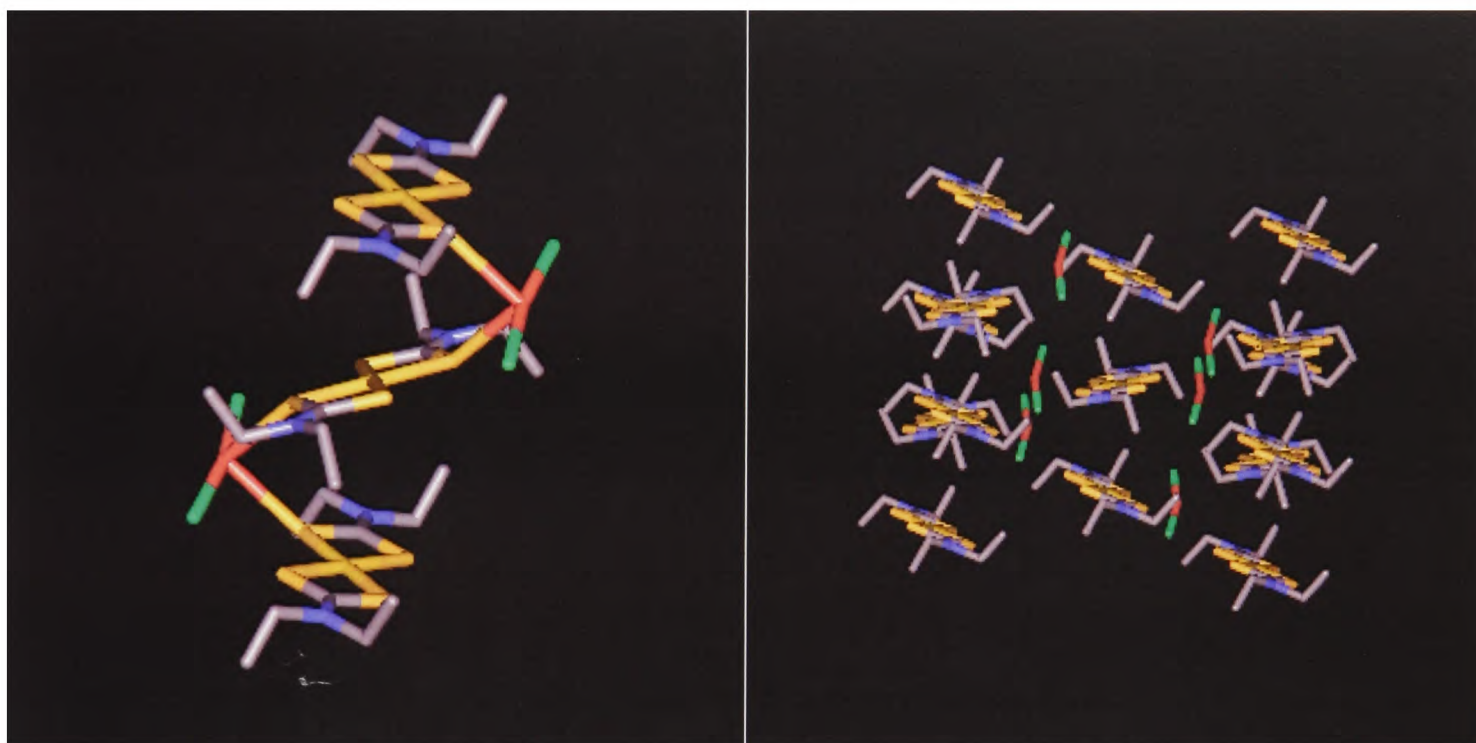


Figure 10 X-ray crystal structure of $\text{Au(dtc)}_2\text{CuCl}_2$. (62) Right: packing diagram (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, Cu – red, Cl – green, Au – gold)

The structure (Figure 10) consists of $\{\text{Au(dtc)}_2\}^+$ cations with copper(I) dichloride (CuCl_2^-) anions. These are linked through intermolecular copper-sulphur interactions (intermolecular copper-sulphur distances are $2.83\text{\AA}$) forming chains along the crystallographic *c*-axis. It is this charge transfer interaction between the copper and sulphur centres which give the crystals their distinctive black colour.

The planar dithiocarbamate units are tilted from their axis due to the interaction with the copper(I) centres, which adopt pseudo tetrahedral geometry, with the CuCl_2^- bent out of its normal linear geometry (with the Cl-Cu-Cl angle being 166.9° and the S-Cu-S angle 86.9°).

	(62)
$d(\text{Au-S}_{\text{inter}}) \text{ \AA}$	2.33, 2.35
$d(\text{N-C(S}_2\text{)}) \text{ \AA}$	1.30
$d(\text{Au-S}_{\text{intra}}) \text{ \AA}$	4.53
$\theta(\text{S-Au-S}_{\text{adj}})^\circ$	75.3
$d(\text{Cu-S}_{\text{inter}}) \text{ \AA}$	2.83
$\theta(\text{S-Cu-S})^\circ$	86.9
$\theta(\text{Cl-Cu-Cl})^\circ$	166.9

Table 3 Selected crystallographic parameters for (62)

The analogous reaction of copper(II) bis-(*N,N'*-diethyldithiocarbamate) (20) with one equivalent of potassium tetrachloroaurate was also undertaken. The reaction was performed in a dichloromethane/acetonitrile (1:1) solution, which was layered with diethyl ether to induce crystallisation. Initially dark green crystals were formed (63), whose structure is shown in Figure 11.

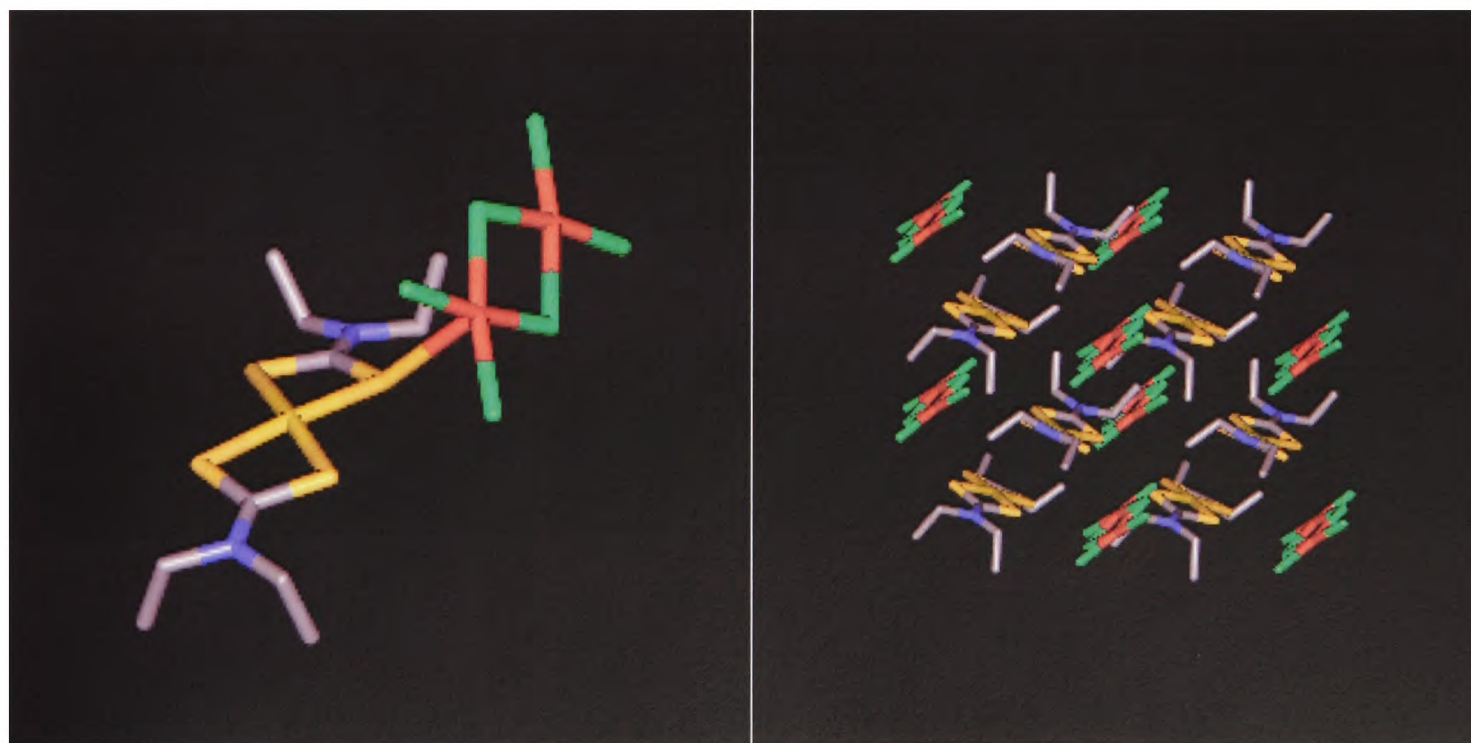


Figure 11 X-Ray crystal structure of $(\text{Au}(\text{dtc})_2)_2\text{Cu}_2\text{Cl}_6$ (square planar Cu) (63) Right: packing diagram (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, Cu – red, Cl – green, Au – gold)

Despite the almost identical reaction conditions to those in the crystallisation of **(62)**, the crystal is of a different composition. The structure is composed of $\{\text{Au}(\text{dtc})_2\}^+$ cations and $\text{Cu}_2\text{Cl}_6^{2-}$ anions situated on crystallographic centres of inversion (Figure 11). The gold(III) dithiocarbamate unit is, once more, planar with gold-sulphur distances consistent with that of the previous structures (2.34 Å). Furthermore, the cationic units do not interact with each other, nor are there any significant intermolecular interactions at the axial sites of the gold atoms, as occurred in **(59)**.

The $\text{Cu}_2\text{Cl}_6^{2-}$ counter anion contains two square planar coordinated copper(II) ions. The terminal copper-chloride bonds are, as expected, longer than the bridging chloride ligands (copper-chloride(terminal) distance is 2.23 Å, while the copper-chloride(bridging) distance is 2.32 Å).

There is again an interaction between the copper atom of the anion and a sulphur atom of a neighbouring cation (copper-sulphur 3.00 Å). Although this can be regarded as producing a 5-coordinate copper atom, there is no significant deviation of the copper atom from the best plane of its four chloride ligands. It is this charge transfer interaction, between the copper centres and the sulphur donors that result in the colouration of the crystals.

As well as the dark green crystals **(63)**, over time orange crystals **(64)** also formed within the same solution. The very dark green crystals and orange polycrystalline aggregates may be clearly distinguished by eye (Figure 12), although both dissolve in water to give a greenish-yellow solution.

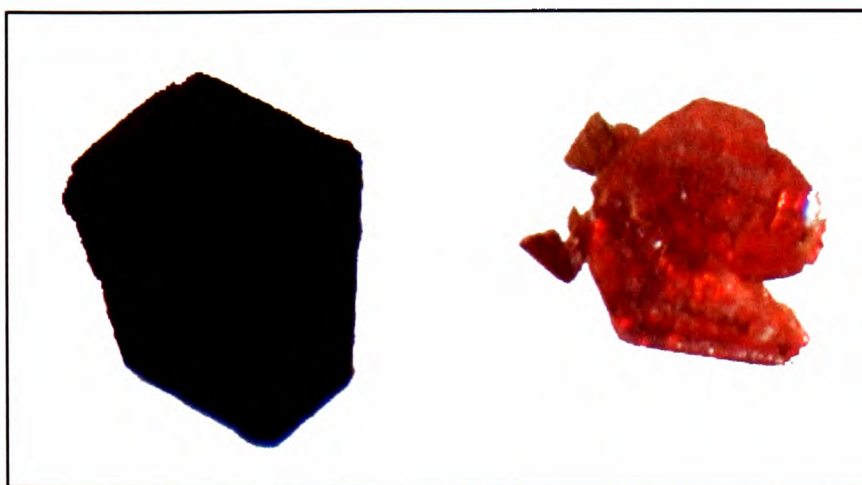


Figure 12 Dark green (63) (left) and orange (64) (right) polymorphs of $(\text{Au}(\text{dtc})_2)_2\text{Cu}_2\text{Cl}_6$

In addition to their difference in physical appearance the two solids can also be clearly distinguished in their solid-state structures. The X-ray crystal structure of a single crystal of the orange complex (64) is displayed in Figure 13.

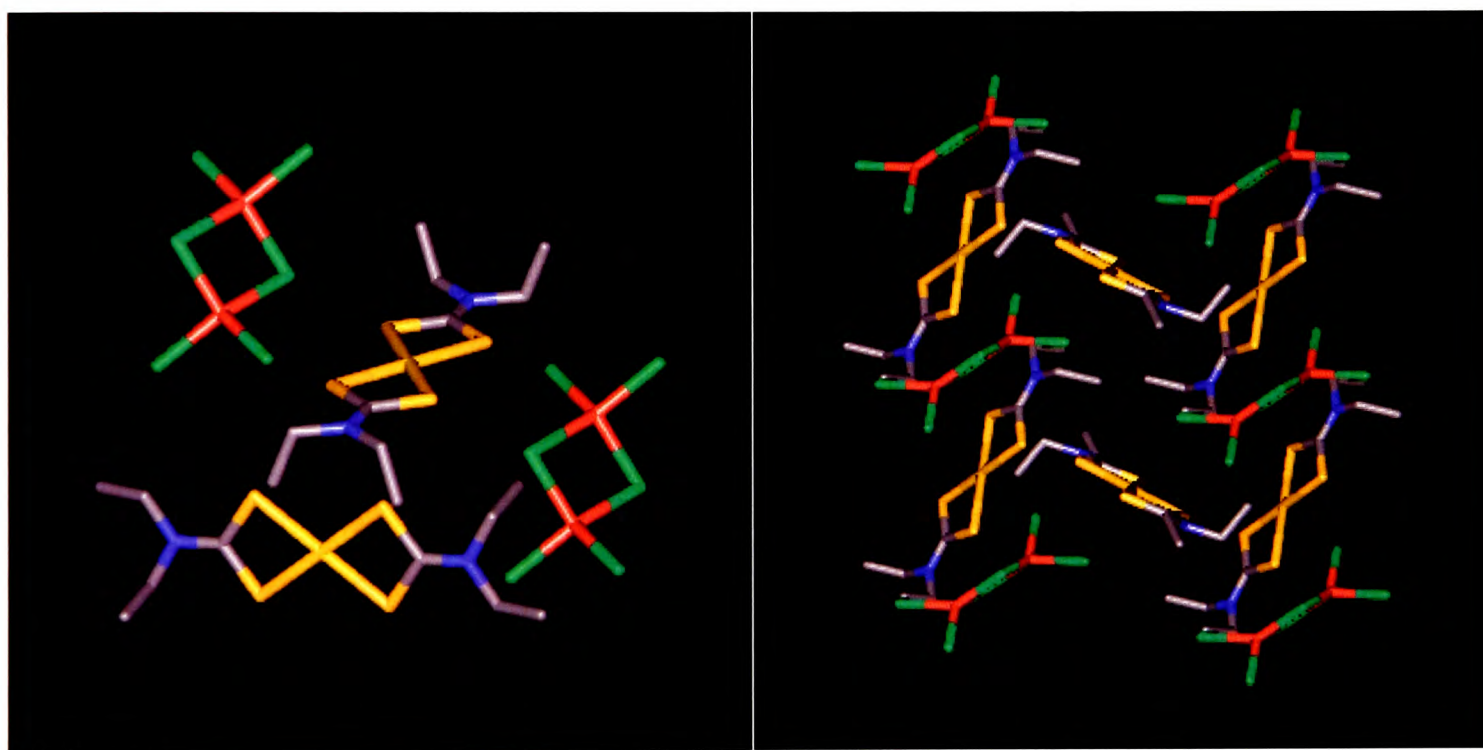


Figure 13 X-ray crystal structure of $(\text{Au}(\text{dtc})_2)_2\text{Cu}_2\text{Cl}_6$ (tetrahedral Cu) (64) Right: packing diagram (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, Cu – red, Cl – green, Au – gold)

The structure of (64) has the same composition as (63), consisting of gold(III) N,N' -diethyldithiocarbamate cations with $\text{Cu}_2\text{Cl}_6^{2-}$ counteranions. There are two crystallographically-distinct types of the former, both located on centres of inversion. The single crystallographic anion is also located on a centre of inversion.

The gold(III) N,N' -diethyldithiocarbamate cationic moieties are structurally similar to those in

the dark green crystals **(63)**. In contrast to the coplanar $\{\text{Au}(\text{dtc})_2\}^+$ complexes in **(63)**, alternate cations along the crystallographic *c*-axis are rotated such that they are perpendicular to each other. This results in a relatively short gold-sulphur interaction between neighbouring cationic units (gold-sulphur bond distance is 3.89Å).

	(63)	(64)
d(Au-S _{inter}) Å	2.34	2.34
d(N-C(S ₂)) Å	1.30	1.30
θ(S-Au-S _{adj})°	75.9	75.9
θ(N-N-Au)°	7.2	0
d(Au-S _{intra}) Å	3.89	3.89
d(Cu-S _{inter}) Å	3.00	4.56
d(Cu-Cu) Å	3.48	3.35
d(Cu-Cl _{terminal}) Å	2.23	2.20, 2.21
d(Cu-Cl _{bridging}) Å	2.32	2.30, 2.31
θ(Cl-Cu-Cl _{terminal})°	95.8	98.4
θ(Cl-Cu-Cl _{bridging})°	82.5	93.1

Table 4 Selected crystallographic parameters for **(63)** and **(64)**

The most significant difference between the two crystal structures is the variation in the structure of the accompanying anion. Whilst the geometry of the copper atoms is essentially planar in the dark green crystals of **(63)**, those in the orange crystals of **(64)** are substantially distorted, adopting a pseudo-tetrahedral array. This difference is highlighted in the interplanar angles between the copper-chloride(bridging) and (terminal) planes, which are 6.11° in the case of the former and 47.6° in the latter. In addition to this difference, the intramolecular copper-copper distances are consequentially different (3.48Å in the former and 3.35Å in the

latter). The copper-chloride bonds are similar to that in the planar anion with, once more the bridging copper-chloride bonds being longer than those of the terminal bonds (copper-chloride(terminal) 2.21 Å, copper-chloride(bridging) 2.31 Å)

The dramatic difference in the appearances of **(63)** and **(64)** is the result of their structural differences. There is an interaction between the axial site of one of the copper atoms and a sulphur of a neighbouring cation in **(63)** (copper-sulphur 3.00 Å), while no such interaction is present in **(64)**. This secondary copper-sulphur interaction results in the charge transfer band, hence the intense colour of the crystals. The structure of **(63)** lacks the copper-sulphur interaction, and so simply appears orange due to the weaker transitions of the gold centre.

The $\text{Cu}_2\text{Cl}_6^{2-}$ anion is fairly well documented in the literature, with the tetrahedral geometry being predominant, although the square planar form is by no means rare²⁷. There are no examples in the literature, however, of two different structures being formed with the $\text{Cu}_2\text{Cl}_6^{2-}$ anion at a single temperature, let alone being crystallised simultaneously. This unusual feature is probably brought about by the similarity in energy between the gold-sulphur secondary interactions and the copper-sulphur interaction, with the geometrically flexible counter-anion able to accommodate both of these structures.

4.1.2 Transmetallation With Gold(I)

Given the difficulties of synthesising gold(I) tetranuclear dithiocarbamate-based macrocyclic complexes from simple aromatically-spaced bis-dithiocarbamate-based ligands, the possibility of creating such structures via a transmetallation reaction was investigated. To examine whether this approach would be successful, a dichloromethane solution of the copper(II) dithiocarbamate complex **(20)** was added to an acetonitrile solution of gold(I). The gold(I) ions were formed by the *in situ* reduction of potassium tetrachloroaurate by its addition to the reducing agent ethyl(2-hydroxyethyl)sulphide. The resulting yellow solid was recrystallised

from dichloromethane/diethyl ether to yield orange crystals (**65**), Figure 14.

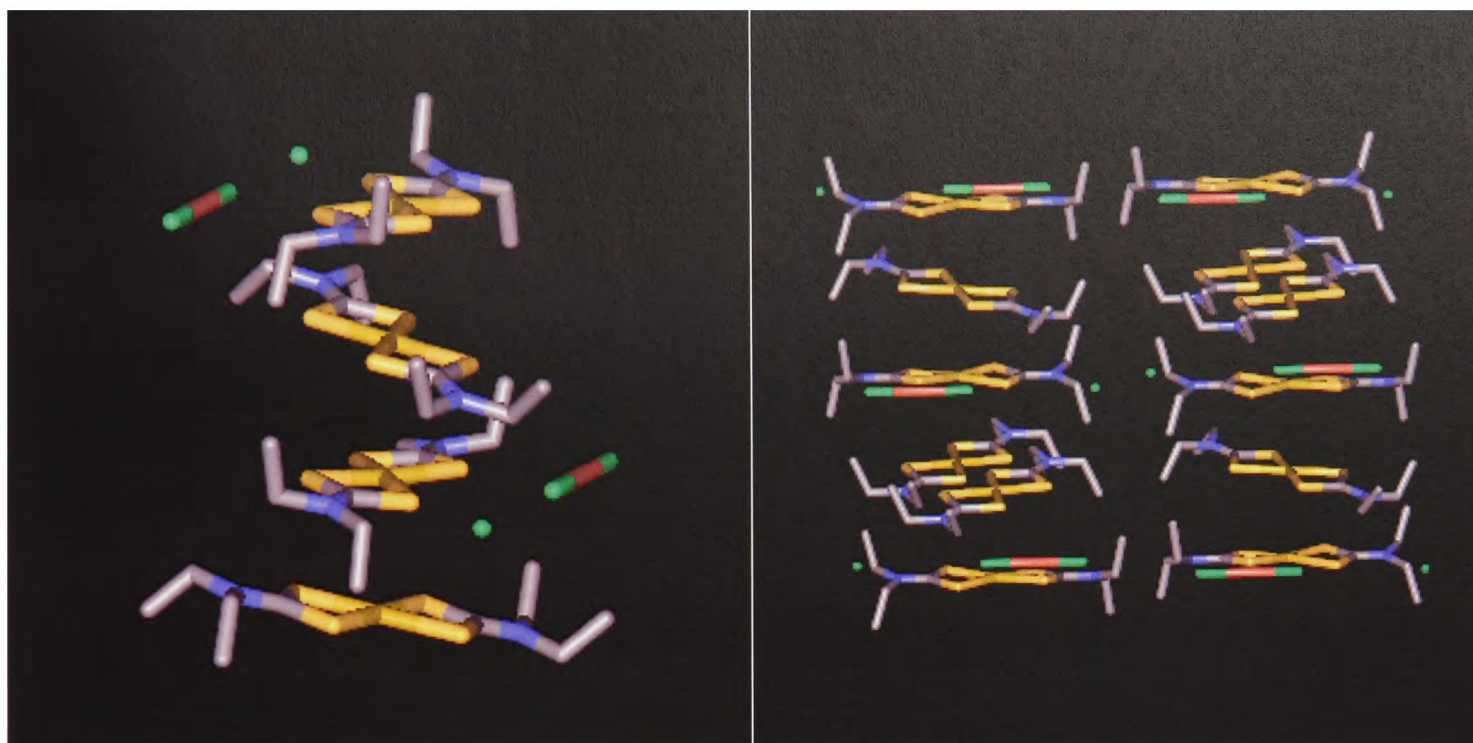


Figure 14 X-ray crystal structure of $(\text{Au}(\text{dtc})_2)_2\text{CuCl}_2\cdot\text{Cl}$ (**65**) Right: packing structure (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, Cu – red, Cl – green, Au – gold)

As can be seen, the desired gold(I) dithiocarbamate was not formed. Although the gold does indeed displace the copper centre for the dithiocarbamate ligands, the gold does not remain in its lower oxidation state. The gold is oxidised to the higher gold(III) state with the displaced copper being reduced to the copper(I) state. This further shows the affinity of the dithiocarbamate ligand for higher oxidation states and the greater stability of the gold(III) state in comparison to the gold(I) oxidation state, in combination with dithiocarbamate ligands.

The structure that (**65**) adopts is different to those previously described. Each moiety within the structure lies on a site with crystallographic symmetry. There are two crystallographically-distinct gold complexes, one of which is located on a two-fold axis and the second on an inversion centre. The copper(I) dichloride counteranion (CuCl_2^-) also lies on a two-fold axis (and is consequently exactly linear). The free chloride anion is also on the two-fold axis.

The gold complexes are arranged in an alternating stack, but there are no obvious gold-sulphur interactions (the shortest non-bonded gold-sulphur distance is $4.08\text{\AA}$). The CuCl_2^-

complex lies between these stacks (shortest copper-sulphur distance 3.27Å). In contrast with the chemically-related compound **(62)**, the gold and copper complexes do not appear to interact significantly.

(65)	
d(Au-S _{inter}) Å	a) 2.34, b) 2.32, 2.34
d(N-C(S ₂)) Å	a) 1.30, 1.31 b) 1.30
θ(S-Au-S _{adj})°	a) 75.3, 75.5 b) 75.4
d(Au-S _{intra}) Å	4.08, 4.23
d(Cu-S _{inter}) Å	3.27
d(Cu-Cl) Å	2.12
θ(Cl-Cu-Cl)°	180

Table 5 Selected crystallographic parameters for (65)

4.1.3 Monofunctionalised Gold(III) Dithiocarbamate Complexes

The synthesis of dinuclear gold(III) dithiocarbamate-based complexes often leads to the formation of solids whose elemental analysis suggests the formation of a mixed salt. In particular, these results have greater than expected values for gold, suggesting that gold-based counteranions such as gold(I) dichloride or tetrachloroaurate are present. The transmetallation reaction between copper(II) bis-(*N,N'*-diethyldithiocarbamate) **(20)** and potassium tetrachloroaurate was repeated, using two equivalents of the latter. This was designed to generate the tetrachloroaurate salt of the desired complex. This reaction was performed in a dichloromethane/acetonitrile (1:1) solvent system, and this led to the formation of an orange solution and subsequent precipitation of a yellow solid.

A single crystal suitable for X-ray analysis, was grown through the recrystallisation of the precipitate from 1,2-dichloroethane/isopropyl ether, yielding pale orange needles. The resulting structure is shown in Figure 15.

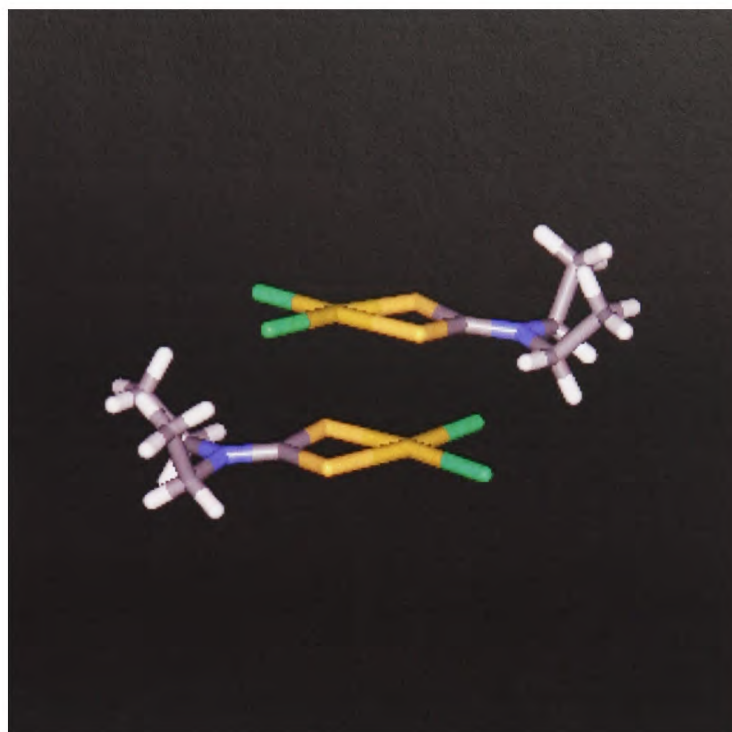


Figure 15 X-ray crystal structure of Au(dtc)Cl_2 (**66**) Key: C – grey, H – white, N – blue, S – yellow, Cl – green, Au – gold)

Analysis of the structure did not reveal the expected $[\{\text{Au(dtc)}_2\}\text{AuCl}_4]$ complex, but that of a monofunctionalised gold(III) dithiocarbamate complex. The structure consisted of discrete Au(dtc)Cl_2 units which have two crystallographically-distinct molecules in the unit cell, related by a non-crystallographic screw axis. As in the case of (**59**), there are significant axial, secondary interactions between the gold centre and one of the sulphur atoms of the dithiocarbamate subunit (gold-sulphur distances are 3.43 and 3.61 Å). The gold-chloride bond lengths in this structure are relatively long (gold-chloride distance ~ 2.33 Å). This is a result of the strong *trans* influence of the sulphur-based ligand with respect to chloride²⁸.

Closer inspection of the crystals shows that when a section of one of the needles is viewed along the crystallographic *b*-axis, it appears orange-red. When viewed perpendicularly to this, it appears bright yellow, i.e. the crystals are strongly pleochronic. This also explains the pale orange appearance of a bulk sample of the randomly oriented ethyl chains within the crystal.

	(66)	Au(S ₂ CN(CH ₂ CH ₂ OH) ₂)Cl ₂ [*]
d(Au-S _{inter}) Å	2.29, 2.31	2.29, 2.31
d(Au-Cl _{inter}) Å	2.32, 2.33	2.32, 2.33
d(N-C(S ₂)) Å	1.30	1.31
θ(S-Au-S _{adj})°	75.7	75.5
θ(Cl-Au-Cl)°	94.3	93.6
d(Au-S _{intra}) Å	3.63	3.61, 3.84

Table 6 Selected crystallographic parameters for (66) ^{*}Data for Au(S₂CN(CH₂CH₂OH)₂)Cl₂ taken from Lock *et al*³¹

Although structures containing a central metal bound to one dithiocarbamate unit and two halides have been previously reported^{29,30}, there has only been one previous X-ray crystal structure determined for these, that of the related Au(S₂CN(CH₂CH₂OH)₂)Cl₂³¹. Selected crystallographic parameters for this are displayed in Table 6, and show a high structural similarity between the two complexes.

The formation of (66) was surprising since the reactions to form the (59) and (62) were both performed with an excess of the gold starting material. The formation of this monofunctionalised structure may be regarded as an intermediate to the synthesis of unsymmetrical dithiocarbamate products. Indeed this methodology has previously been used to generate organometallic³² or boron-based cluster architectures^{33,34} from dihalo-gold(III) *N,N'*-diethyldithiocarbamate complexes (Figure 16). The formation of these organometallic or boron-based cluster complexes is possibly due to the strong and irreversible nature of the bonds that are formed.

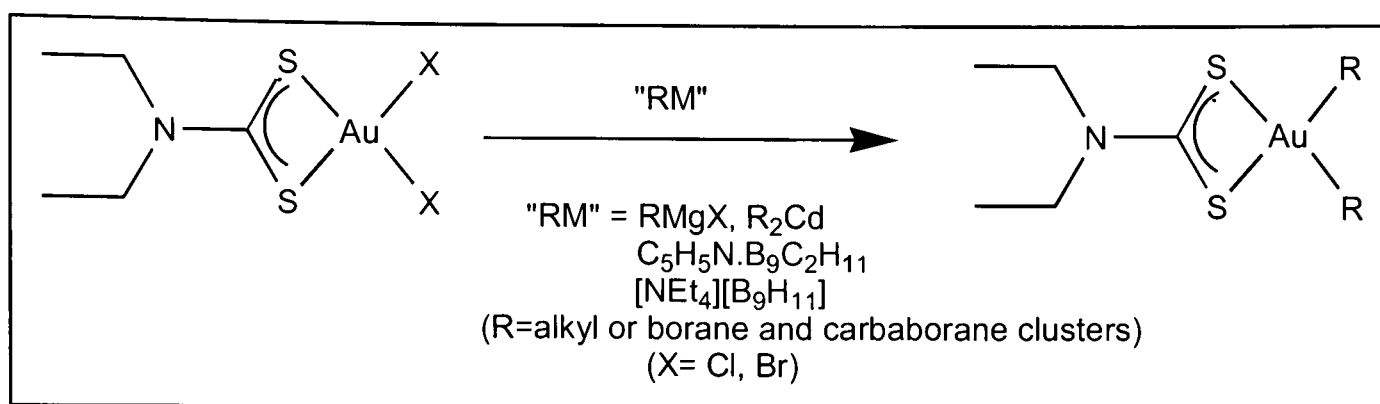
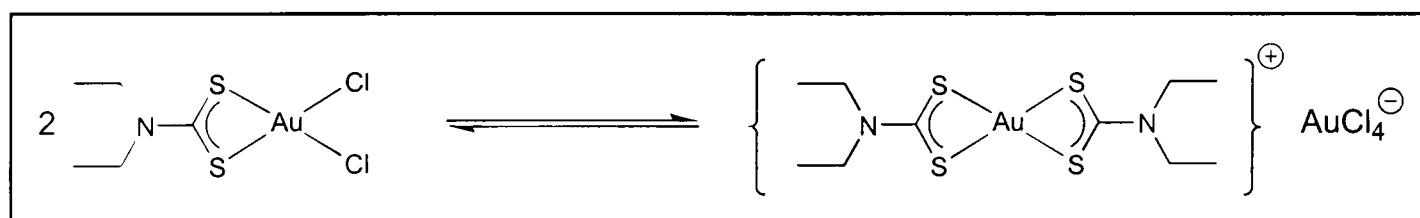


Figure 16 Formation of unsymmetrical Au(III) dithiocarbamate complexes

Whilst electron ionisation mass spectrometry revealed the presence of Au(dtc)Cl_2 , analysis of **(66)** by electrospray mass spectrometry revealed a large peak corresponding to the $\{\text{Au(dtc)}_2\}^+$ cation. In addition, the ^1H NMR spectrum of **(66)**, whilst only two peaks corresponding to the CH_2 and CH_3 protons are observed, these peaks appear to be the result of two overlapping quartets and triplets respectively. This, in combination with electrospray mass spectrometry evidence, suggest that **(66)** exists in equilibrium with its tetrachloraurate salt in solution, with the gold(III) dithiocarbamate bonds displaying a degree of lability (Figure 17).

Figure 17 Proposed solution state equilibrium of **(66)**

4.1.4 Nickel-based Counteranions

It has been demonstrated that the metal centre within copper(II) dithiocarbamate complexes can be displaced through the addition of tetrachloraurate salts to yield the corresponding gold(III) dithiocarbamate complexes. Electrospray mass spectrometry has shown that nickel(II) dithiocarbamate complexes may also form gold(III) dithiocarbamate cations via an analogous transmetallation reaction. The product of this reaction was also studied crystallographically. The mononuclear nickel(II) bis-(*N,N'*-diethyldithiocarbamate) complex **(21)** was combined with potassium tetrachloraurate in a dichloromethane/acetonitrile (1:1)

solution. The resultant green solution was layered with diethyl ether and this generated lime green crystals (**67**) whose structure was determined and is displayed in Figure 18.

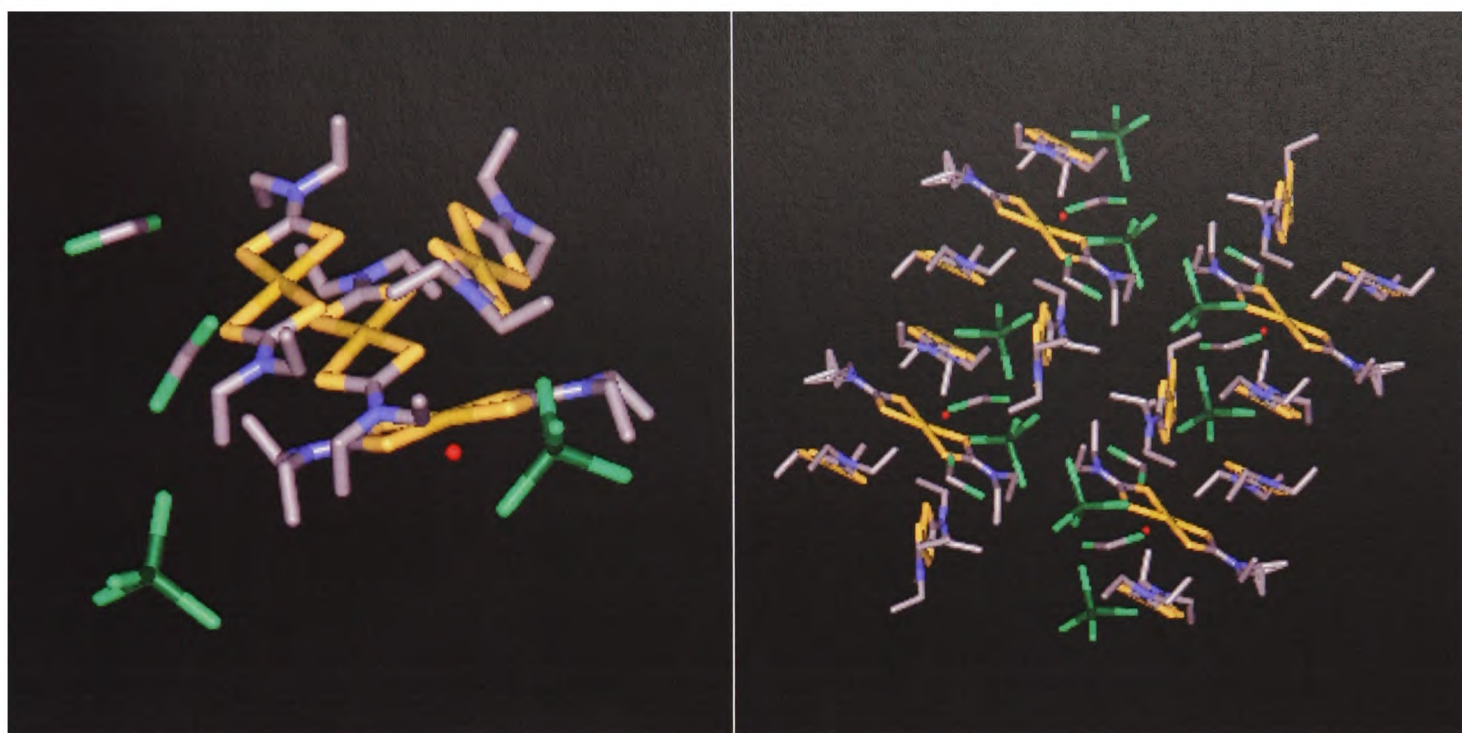


Figure 18 X-ray crystal structure of $\{\text{Au}(\text{dtc})_2\}_2 \cdot \text{NiCl}_4 \cdot 2\text{CH}_2\text{Cl}_2 \cdot \text{H}_2\text{O}$ (**67**) Right: crystal packing diagram (hydrogen atoms omitted for clarity, Key: C – grey, N – blue, S – yellow, O – red, Cl – green, Ni – dark green, Au – gold)

Once more, the metal centre within the dithiocarbamate complex has been displaced by the gold(III) ion. The accompanying counteranion is the nickel-based pseudo-tetrahedral nickeltetrachloride (NiCl_4^{2-}). The asymmetric unit of the crystal contains four crystallographically-distinct gold complexes, two nickel complexes, two dichloromethane molecules and a single water molecule. The thermal parameters of all the solvent atoms are large, suggesting these to be disordered. Only the disorder of the ethyl group can be resolved. The gold-based cations are associated by weak axial interactions with sulphur atoms of other complexes to form a tetramer (intramolecular gold-sulphur distances 3.33, 3.50, 3.48, 3.40 Å). There are not, however, any significant anion-cation interactions.

(67)	
d(Au-S _{inter}) Å	a) 2.33, 2.34 b) 2.33, 2.35 c) 2.33, 2.34 d) 2.33, 2.35
d(N-C(S ₂)) Å	a) 1.30, 1.31, b) 1.31 c) 1.29, 1.30, d) 1.30
θ(S-Au-S _{adj})°	a) 75.1, 75.2 b) 75.3, 75.4 c) 75.4, 75.5 d) 75.3, 75.5
θ(N-N-Au)°	a) 6.2, b) 1.2 c) 3.0, d) 6.4
d(Au-S _{intra}) Å	a) 3.48, b) 3.50 c) 3.33, d) 3.40
d(Ni-Cl) Å	a) 2.26, 2.27 b) 2.25, 2.26
θ(Cl-Ni-Cl)°	a) 103.4, 108.7, 110.0, 122.2 b) 107.7, 110.6, 110.9, 118.0

Table 7 Selected crystallographic parameters for (67)

4.2 Dinuclear Macrocyclic Complexes

The previous sections within this Chapter have shown that with simple mononuclear copper(II) and nickel(II) dithiocarbamate complexes (20) and (21) it is possible to substitute the metal centre for gold(III) through the addition of a tetrachloroaurate salt. It was further investigated whether this transmetallation reaction could be performed on dinuclear macrocyclic dithiocarbamate-based complexes, such as those described in Chapter Two, to generate analogous gold(III)-based complexes.

A variety of nickel(II) and copper(II) dithiocarbamate-based complexes were treated with

potassium tetrachloroaurate to yield the corresponding dinuclear gold(III) structures. Typically, this was achieved by the addition of an acetonitrile solution of the tetrachloroaurate salt to a dichloromethane solution of the metal complex. Stirring at room temperature led to the formation of golden yellow and light green solutions for copper(II) and nickel(II) complexes respectively.

A number of *m*-xylyl spaced complexes were prepared via this method (Scheme 10). Analysis of these solutions by electrospray mass spectrometry clearly showed the formation of the dicationic macrocyclic complexes. The resultant peaks show excellent correlation with predicted isotopic models. Additionally, the electrospray mass spectra of the gold(III) macrocyclic complexes illustrate that this transmetallation reaction offers a clean route for synthesising the desired dicationic complexes, with no evidence of the previously seen mixed-valence compounds being formed. The electrospray mass spectrum of **(71)** is displayed in Figure 19.

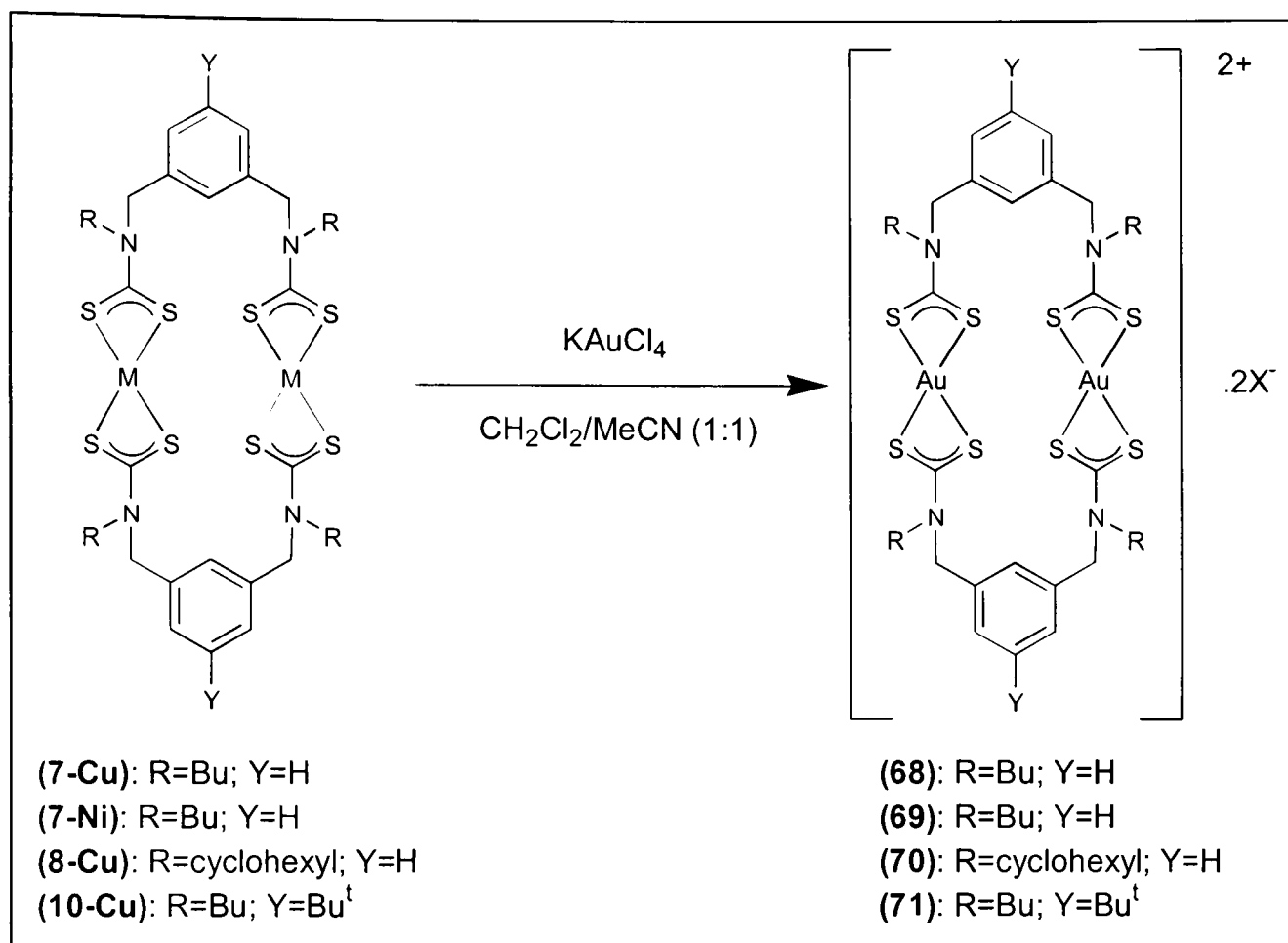
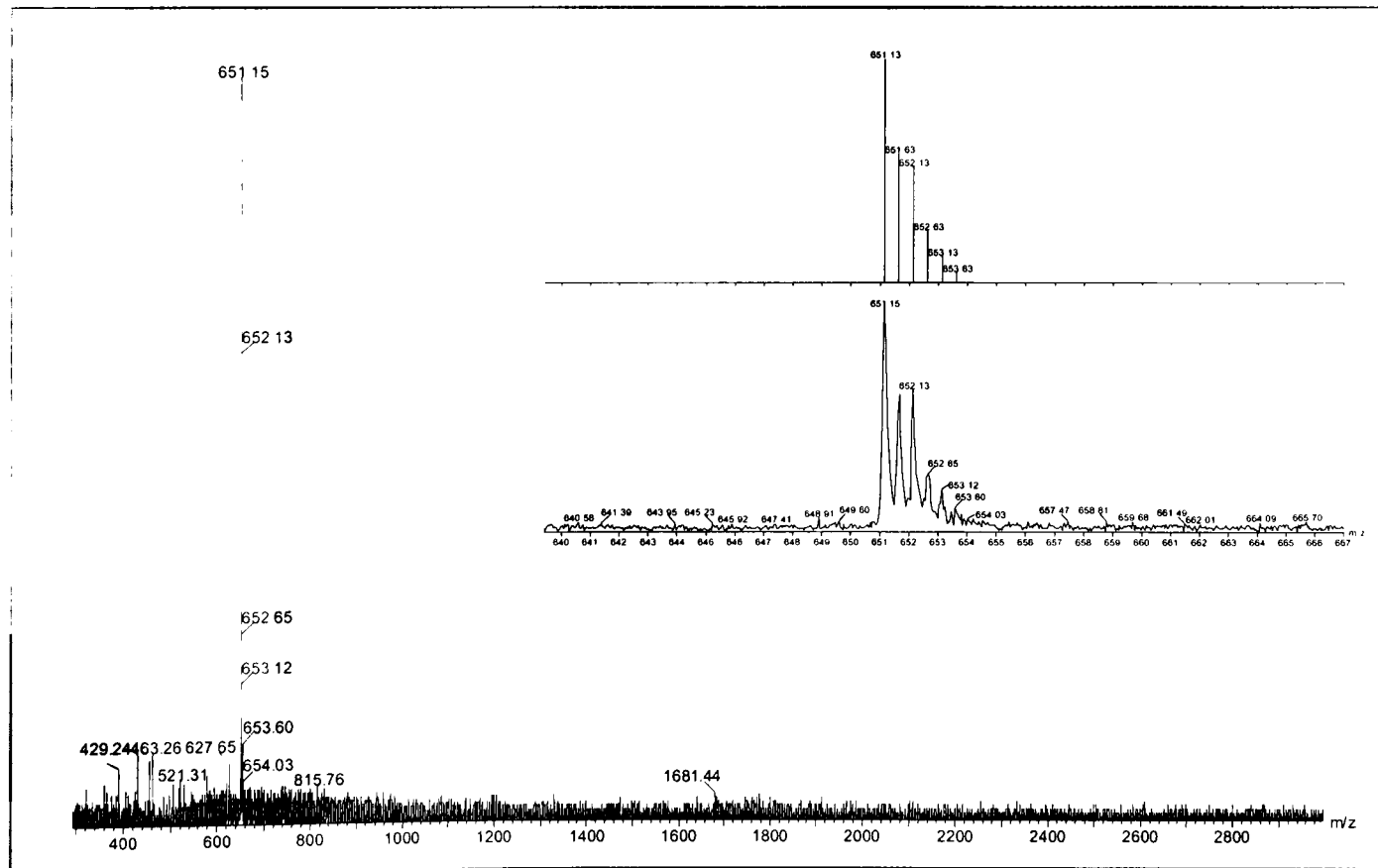
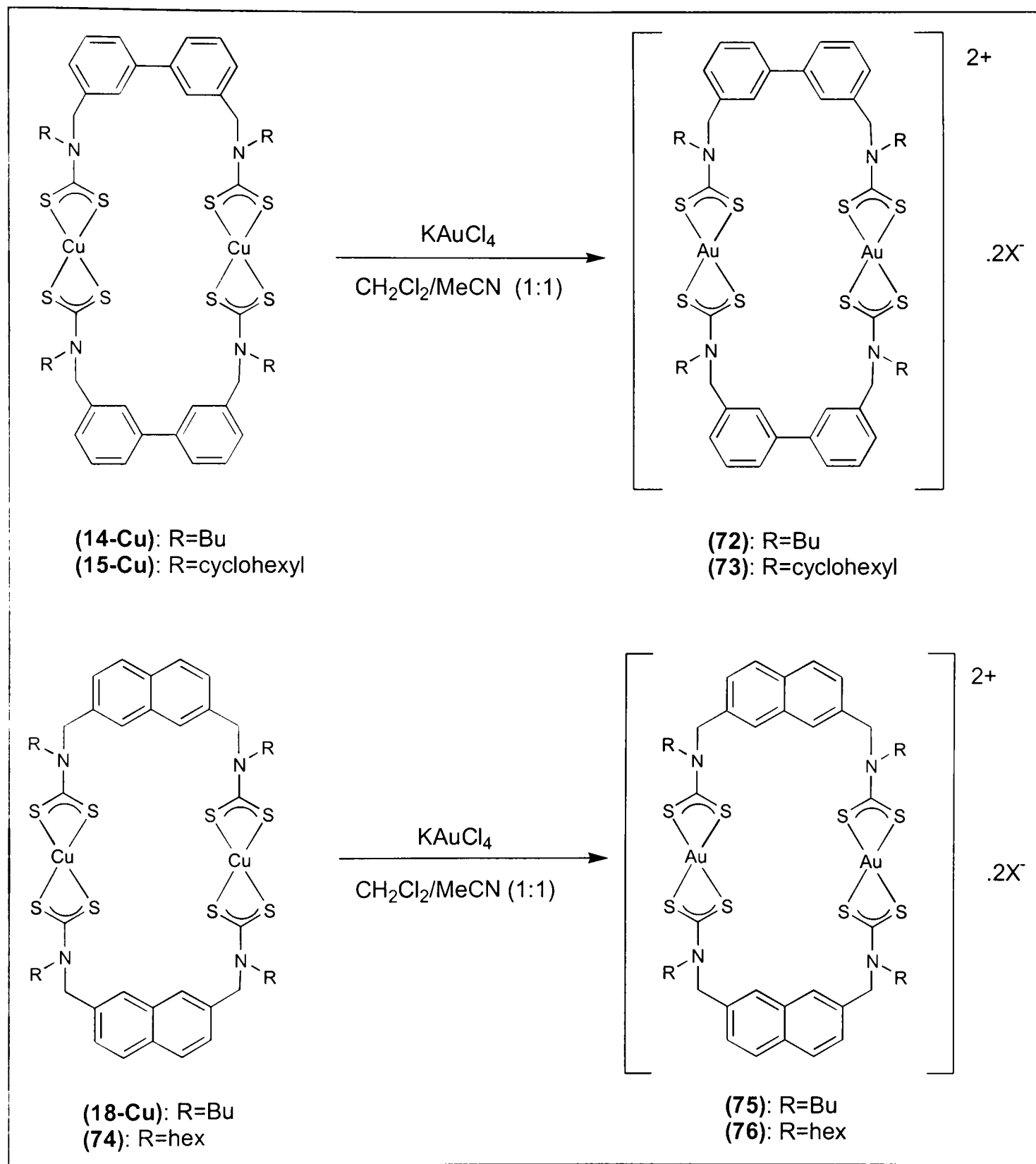
Scheme 10 Transmetallation of *m*-xylyl spaced macrocyclic complexes

Figure 19 Transmetallation of (10-Cu) to form the dinuclear Au(III) complex (71)

Analogous transmetallation reactions with the 3,3'-biphenyl spaced complexes (**14-Cu**) and (**15-Cu**), the naphthyl spaced structures (**18-Cu**) and the *n*-hexyl chained analogue (**74**)³⁵

were undertaken (Scheme 11). These syntheses also resulted in the formation of the corresponding dinuclear gold(III) dithiocarbamate macrocyclic complexes.



Scheme 11 Formation of dinuclear Au(III) dithiocarbamate architectures via transmetalation of 3,3'-biphenyl and naphthyl spaced complexes

Whilst the ^1H NMR spectra of the resultant gold(III) complexes display peaks consistent with the ligands within the structure, these were often broad. This is likely to be due to the presence of paramagnetic counteranions accompanying the cationic structures.

Unfortunately, elemental analysis of the dinuclear gold(III) structures formed via the transmetallation reaction failed to give a conclusive answer as to the nature of the counteranions present. The resulting data suggested that a range of copper/nickel and halide complexes were present as counteranions. This again highlights the difficulty of working with gold(III) coordination complexes and backs up the observation that a variety of counteranions result even from simple acyclic transmetallation reactions as evidenced from the variety of X-ray crystal structures of the monomeric $\{\text{Au}(\text{dtc})_2\}^+$.

The complexes **(72)**, **(73)**, **(75)** and **(76)** were all analysed by electrospray mass spectrometry. Whereas the spectra of the *m*-xylyl spaced complexes showed only one peak corresponding to the doubly charged species, those of the larger spaced complexes displayed more varied spectra. For example, examination of the electrospray mass spectrum of **(73)** revealed a number of adducts with anions (Figure 20). This demonstrates the potential of gold(III) dithiocarbamate-based complexes to act as hosts for anionic guests. The macrocycle forms adducts with chloride, copper(I) dichloride and tetrachloroaurate anions. Since these complexes are not observed with the analogous *m*-xylyl spaced macrocycles, which have been shown to have very small cavities, the larger cavities may accommodate the negatively charged guest. It is also likely that the formation of such cascade complexes may be favourable as the included anion would reduce the repulsive intramolecular cation-cation interactions.

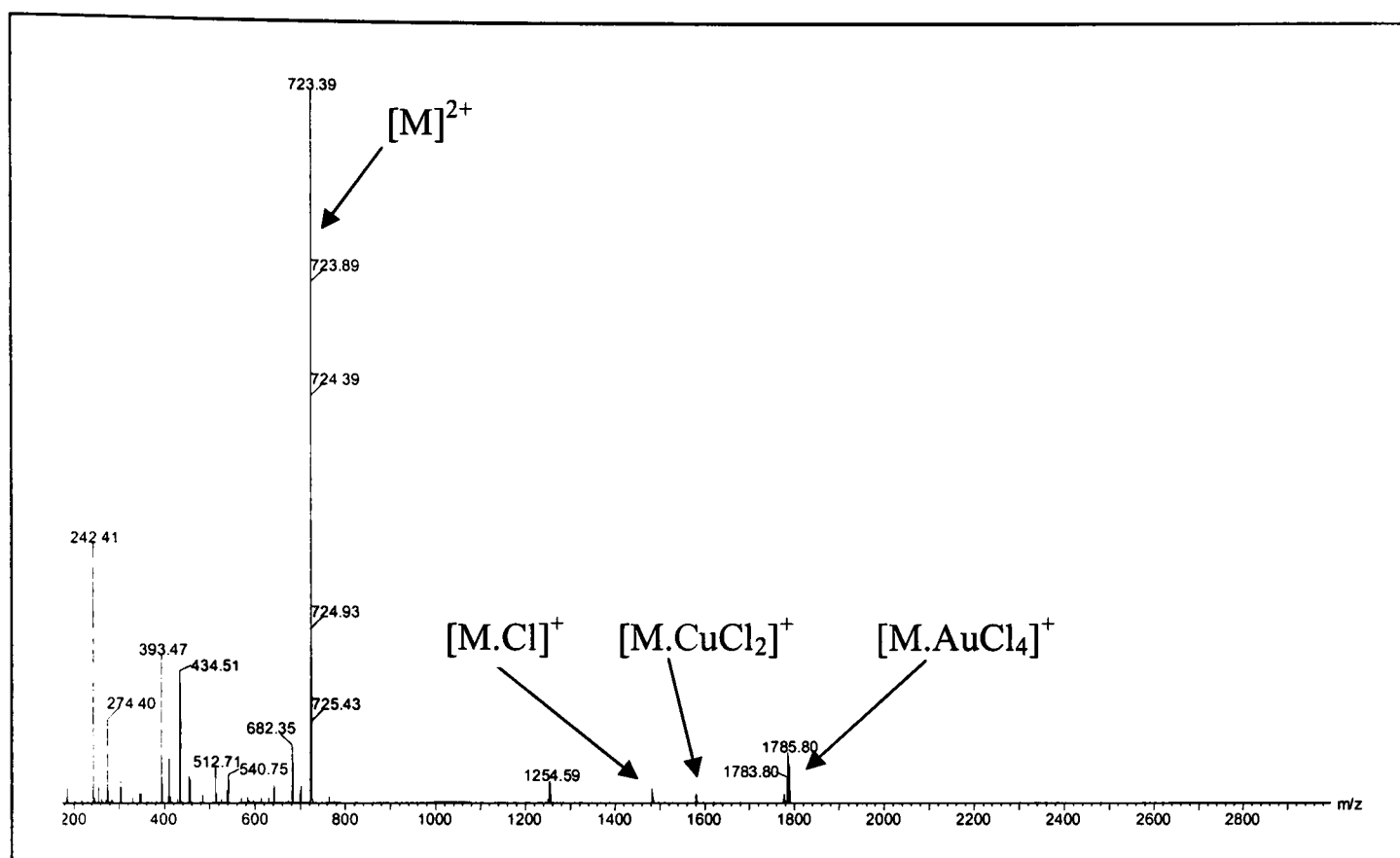


Figure 20 Transmetallation of (15-Cu) to (73)

A further notable feature resulting from these transmetallation reactions is the observation of partially exchanged complexes. For example, where only one of the available metal centres has been transmetallated; hence a mixed heterodinuclear metal species is formed. This is demonstrated in the transmetallation of the naphthyl spaced complex (74) (Figure 21). Here, in addition to the displacement of the two copper(II) centres by gold(III) $[Au_2L_2]^{2+}$ a peak corresponding to the exchange of just one metal centre $[AuCuL_2]^+$ is also seen. Similar to the displacement in (15-Cu), peaks are also observed for the formation of adducts with copper(I) dichloride and tetrachloroaurate anions, possibly suggesting the inclusion of these anions within the charged cavity of the complex.

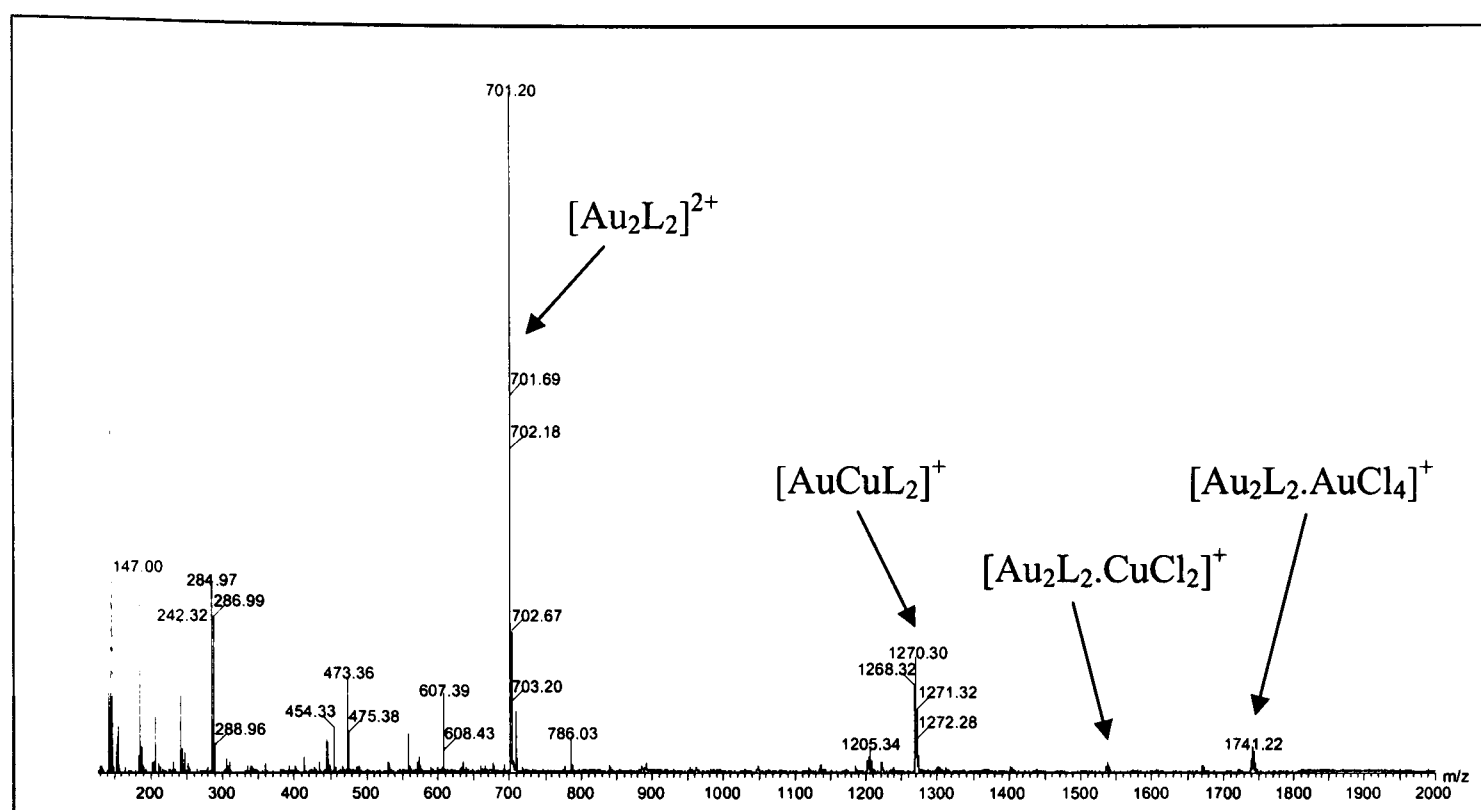
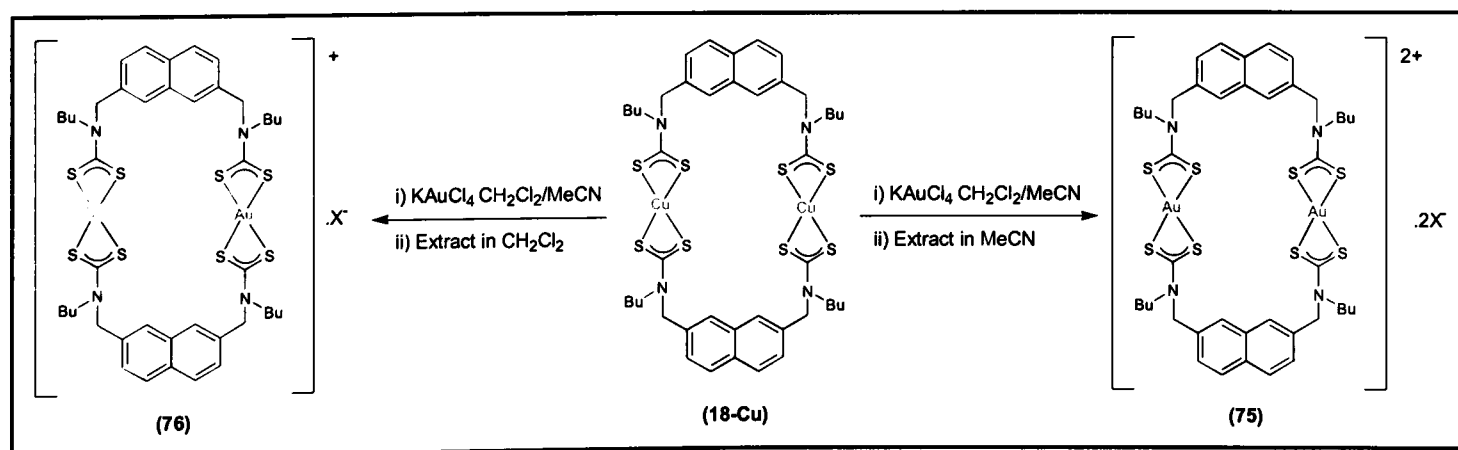


Figure 21 Transmetallation of (74) upon addition of 2.0 equivalents of KAuCl_4

Attempts were made to isolate the mixed-metal complex. Initially this was tried using 5mg of the complex (18-Cu). 1.5 equivalents of potassium tetrachloroaurate were added to the dinuclear complex and the solution stirred at room temperature for 18 hours. It was found that evaporation of the resultant golden solution and subsequent extraction of the crude product with dichloromethane yielded the monocationic product (76), whilst extraction of the remaining product with acetonitrile exclusively gave the dicationic product (75) (Scheme 12).



Scheme 12 Transmetallation of (18-Cu)

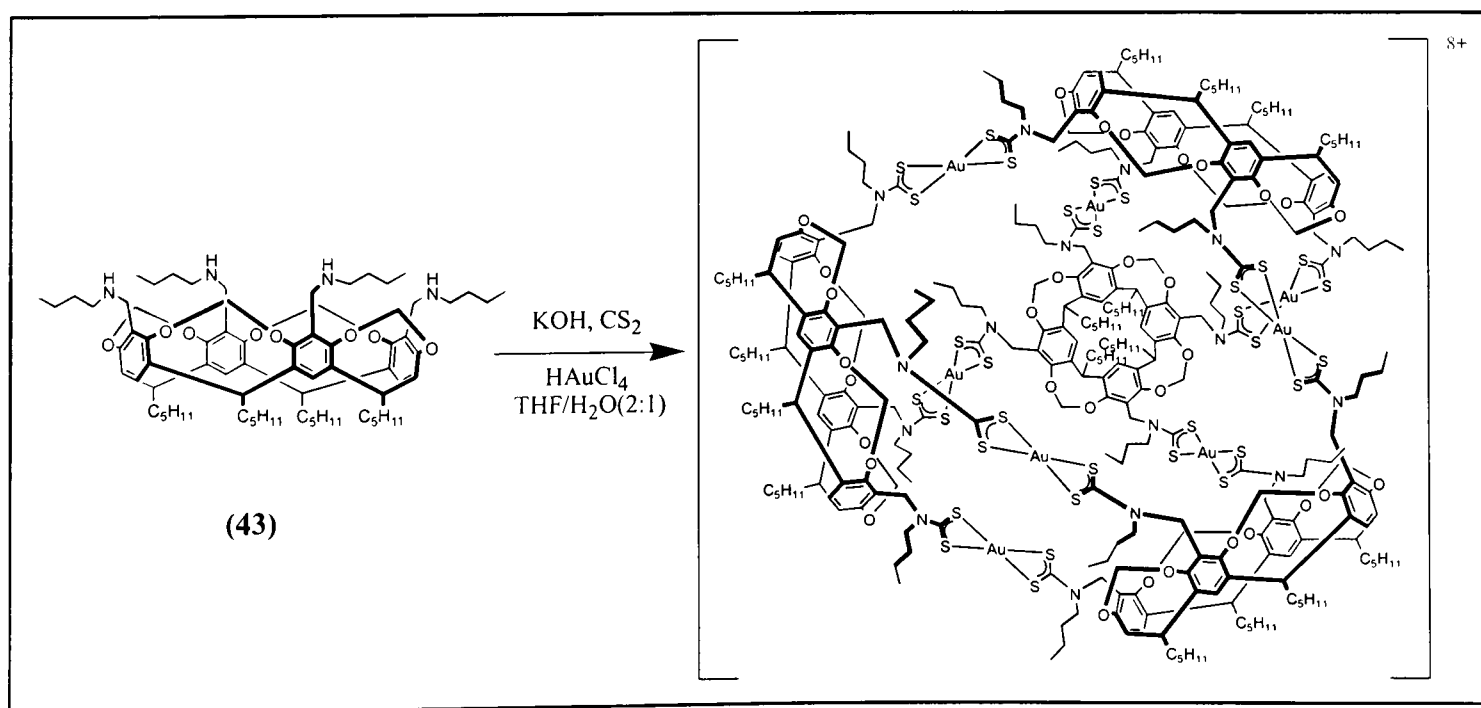
However, attempts to scale up this reaction proved unsuccessful, with the subsequent extractions failing to separate the two products.

5 Gold(III) Resorcinarene Complexes

It has been shown within this Chapter that the gold(III) dithiocarbamate linkage can be used to synthesise dinuclear macrocyclic complexes. This is both via a direct reaction between a potassium dithiocarbamate salt and a tetrachloroaurate salt, and by the displacement of copper(II) or nickel(II) in a preformed bimetallic macrocycle. Furthermore, it was demonstrated in Chapter Three that dithiocarbamate-functionalised resorcinarenes are able to form multinuclear nano-dimensional complexes with first and second row transition metals. An investigation was undertaken as to whether gold(III) dithiocarbamate complexes could also be developed from the tetra-dithiocarbamate functionalised resorcinarene cavitand scaffold.

5.1 Direct Reaction

Initially the synthesis of a gold(III) dithiocarbamate functionalised resorcinarene cavitand was attempted by a one-pot reaction with the tetra-amino cavitand **(43)**, potassium hydroxide, carbon disulphide and hydrogen tetrachloroaurate in tetrahydrofuran/water (2:1) (Scheme 13).



Scheme 13 Attempted synthesis of Au(III) dithiocarbamate functionalised resorcinarene cavitand

Analysis of the brown solution using electrospray mass spectrometry, revealed the presence of an octanuclear gold(III) dithiocarbamate complex, although this was accompanied by numerous by-products, presumably a result of the reduction of the gold centres by the water present in the reaction as has been previously observed. This demonstrates that the square planar gold(III) centre directs the assembly to form an analogous octanuclear tetrahedral structure, as observed with both copper(II) and copper(III) ions (47). This is in contrast to the square based pyramidal coordination complexes of the zinc(II) (48) and cadmium(II) (49) dithiocarbamates which force the complex to adopt a hexanuclear loop structure (Figure 22).

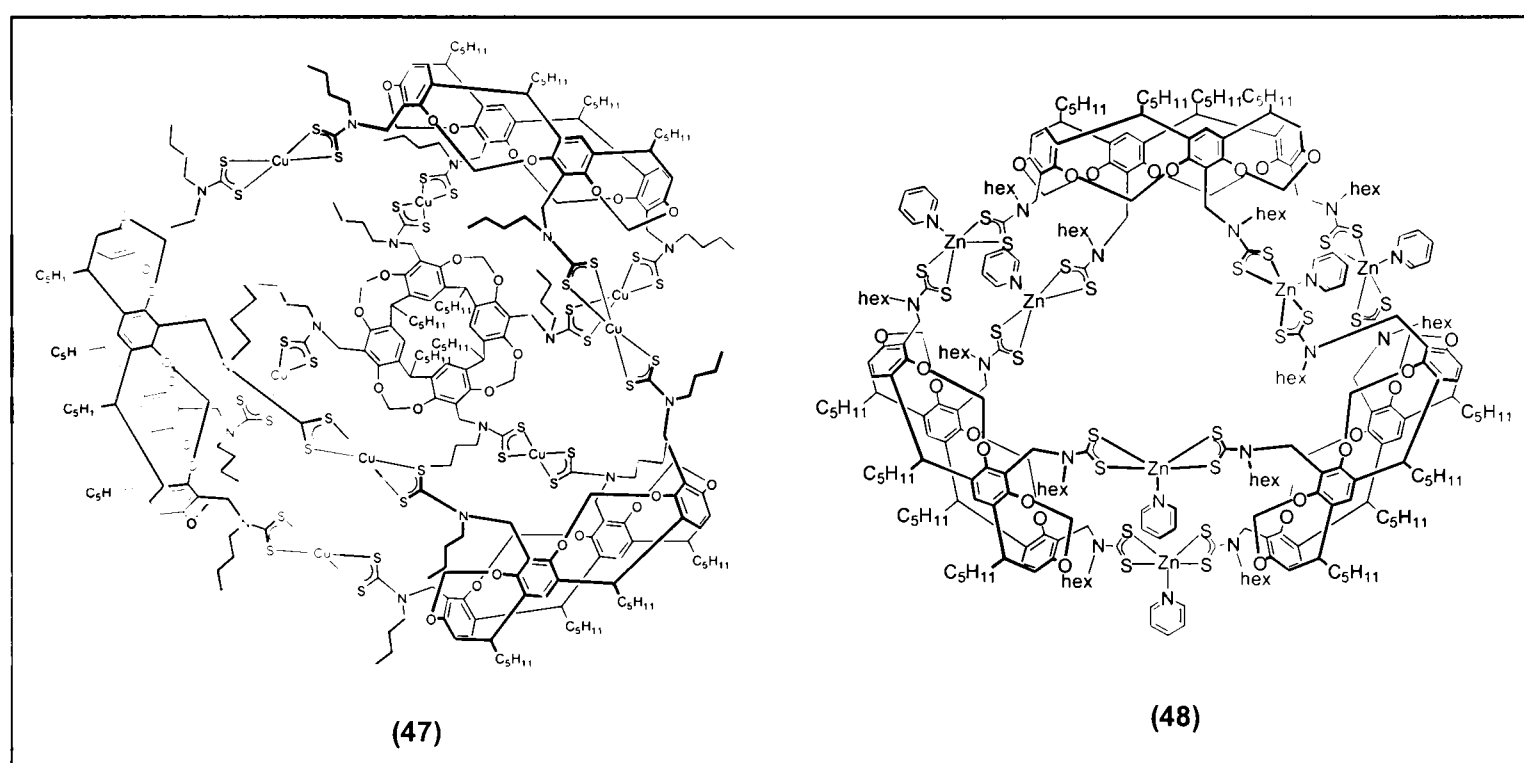


Figure 22 Nano-dimensional resorcinarene cavitand dithiocarbamate complexes of Cu(II) (left) and Zn(II) (right)

5.2 Transmetallation

Whilst the reaction to synthesise the gold(III) dithiocarbamate functionalised resorcinarene cavitand was possible via a direct reaction, this route generated a range of products. The analogous reaction was performed using a transmetallation reaction, in order to ascertain whether this method offers a cleaner reaction. This also allows an investigation as to whether it is possible to displace a number of metal centres whilst maintaining the same structure.

An excess of hydrogen tetrachloroaurate was added to a solution of the octanuclear copper(II) dithiocarbamate functionalised resorcinarene cavitand complex. A rapid colour change from brown to gold was observed. The resulting mixture was injected into the electrospray mass spectrometer. The spectrum obtained from this experiment is displayed in Figure 23.

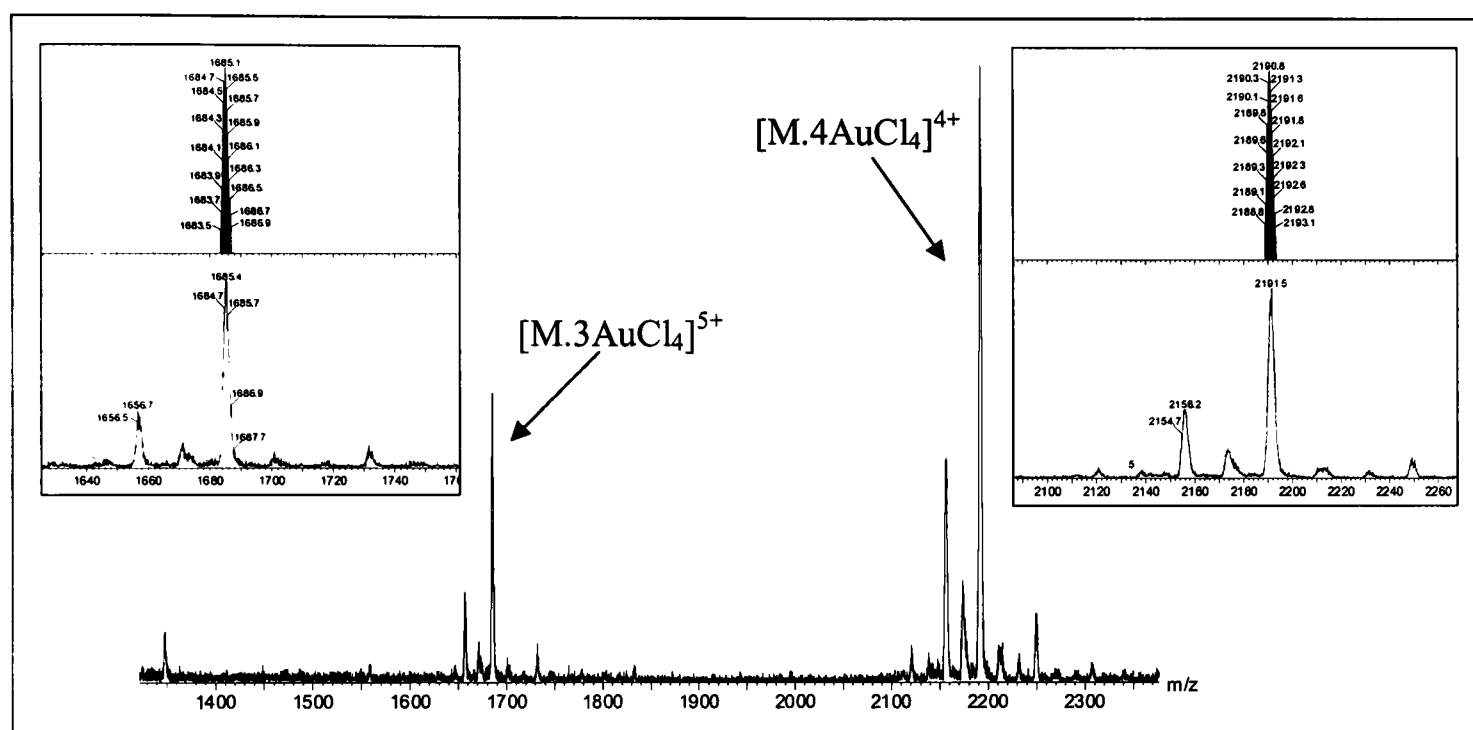


Figure 23 Electrospray mass spectrum of transmetallation of the Cu(II) tetrameric complex with H₂AuCl₄ (left inset) [M.3AuCl₄]⁵⁺ peak and predicted isotopic model, (right inset) [M.4AuCl₄]⁴⁺ peak and predicted isotopic model

The spectrum shows that addition of hydrogen tetrachloroaurate to the octanuclear complex results in the rapid displacement of all eight copper(II) metal centres for gold(III). The product is the same through the transmetallation route as it is from the direct reaction from the parent amine.

The resultant complex is stabilised by the formation of adducts with excess tetrachloroaurate anion. It is possible that these anions may be situated within the central cavity of the cage-like structure. Such an interaction may well be necessary to maintain the structure as in its absence the mutual electrostatic repulsion between the positively-charged gold(III) centres within the structure may result in its instability. Despite the presence of these stabilising counteranions within the architecture, re-recording the electrospray mass spectrum after ten minutes revealed that the assembly had decomposed. Unfortunately, attempts to isolate the octanuclear

complex via the addition of eight equivalents or an excess of tetrachloroaurate proved unsuccessful.

A similar transmetallation reaction was also attempted starting from the hexanuclear zinc(II) dithiocarbamate resorcinarene-based complex (**48**). Unfortunately, analysis by electrospray mass spectrometry of the resultant solution did not reveal the presence of any nano-dimensional products, with only fragmentation peaks being observed. This is disappointing considering the ability of mononuclear zinc(II) dithiocarbamate complexes to undergo transmetallation reactions.

6 Kinetics of Transmetallation Reactions

Gold(III) has been shown to displace both copper(II) and nickel(II) metal centres from both simple mononuclear as well as dinuclear and octanuclear dithiocarbamate-based metal complexes. These reactions were observed to be relatively fast, as they may be followed through the obvious visual colour change to a golden solution. The relative rates of these reactions were studied using UV-vis spectroscopy on a range of structures.

A useful indication of the rate of a chemical reaction is the measurement of its half-life, $t_{1/2}$. This is the time taken for the concentration of the reactant to fall to half of its initial value³⁶. Measurement was achieved via the observation of the UV-vis spectra after the addition of a quantity of potassium tetrachloroaurate corresponding to the number of metal centres within the original structure. It was not possible to study the reactions under pseudo-first order conditions as it has been shown that the addition of an excess of tetrachloroaurate to a dithiocarbamate complex leads to the formation of a mono-dithiocarbamate complex (e.g. (**66**)) being formed, not the desired bis-substituted gold(III) complex.

The effect over time of the addition of two equivalents of potassium tetrachloroaurate to a dichloromethane/acetonitrile (1:1) solution of (**10-Cu**) is displayed in Figure 24. The most

striking aspects of the spectrum are the emergence of a new peak in the spectrum corresponding to the gold(III) dithiocarbamate product at 317nm, and the disappearance of the copper(II) dithiocarbamate band at 427nm. The rate of these processes is shown in Figure 25 and the calculated half lives for the copper(II) dithiocarbamate complexes are displayed in Table 8. Unfortunately, it was not possible to accurately calculate similar times for the analogous nickel(II) dithiocarbamate complexes due to the overlap between the emerging gold and disappearing nickel-based electronic spectral bands.

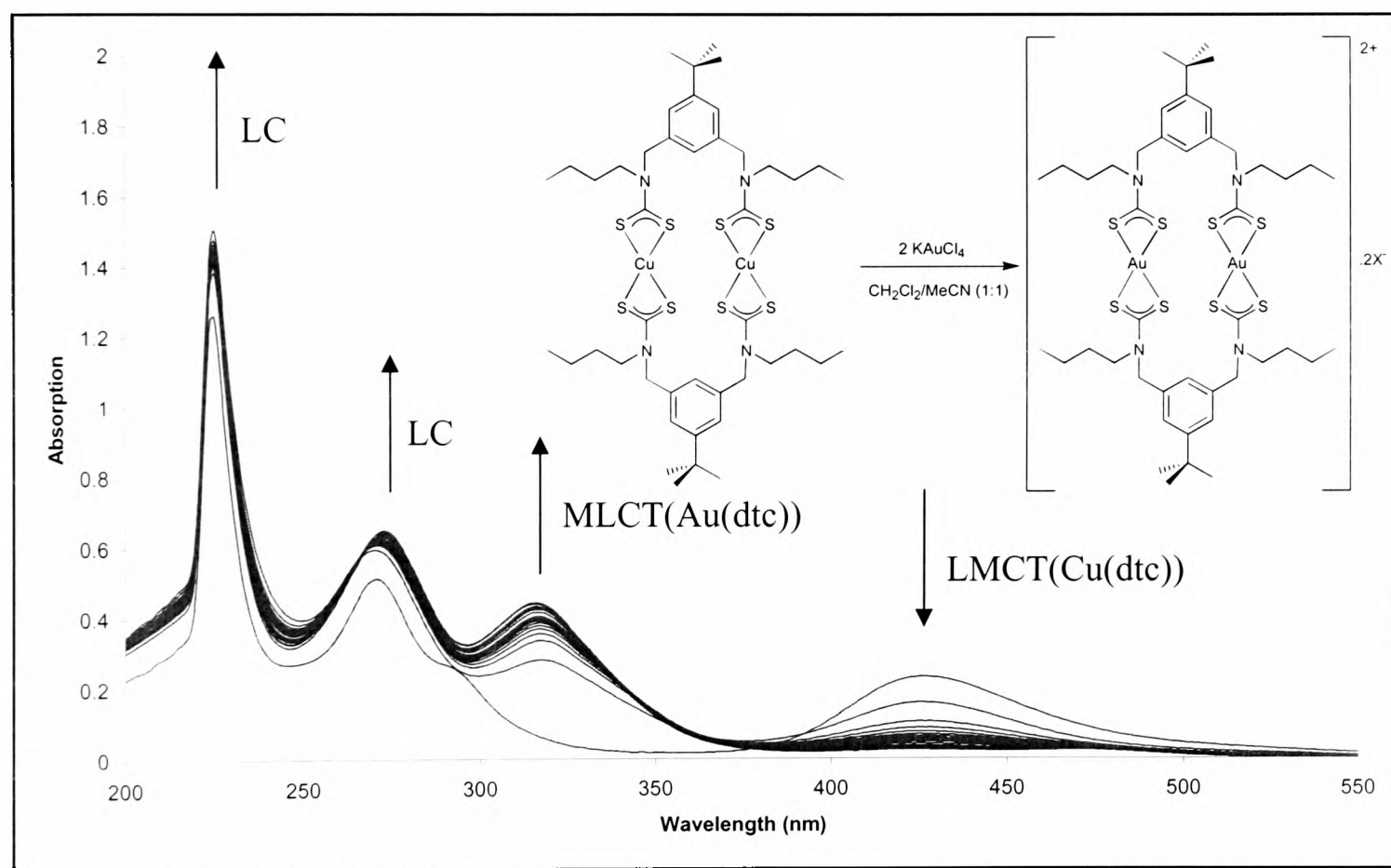


Figure 24 UV-vis spectra of (10-Cu) recorded every 30s after the addition of 2.0 equivalents of KAuCl₄ in MeCN/CH₂Cl₂ (1:1) 293K

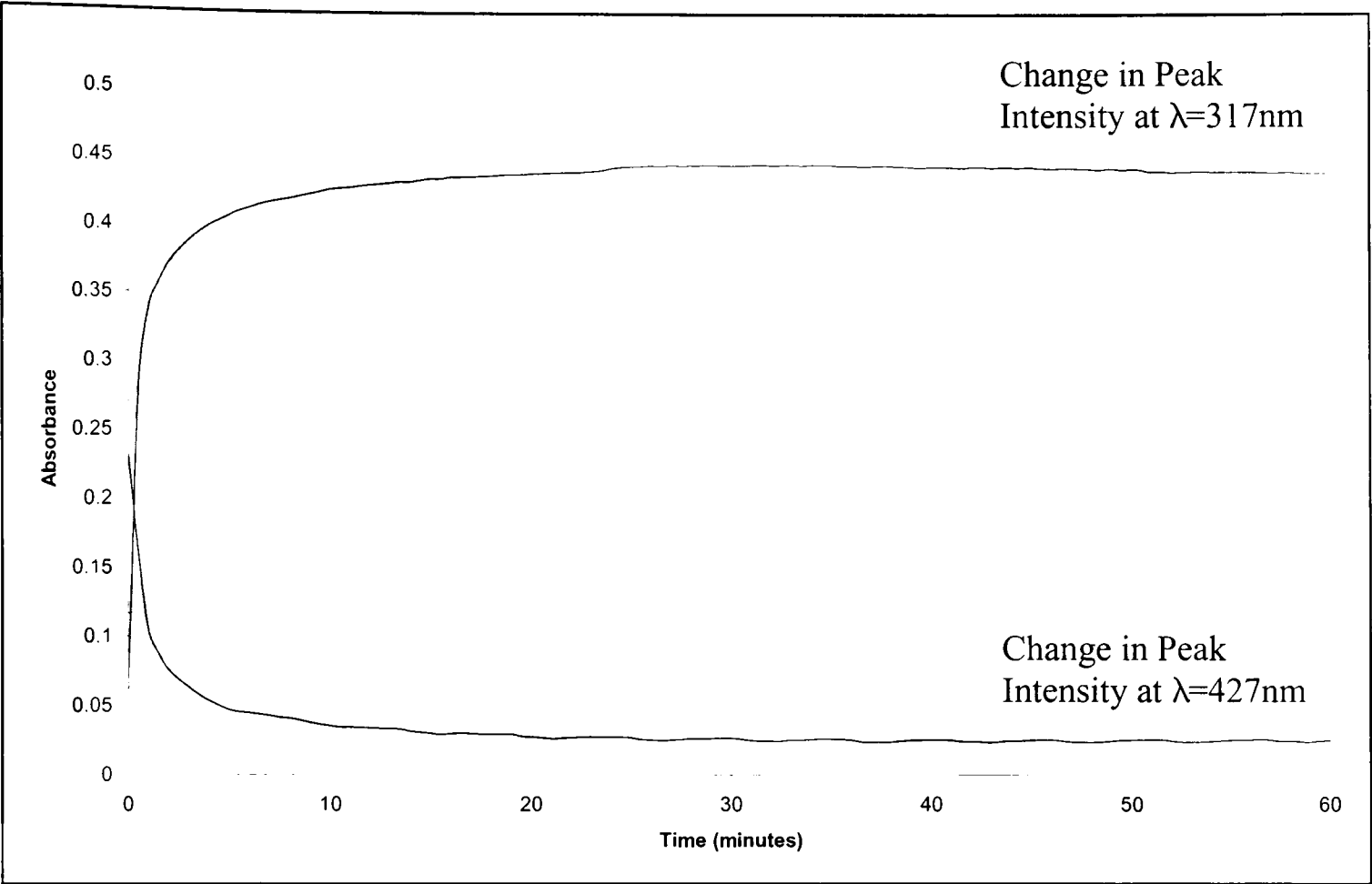


Figure 25 Change in the absorbance over time in the UV-vis Spectrum of (10-Cu) upon the addition of 2.0 equivalents of KAuCl₄

	Spacer	t _½
(20)	-	13 mins
(10-Cu)	<i>m</i> -xylyl	1min 30s
(14-Cu)	3,3'-biphenyl	11 mins
(15-Cu)	4,4'-biphenyl	13 mins
(18-Cu)	2,7-naphthyl	15 mins
(47)	resorcinarene	30s

Table 8 Half-lives of Cu(II) dithiocarbamate complexes upon the addition of sufficient potassium tetrachloroaurate to generate the corresponding Au(III) complex

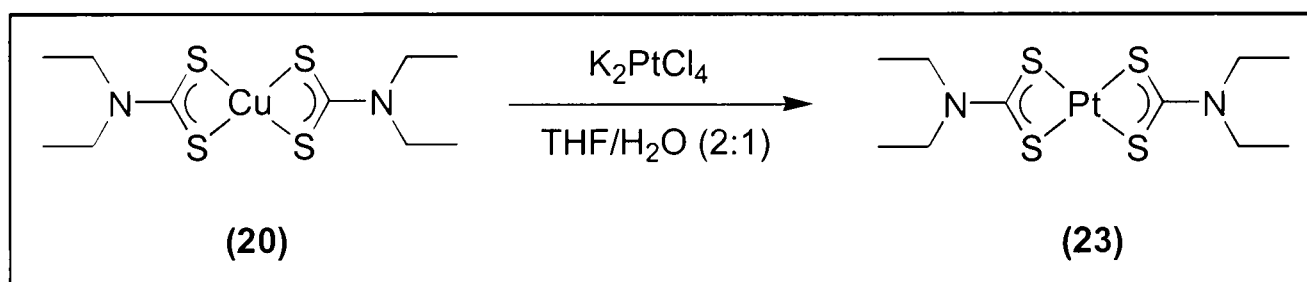
Table 8 clearly illustrates that the nature and size of the aromatic spacer in the dinuclear copper(II) complexes has a significant effect upon the rate of exchange. In the case of the

dinuclear macrocycles with a large spacing group (i.e. **(14-Cu)**, **(15-Cu)** and **(18-Cu)**) the half-lives are similar to those of the mononuclear complex **(20)**. This suggests the exchange of the two copper centres are taking place independently of each other, possibly due to the relatively large through space metal-metal distances. However, in the case of the *m*-xylyl spaced macrocycle the time taken to exchange the gold centres is significantly shorter than that of the mononuclear complex. Here, there appears to be a significant cooperative effect. This is somewhat surprising as it may be expected that arranging two positively-charged centres in close proximity would lead to a mutual electrostatic repulsion and hence a slower half-life time. This positive cooperativity may be a result of the increasing bond lengths on changing from copper(II) to gold(III) centres (typical bond distances in dithiocarbamate complexes: copper(II)-sulphur 2.28 Å, gold(III)-sulphur 2.33 Å). Although the difference in bond lengths may appear small, it may place significant strain upon the small macrocycle, resulting in weaker coordination of the second metal, hence making it easier to displace. This is also consistent with the observation of stable mixed metal macrocyclic complexes of the larger spaced structures, where ring strain would be expected to be significantly reduced. The *m*-xylyl spaced complexes do not generate such mixed metal complexes, due to the greater stability of the bis-gold structures.

Similarly, addition of eight equivalents of potassium tetrachloroaurate to the octanuclear copper(II) dithiocarbamate functionalised resorcinarene complex **(47)** led to the rapid displacement of all the copper metal centres. Transmetallation of this complex was 25 times more rapid than the monomeric copper(II) dithiocarbamate complex **(20)**, thus a significant positive cooperative effect is observed. This is probably due to the increasing bond length on changing from a copper(II) to a gold(III)-based architecture. This would result in a significant degree of strain upon the cage-like architecture, if a heterometallic structure were formed.

7 Platinum(II) Transmetallation Reactions

Given the success in using the transmetallation reaction in introducing gold(III) centres into dithiocarbamate complexes an investigation as to whether the isoelectronic platinum(II) ion could also undergo this reaction was undertaken. The soft platinum(II) ion would also be expected to have a high affinity for the sulphur-based ligands. It was necessary to perform the reaction in a tetrahydrofuran/water (2:1) solvent system, due to solubility constraints. Addition of potassium tetrachloroplatinate to the copper(II) dithiocarbamate-based complex (20) did also result in the transmetallation of the copper for a platinum centre resulting in the formation of (23) (Scheme 14). However, it was found that the rate of this reaction was significantly slower than of the analogous displacement using gold, with reaction times in the order of days, in comparison to the minutes observed in the analogous gold(III) exchange.



Scheme 14 Transmetallation of (20) via the addition of potassium tetrachloroplatinate

7.1 Dinuclear Calix[4]Arene Dithiocarbamate Complexes

It has been demonstrated the bis-(aminomethyl)-functionalised calix[4]arene frameworks can undergo metal-directed self-assembly reactions to generate dinuclear dithiocarbamate-based complexes³⁷. Transmetallation of a copper(II)-based structure (77) was attempted with platinum(II) (Figure 26).

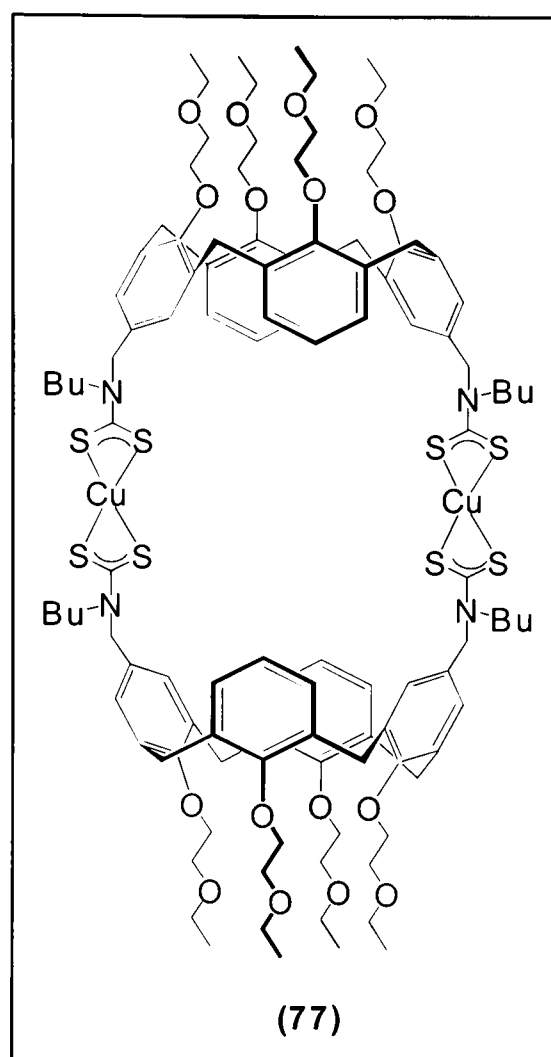


Figure 26 Dinuclear Cu(II) dithiocarbamate-based calix[4]arene complex (77)

Interestingly, a previous attempt to synthesise the desired platinum complex proved unsuccessful via a one-pot reaction³⁸. A transmetallation reaction was therefore performed, in order to elucidate whether this alternative method would prove more successful.

The exchange of the copper(II) centres of a dinuclear complex was attempted through the addition of potassium tetrachloroplatinate in a tetrahydrofuran/water (2:1) solvent system. A nanomolar solution of the preorganised copper(II) complex (77) was stirred at room temperature for seven days. Analysis of the solution by electrospray mass spectrometry revealed the formation of the desired platinum(II) complex (Figure 27). The resulting spectrum displays both peaks for monocationic complexes with alkali metals, in addition to the more prominent peaks, corresponding to the complexation of the desired bis-platinum complex with two alkali metal cations.

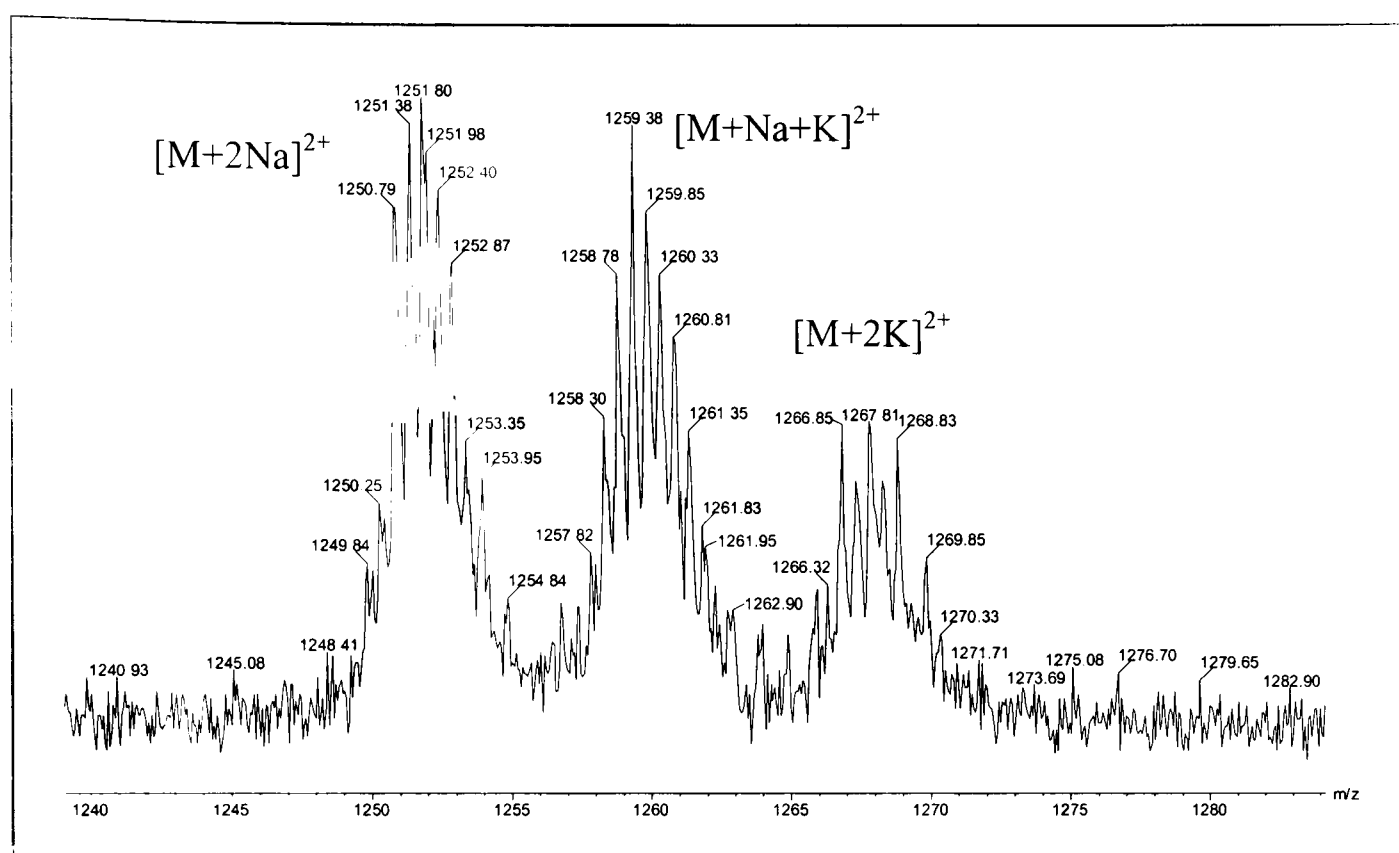


Figure 27 Electrospray mass spectrum of the Pt(II) transmetallation of (77) after coinjection of sodium and potassium hexafluorophosphate

This demonstrates that where the direct one-pot synthesis reaction is unsuccessful, a transmetallation reaction provides an alternative synthetic route.

8 Conclusion

It has been shown in this Chapter that the positively-charged gold(III) bis-dithiocarbamate unit may be incorporated into a range of assemblies. New dinuclear gold(III) dithiocarbamate macrocyclic complexes have been prepared by two different synthetic methods. Firstly, the reaction of a bis-potassium dithiocarbamate salt containing a simple aromatic spacer group with tetrachloroaurate yields the desired macrocyclic dicationic complex. In addition, it has been demonstrated that a transmetallation reaction occurs upon the addition of a tetrachloroaurate salt to a solution of a preformed copper(II) or nickel(II) dithiocarbamate macrocyclic complex. Elemental analysis of the complexes has revealed, however, that a major problem with all these reactions is elucidating the nature of the accompanying counteranion. This problematic feature has been highlighted via a series of crystallisations.

which illustrates that both direct and transmetallation synthetic methods result in a range of counteranions being generated. In mononuclear gold(III) dithiocarbamate complexes, it has been possible to displace these anions for a non-coordinating anion. However, with multinuclear complexes, this has not proved possible. This may be a result of the counteranion playing an integral part in stabilising the dinuclear structures.

In addition to the generation of dinuclear gold(III) complexes, an octanuclear gold(III) resorcinarene dithiocarbamate-based complex was prepared. This was achieved via both a direct one-pot reaction, and a transmetallation reaction from a pre-formed copper(II)-based octanuclear complex, which resulted in a significantly cleaner reaction.

The rate of transmetallation was examined by the measurement of the half-lives of a range of copper(II) dithiocarbamate-based complexes. It was found that the exchange of the copper(II) centres of *m*-xylyl spaced macrocycles and the octanuclear copper(II) resorcinarene complex (**47**) resulted in a rapid reaction. This positive cooperativity is possibly a result of the increasing metal-sulphur bond length resulting from the first row transition metal displaced by the third row metal, adding strain to the partially-substituted, heterometallic structures. It has also been demonstrated that larger macrocyclic complexes can undergo partial-metal exchange. This leads to the possibility of generating mixed metal architectures.

Transmetallation reactions have been extended to the isoelectronic platinum(II) ion, which also displaces first row transition metals in dithiocarbamate complexes, although this is achieved at a significantly slower rate than the corresponding exchange with gold(III). The platinum(II) transmetallation reaction has been used to produce a platinum(II) dithiocarbamate-based dinuclear calix[4]arene complex that could not be prepared via a direct one-pot reaction from its parent bis-amine.

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Chapter Five

Interpenetrating

Dithiocarbamate Complexes

Chapter Five: Interpenetrating Dithiocarbamate Complexes

1 Introduction

It has long been a desire of the chemist to be able to synthesise interlocked molecules¹. Apart from their aesthetic beauty, they possess interesting topological, electronic and dynamic properties^{2,3,4}. A range of these interpenetrating systems have already been discussed in Chapter One, with the most common being catenanes, rotaxanes and pseudo-rotaxanes. These architectures have been formed both by the use of metal-directed self-assembly as well as via organic templated methodologies.

In recent years, the use of interpenetrating species has been at the forefront of nanotechnology. These mechanically interlocked architectures have offered the possibility of generating a range of molecular machines and devices^{5,6}. For example, systems where an external stimulus is able to perturb the molecular topology, have proved particularly attractive for this purpose. It is possible that the development of such arrays will lead to the fabrication of devices capable of writing, reading and storing information of the nanometre scale⁷.

1.1 Tetrathiafulvalene

Square planar transition metal dithiocarbamate complexes can be considered as an inorganic analogue to the well-known electron-rich organic redox-active tetrathiafulvalene (TTF) (Figure 1). The TTF moiety has been demonstrated to interact with a range of cationic^{8,9} and electron-deficient guests, such as C_{60} ^{10,11}. This preference for electron-deficient guests has recently been utilised in the development of a variety of interlocked molecules.

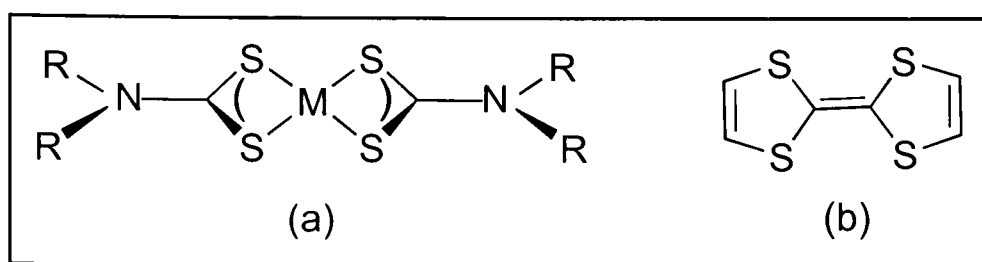


Figure 1 Structural similarity between a) square planar transition metal dithiocarbamate complexes and b) tetrathiafulvalene (TTF)

For example, the tetrathiafulvalene unit is able to form a pseudo-rotaxane structure with a tetracationic paraquat-derivatised cyclophane¹² (Figure 2). Examination of the UV-vis spectrum of the pseudo-rotaxane in either acetonitrile or aqueous solutions reveals a broad band at 850nm, due to a charge-transfer interaction between the electron-rich TTF unit and the electron-deficient bipyridinium groups of the cyclophane. In addition, it was possible to regulate the threading process by the use of redox-control¹³. Addition of a mild oxidant, such as iron(III) perchlorate, results in the oxidation of the TTF unit to a radical cation. This leads to the dethreading of the assembly, due to the electrostatic repulsions within the pseudo-rotaxane complex. However, addition of a stoichiometric amount of the reductant ascorbic acid, results in the reformation of the pseudo-rotaxane, illustrating the reversibility of this process.

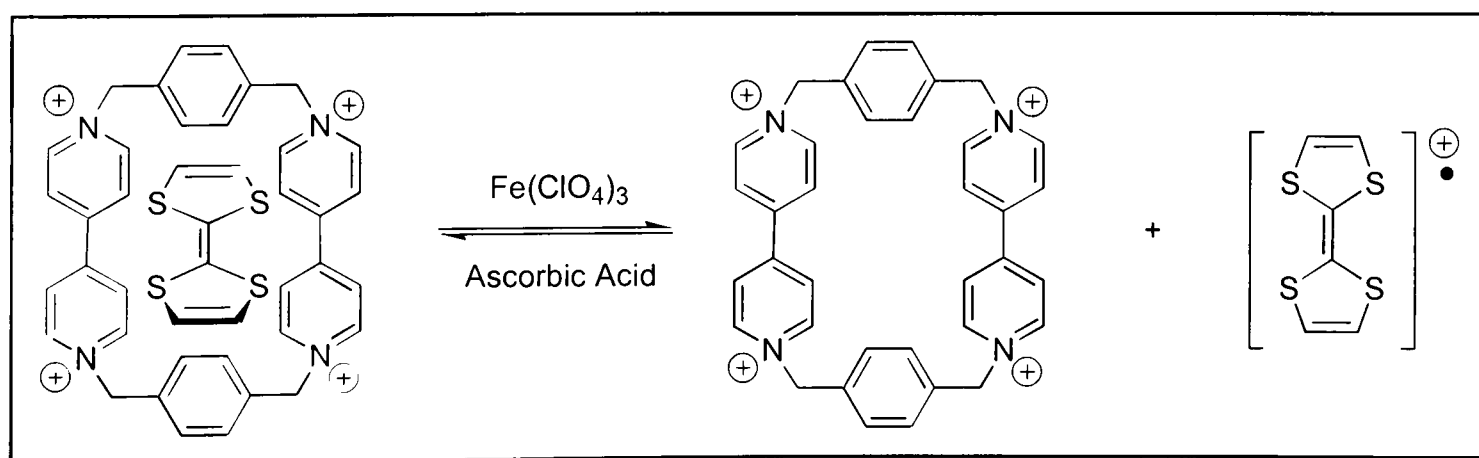


Figure 2 Inclusion of TTF within a tetracationic paraquat-derivatised cyclophane

The subsequent functionalisation of the TTF motif has resulted in its incorporation into a range of more complex interlocked architectures, such as rotaxanes and catenanes¹⁴.

1.2 Aims of the Chapter

The work described in this Chapter outlines the potential use of the dithiocarbamate-based macrocyclic complexes, described in Chapters Two and Four, to generate a range of interlocking systems. It has been shown within these Chapters, that dinuclear transition metal dithiocarbamate-based macrocyclic complexes may be formed with a variety of metal centres and sizes of cavities. Larger macrocyclic complexes may prove attractive for the generation of such interpenetrating architectures. For example, in the X-ray crystal structure of **(18-Cu)**, it is shown that the macrocycle is able to accommodate a dichloromethane molecule within its central cavity. These structures may be capable of including other suitable guest molecules to generate a range of interpenetrating structures.

The copper(II) dithiocarbamate linkage may prove to be particularly attractive for the generation of interlocked structures due to its labile nature¹⁵. This lability has been demonstrated in previous Chapters in allowing both the formation of asymmetrical dithiocarbamate complexes and the inclusion of large guest species into dithiocarbamate cage-like architectures. The dithiocarbamate ligand's ability to stabilise a range of oxidation states and the affinity that its electron-rich complexes exhibit for electron-deficient guests may prove useful in generating interpenetrating structures.

2 Non-Templated Catenane Synthesis

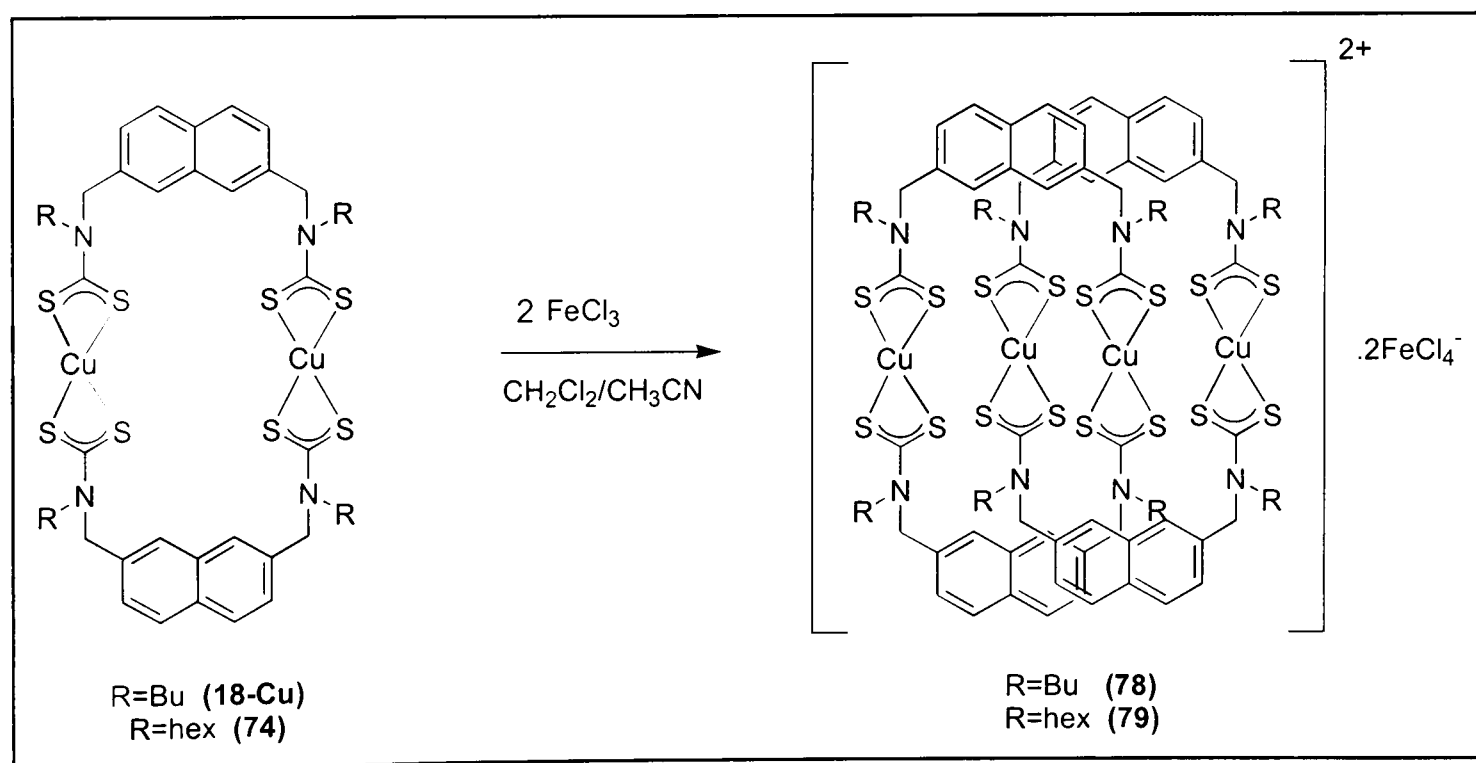
In general, the creation of interpenetrating architectures has relied on an initial templation process. This generates an intermediate species that is subsequently trapped by an irreversible cyclisation or stoppering reaction. This stepwise process can, however, be both time-consuming and inefficient (Chapter One).

More recently, a range of interlocked systems have been generated under thermodynamic control, i.e. they are prepared via reversible reactions such as ring-opening/closing steps. For

example, Fujita and co-workers have demonstrated that the lability of the palladium-pyridyl bond can be used in combination with aromatic hydrophobic bonding between preformed macrocycles in aqueous solution to form [2]catenanes in quantitative yields^{16,17}. The preparations of these structures are highlighted in Chapter One.

2.1 Dithiocarbamate-based [2]Catenanes

It was recently established that the partial oxidation of naphthyl-spaced copper(II) dithiocarbamate-based macrocyclic complexes generated [2]catenanes, in near quantitative yields¹⁸. Here, the partial oxidation of the macrocycles (**18-Cu**) and (**74**) with iron(III) chloride results in the serendipitous formation of an interlocked [2]catenane structure (**78**) and (**79**) respectively (Scheme 1).



Scheme 1 [2]Catenane synthesis from partial oxidation of dinuclear Cu(II) dithiocarbamate-based naphthyl-spaced macrocyclic complexes

The formation of the [2]catenane architecture was confirmed by electrospray mass spectrometry, elemental analysis and X-ray crystallography (Figure 3). Examination of the bond lengths within the X-ray crystal structure of (**78**) provides evidence that a mixed-valence complex is produced, with alternate copper(II) and copper(III) metal centres within the

[2]catenane i.e. Cu(II)Cu(III)Cu(II)Cu(III). It is believed that the formation of the interlocked structure is driven by favourable donor-acceptor axial interactions between dithiocarbamate ligand sulphur donors and metal centres, with each catenane exhibiting short intramolecular copper-sulphur contacts.

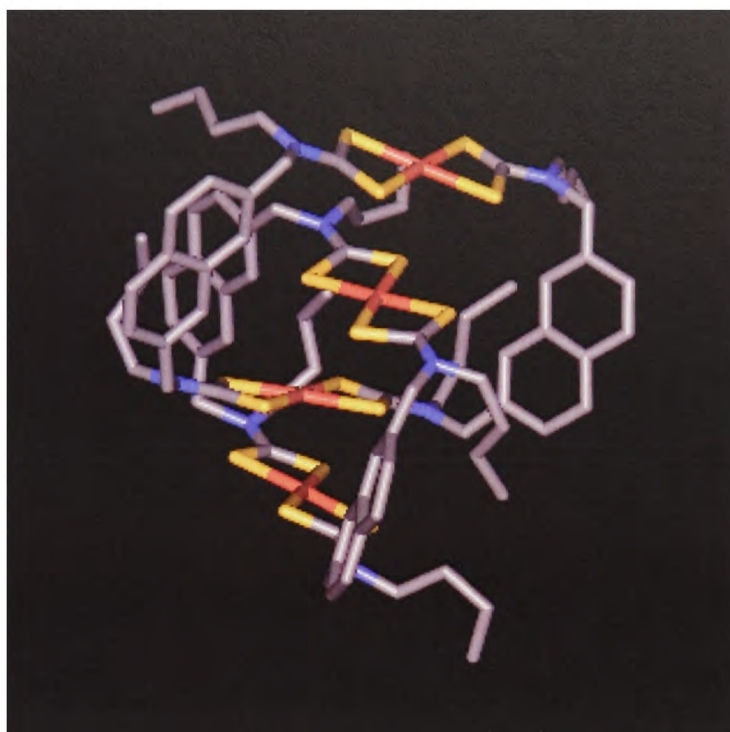
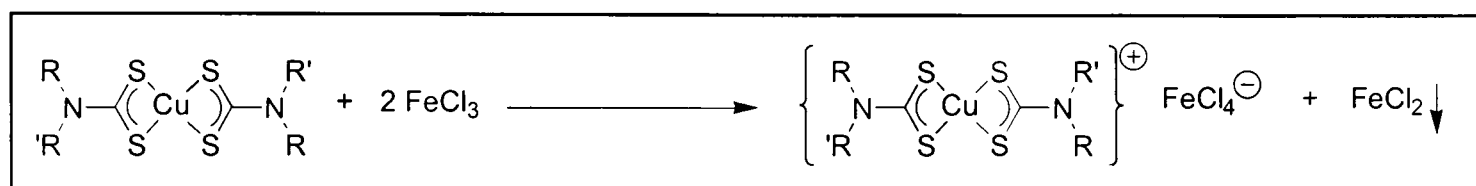


Figure 3 X-ray crystal structure of Cu(II/III) dithiocarbamate naphthyl-spaced [2]catenane (**78**) counteranions and hydrogens omitted for clarity

The electrochemical properties of the [2]catenane differ significantly from those of the macrocyclic reactant. The free macrocyclic complex (**18-Cu**) exhibits a single, broad oxidation wave in its cyclic and square wave voltammograms indicative of overlapping waves corresponding to both copper(II) centres being oxidised at similar potentials. However, the interlocked structure (**78**) displays two distinct waves corresponding to the copper(II/III) redox couple. It is noteworthy that the first catenane oxidation occurs at a significantly less anodic potential ($\Delta E=120\text{mV}$) than that of the macrocycle. This observation suggests that the stabilisation of the copper(III) oxidation state is a direct consequence of the unique topological arrangement of the [2]catenane.

2.2 Catenane Synthesis and Characterisation

The synthesis of the [2]catenane (**78**) was repeated. This was achieved through the addition of two equivalents of iron (III) chloride to the macrocycle (**18-Cu**). The oxidation of one copper(II) dithiocarbamate complex requires the addition of two equivalents of iron(III) chloride¹⁹ (Scheme 2). The addition of two equivalents of the oxidant, therefore, resulted in the oxidation of half of the copper centres within the sample.



Scheme 2 Oxidation of Cu(II) dithiocarbamate complexes with FeCl₃

The resulting interlocked structure was isolated as the iron(III) tetrachloride salt in 91% yield (Scheme 2). The resulting black solid was characterised by electrospray mass spectrometry and elemental analysis. The electrospray mass spectrum of (**78**) revealed weak signals for both the mono- and dicationic states of the catenane (*m/z* 2048.8 and 1024.6 respectively). However, a significantly better resolved spectrum, with greater ion counts, was obtained upon the addition of the oxidant nitrosium tetrafluoroborate prior to the injection of the [2]catenane to the electrospray mass spectrometer²⁰. This results in the *in situ* oxidation of the copper(II) dithiocarbamate-based complex, within the mass spectrometer. The resulting spectrum was able to be recorded using ambient temperatures and low cone voltages, aiding the detection of the desired cationic species (Figure 4).

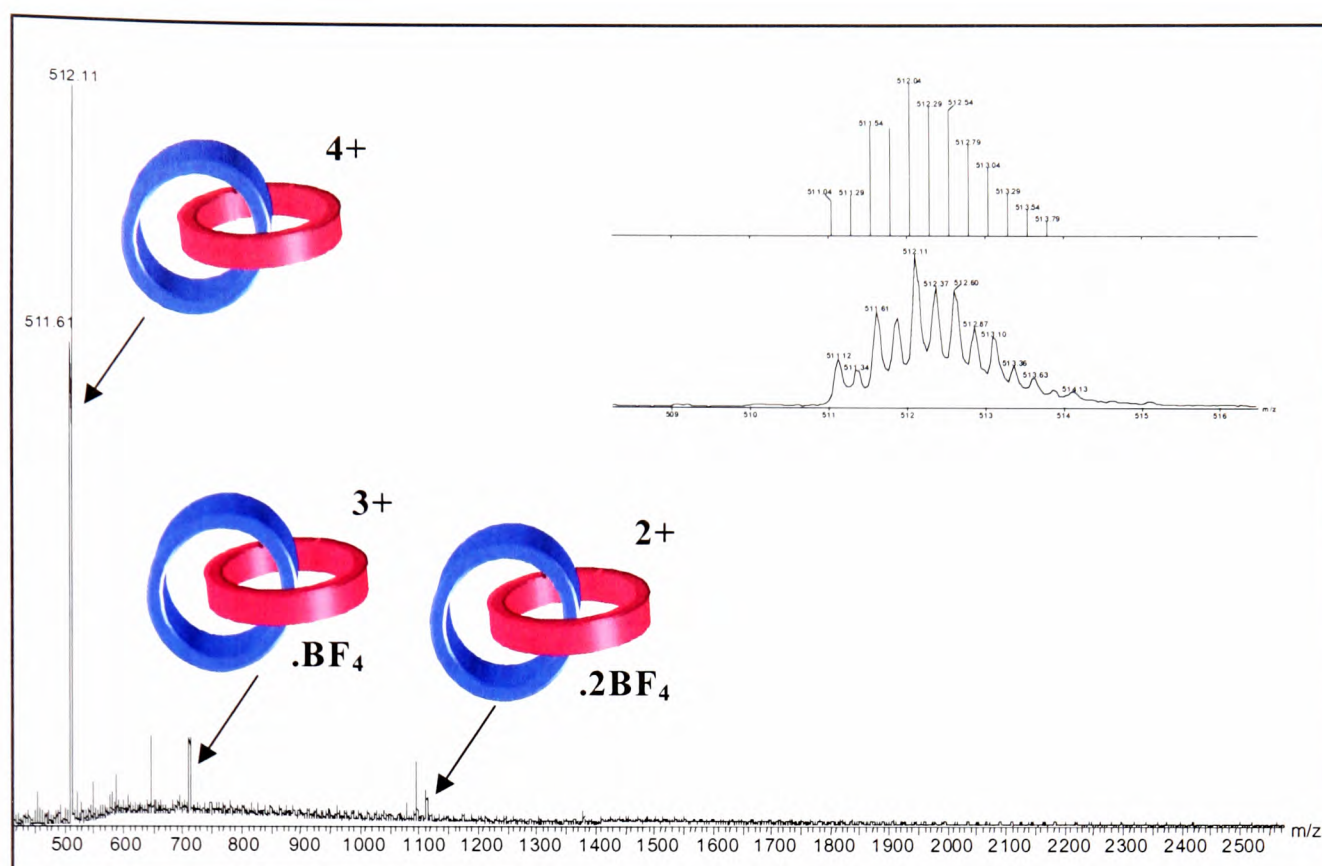


Figure 4 Electrospray mass spectrum of (78) oxidised *in situ* by NOBF_4 Inset $[\text{M}]^{4+}$ peak and (above) predicted isotope model

The spectrum was recorded under extremely mild conditions, which resulted in the generation of a high quality spectrum, with little fragmentation being observed. The main peak of the spectrum (m/z 512.1) shows quarter-integer spacing. This indicates that the peak is due to the previously unseen tetracationic catenane $[\text{78}]^{4+}$ (which is stable only on the time-scale of the experiment) and not the dissociation product, the dicationic macrocycle $[\text{18-Cu}]^{2+}$. This is clearly shown in Figure 4(inset) which also demonstrates the excellent correlation between the predicted and actual isotopic models. Further catenane peaks corresponding to the tri- and dicationic states are also observable at m/z values of 711.8 and 1111.2, respectively. These are due to the formation of adducts with one and two tetrafluoroborate counteranions, respectively.

Interestingly if the oxidant is co-injected with the catenane, the tetra-cationic state is no longer observed and the dicationic macrocyclic dissociation product $[\text{18-Cu}]^{2+}$ is seen. This is a result of the interlocked structure breaking apart over time, probably as a result of the high electrostatic cost of possessing four positive charges in close proximity to one another.

It is also interesting to note that the interlocked [2]catenane structure only forms after the partial oxidation of the copper centres. Experiments were undertaken where solutions of (**18-Cu**) were left open to the atmosphere in the absence of an oxidant, as well as in the presence of four equivalents of the oxidant iron(III) chloride. In the former example, neither of the metal centres were oxidised and in the latter both centres were oxidised to copper(III) centres. The electrospray mass spectra of both of these solutions were recorded after 24 hours.

In both cases, there was no evidence of the formation of the interlocked structure (**78**). In the absence of the oxidant, although the copper(II) dithiocarbamate bonds are labile and can interpenetrate, there is no driving force for this to occur. Similarly, when both of the metal centres are oxidised, the formation of the interpenetrated structure is no longer favoured, due to the resultant electrostatic repulsions in bringing four positively charged centres together into close proximity. This illustrates the importance of the partial oxidation of the copper centres to form the interlocked architecture.

3 Mixed-Ligand Catenane Syntheses

Since it has been established that the partial oxidation of naphthyl spaced copper(II) dithiocarbamate macrocyclic complexes (**18-Cu**) and (**74**) yield interlocked structures, investigations into whether similar copper(II) dithiocarbamate-based macrocyclic complexes (synthesised in the work detailed in Chapter Two) are also able to form analogous catenane architectures were pursued. This was initially undertaken via the partial oxidation with iron(III) chloride of the *m*-xylyl spaced and 3,3'-biphenyl spaced macrocycles (**10-Cu**) and (**13-Cu**). Unfortunately, analysis of the resultant solutions by electrospray mass spectrometry only revealed the presence of the dinuclear macrocyclic complexes and not any interlocked species. This is, perhaps, not surprising in the case of the *m*-xylyl spaced complex (**10-Cu**), where the molecular cavity is too small to accommodate a threaded molecular species.

However, in the case of the larger 3,3'-biphenyl spaced structure (**13-Cu**), where the cavity size is of comparable dimensions to that of the naphthyl spaced complex (**18-Cu**) it is perhaps more surprising.

Due to the structural similarity between the 3,3'-biphenyl and naphthyl spaced copper(II) dithiocarbamate-based macrocycles (**13-Cu**) and (**18-Cu**), it was examined as to whether it is possible to generate a mixed ligand catenane, i.e. where one ring of (**13-Cu**) interlocks one of (**18-Cu**) (Figure 5).

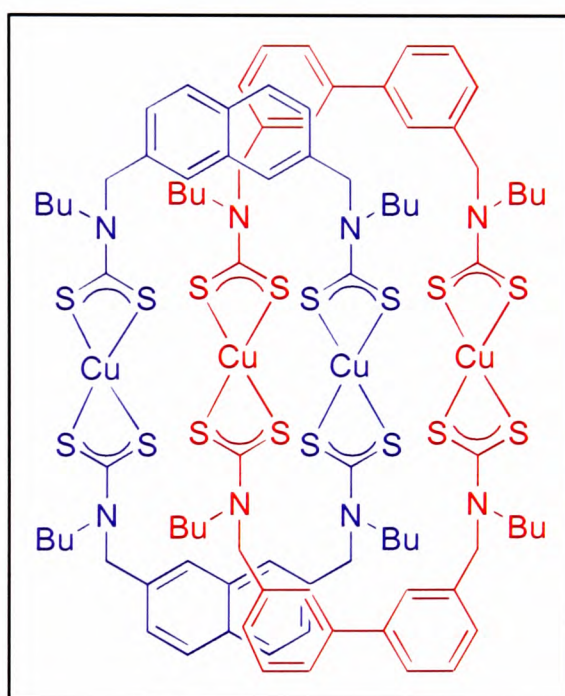


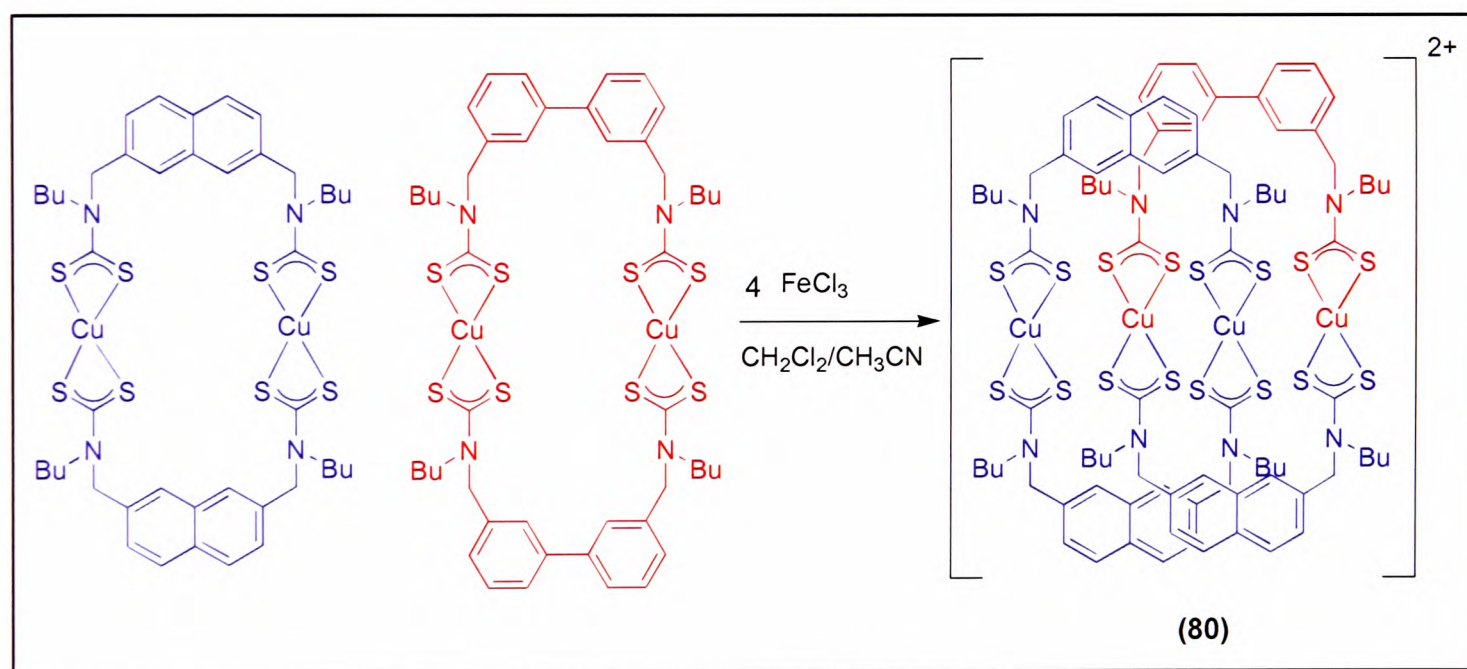
Figure 5 Mixed-ligand [2]catenane

In order to synthesise the mixed-ligand system an equimolar dichloromethane solution of the two copper(II)-based macrocycles (**13-Cu**) and (**18-Cu**) was prepared. Sufficient iron(III) chloride in order to oxidise half the metal centres (i.e. four equivalents), was dissolved in the minimum amount of acetonitrile and added to solution. This was stirred at room temperature for 18 hours and analysed by electrospray mass spectrometry. Prior to injection of the sample a large excess of the oxidant nitrosium tetrafluoroborate was injected into the spectrometer, in order to oxidise the copper(II) centres within the sample *in situ*, to aid identification of the products.

Analysis of the resulting spectrum failed to reveal the presence of the desired product, with

significant peaks corresponding to the previously synthesised [2]catenane (**78**), again highlighting the high thermodynamic stability of this structure. However, the electrospray mass spectrum did also show the presence of another interlocked structure, a mixed-ligand product (**80**) (Scheme 3).

The formation of this mixed-ligand product is clearly shown in its electrospray mass spectrum, which shows the doubly-charged and (less well resolved) triply-charged states of the product. The peaks, which exhibit a good correlation with predicted isotope patterns, display half- and third-integer splittings, respectively. This enables their characterisation as the di- and tricationic peaks of the interlocked structure (Figures 6 and 7).



Scheme 3 Synthesis of mixed-ligand [2]catenane (**80**)

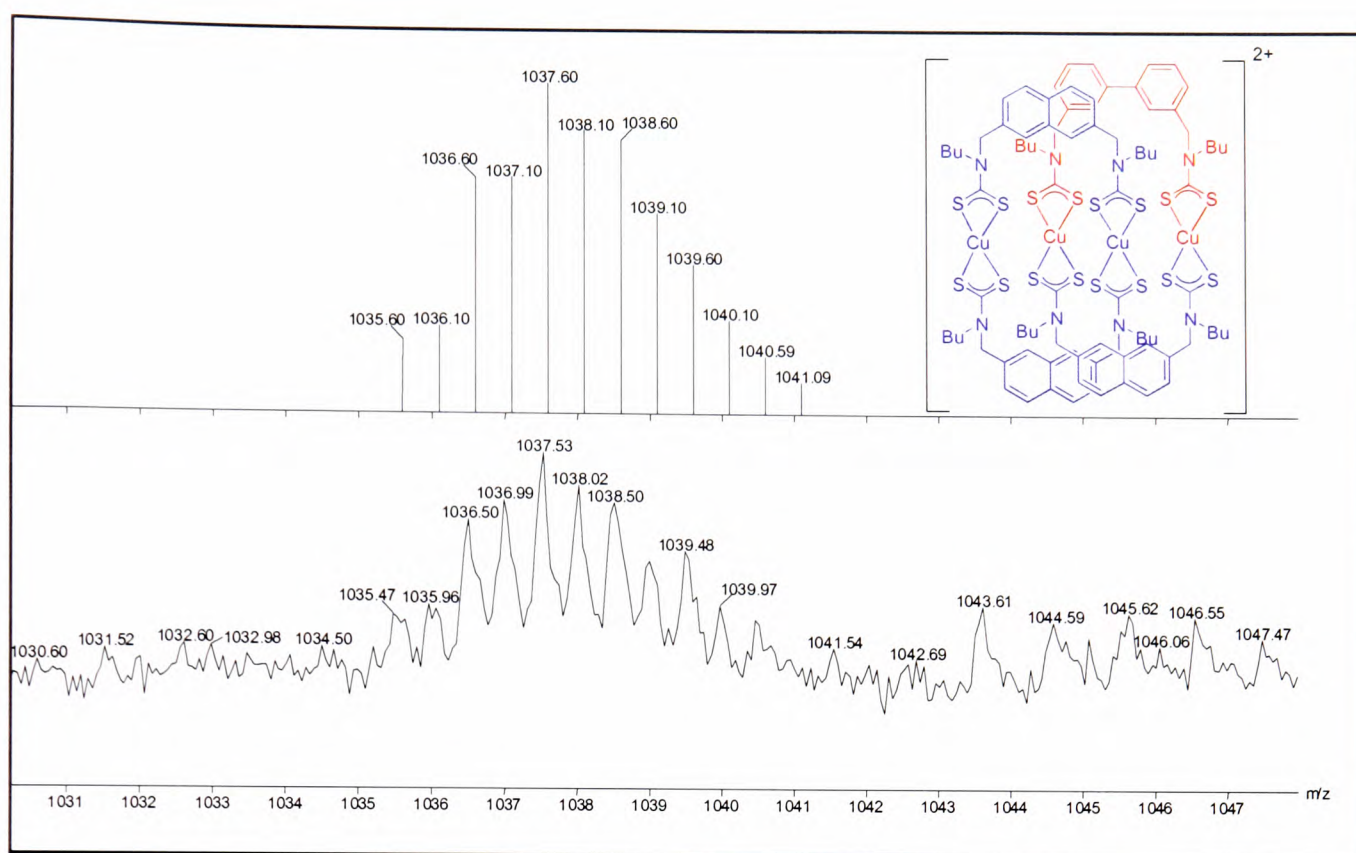


Figure 6 Electrospray mass spectrum and predicted isotope model (upper) of $[80]^{2+}$ [2]catenane

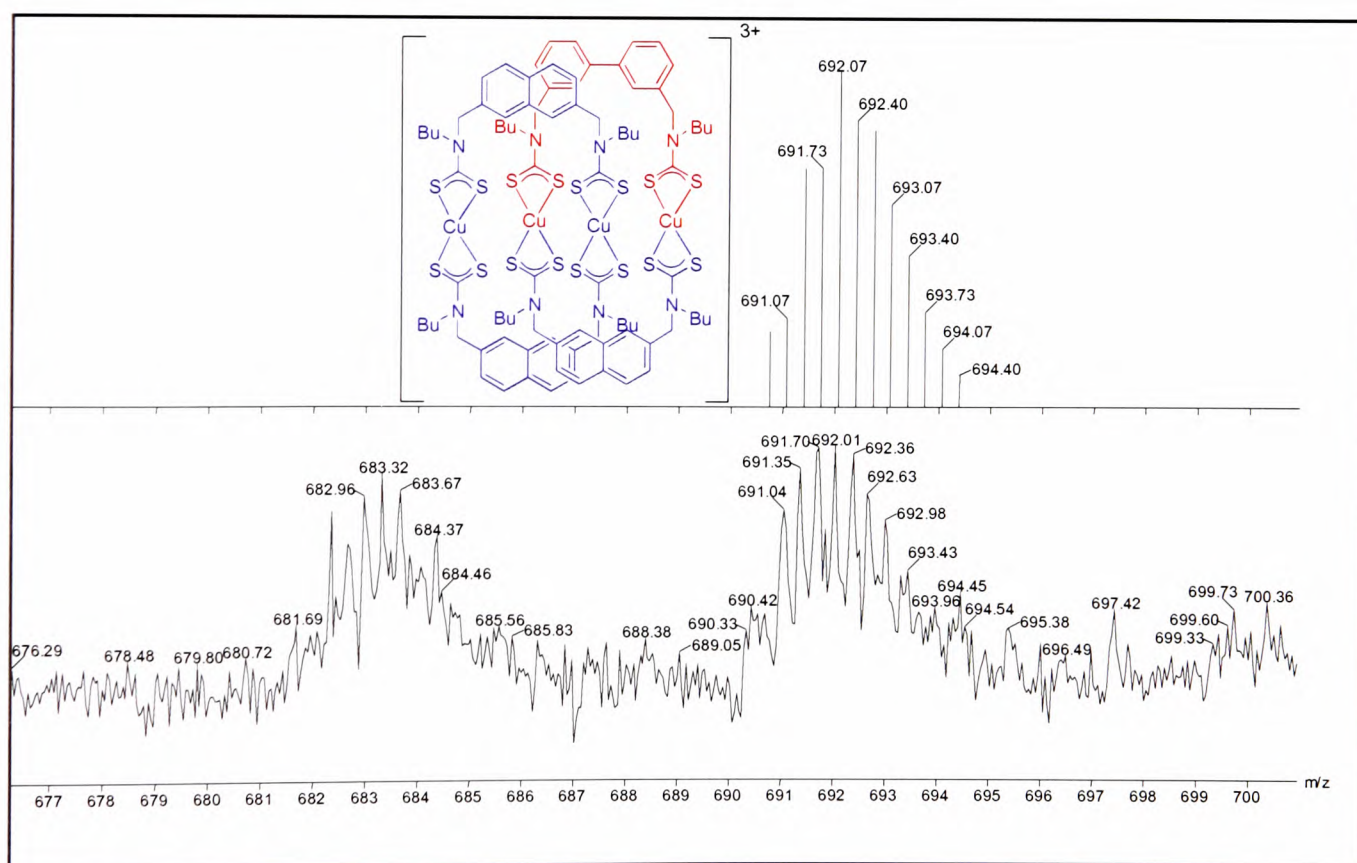


Figure 7 Electrospray mass spectrum and predicted isotope model (above) of $[80]^{3+}$ [2]catenane (right hand peak) and $[78]^{3+}$ [2]catenane (left hand peak)

This result illustrates that macrocycles (13-Cu) and (18-Cu) are labile and are able to exchange ligands to form an unsymmetrical macrocycle (as previously seen in copper(II) dithiocarbamate-based macrocycles in Chapter Two). The formation of a mixed-ligand

macrocyclic complex is possible since the naphthyl and 3,3'-biphenyl spacers are similar in size, hence the resultant macrocyclic complex does not have a significant amount of strain within it. The asymmetric macrocycle on oxidation is then able to entwine with a molecule of **(18-Cu)** to form a [2]catenane.

This illustrates the vital issue of the size of the macrocyclic cavity in catenane formation. In the case of the naphthyl spaced system, **(18-Cu)**, the two copper(II) dithiocarbamate moieties are the ideal distance apart to accommodate an electron-deficient guest (an oxidised copper(III) centre) within the macrocyclic cavity. This guest is then stabilised via favourable axial charge transfer interactions with the electron-rich sulphur donors.

The copper-copper bond length in the X-ray crystal structure of **(18-Cu)** is 7.62 Å; whilst the analogous distance in **(13-Cu)** is estimated, by molecular modelling, to be 8.43 Å (Chapter Two). It is therefore likely that in the larger macrocycle, **(13-Cu)**, the copper(II) centres are too far apart to both interact with an interpenetrating electron-deficient guest, hence no catenane formation is observed.

Where there is a mixture of the two complexes **(13-Cu)** and **(18-Cu)**, ligand exchange reactions are rapidly occurring. This is due to the lability of the copper(II) dithiocarbamate bonds and the structural similarity of the two structures enabling the formation of the asymmetric macrocycle (presumably with an intermediate copper-copper distance). In this case, therefore, the three potential dinuclear macrocycles are in a thermodynamic equilibrium between each other. Since the oxidant iron(III) chloride is also present within the solution, this enables the macrocycles to subsequently catenate. A combinatorial library^{21,22} between the three potential macrocycles and six possible [2]catenane products is therefore set up (Figure 8). Of these six possible tetranuclear products only two **(74)** and **(80)** were observed, suggesting that only those two products have the appropriate cavity sizes to stabilise the formation of the interlocked structures.

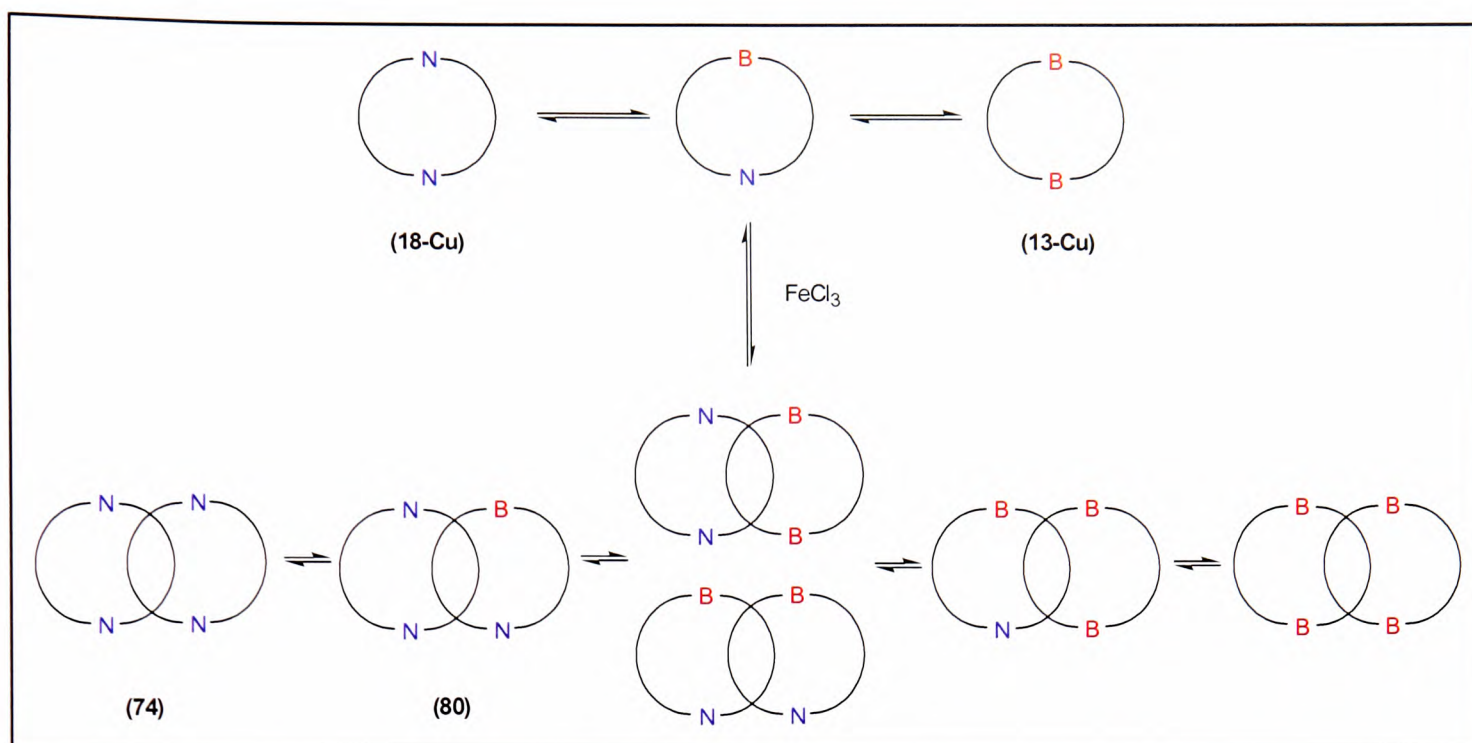


Figure 8 Combinatorial library of macrocyclic and [2]catenane products (Key: N: naphthyl spacer, B: 3,3' biphenyl spacer within dinuclear Cu(II) dithiocarbamate complexes)

4 Mixed-Metal Interpenetrating Structures

It has been established that the formation of the [2]catenane (78) is stabilised by charge transfer interactions between interpenetrating copper(II) and copper(III) dithiocarbamate units. Favourable axial interactions between the electron-deficient metal centres and optimally spaced sulphur donors, result in the high thermodynamic stability of the structure.

Gold(III) dithiocarbamate complexes have been shown to adopt the same square planar geometry as both copper(II) and copper(III) dithiocarbamate systems, whilst also possessing a permanent positive charge (Chapter Four). An investigation as to whether these charged analogues could be used to generate interpenetrating systems was therefore undertaken. Such systems should spontaneously self-assemble into the thermodynamic, interlocked product, thus avoiding the necessity of using an oxidant to drive the reaction.

It has previously been demonstrated by Gal *et. al.* that gold(III) dithiocarbamate complexes co-crystallise with copper(II) and copper(III) dithiocarbamate complexes²³. This structure (Figure 9) shows stacks alternate copper(II) and copper(III)/gold(III) dithiocarbamate

complexes. These stacks are stabilised by the formation of favourable axial metal-sulphur interactions between the electron-rich sulphur donors and the electron-deficient metal(III) centres. It is these favourable interactions that may be utilised to generate mixed-metal interpenetrating structures.

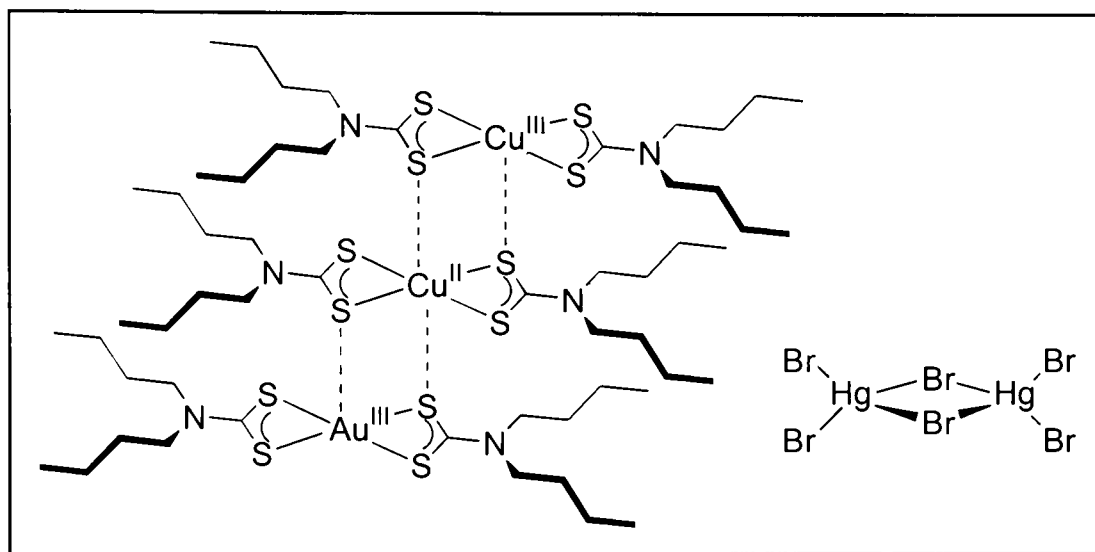
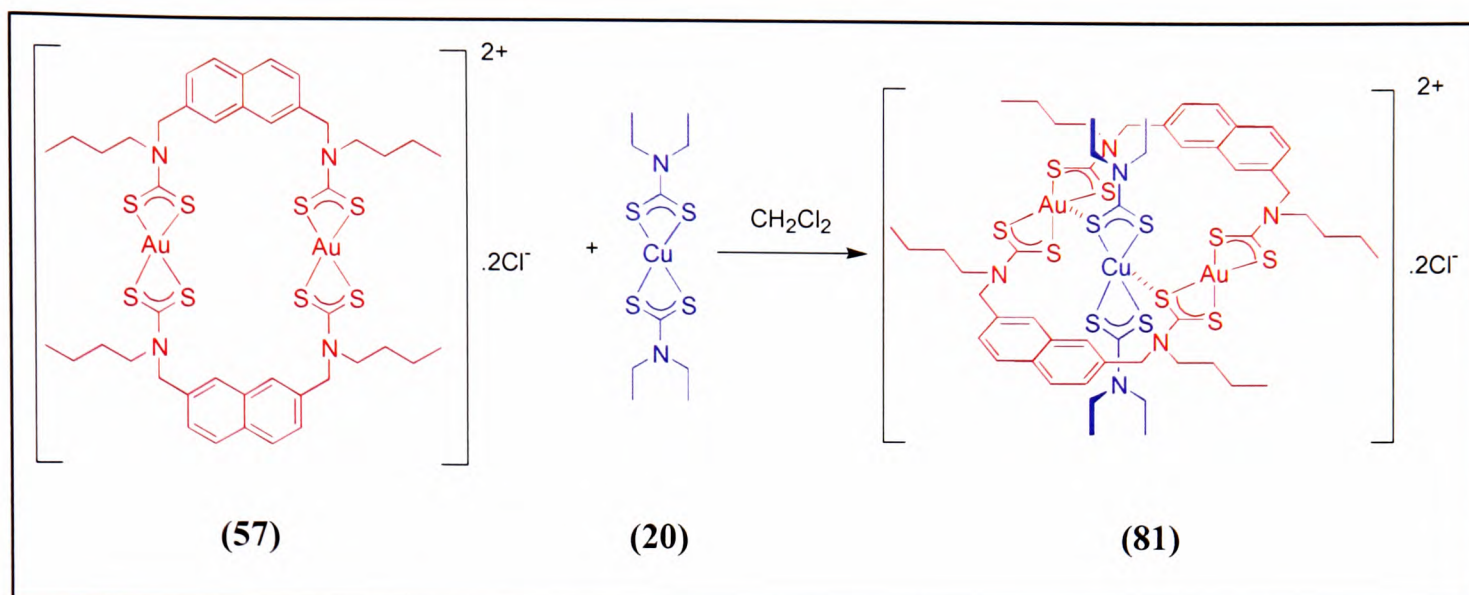


Figure 9 X-ray crystal structure of $[(\text{Cu}_2\text{Au})(\text{Bu}_2\text{dtc})_6][\text{Hg}_2\text{Br}_6]$

4.1 Pseudo-Rotaxane Formation

It was proposed that the interaction between the electron-deficient gold(III) dithiocarbamate unit and the electron-rich copper(II) dithiocarbamate group may be used to generate a pseudo-rotaxane. This was initially attempted using copper(II) bis- $(N,N'$ -diethyldithiocarbamate) (**20**) as a thread and the dicationic gold(III) naphthyl spaced host (**57**) as a macrocycle. It was hoped that the electron-deficient guest would thread through the electron-rich host, as illustrated in Scheme 4, to form the desired pseudo-rotaxane (**81**).



Scheme 4 Synthesis of mixed-metal pseudo-rotaxane

This interaction was initially investigated with electrospray mass spectrometry. A solution of (57) with five equivalents of (20) was prepared (in 99:1 acetonitrile/dichloromethane) and injected into the mass spectrometer. The resulting spectra are displayed in Figures 10 and 11.

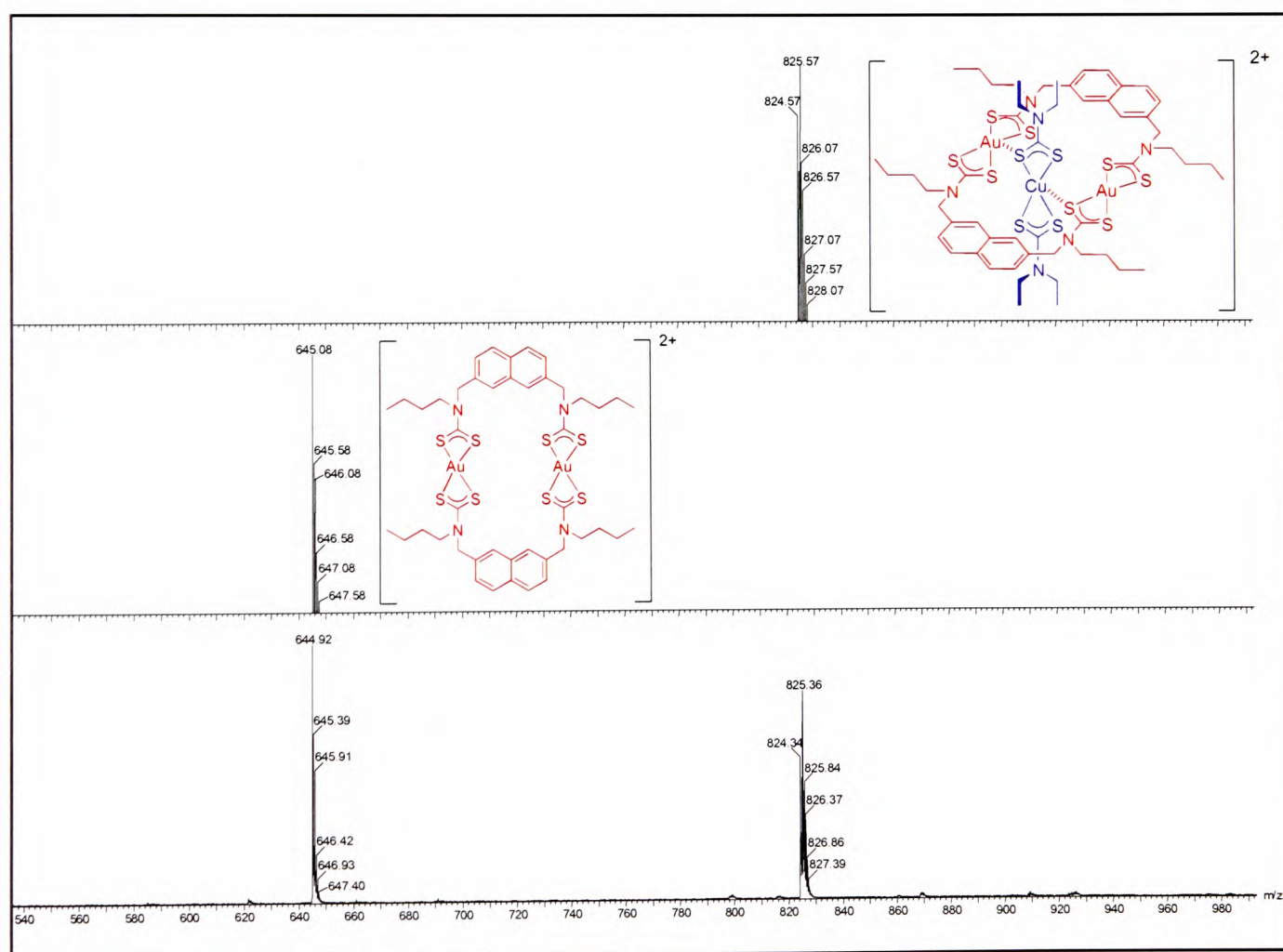


Figure 10 Electrospray mass spectrum of (81), (57) in the presence of 5.0 equivalents of (20) bottom: actual spectrum, above: predicted isotope models for (middle) (57) and (upper) (81)

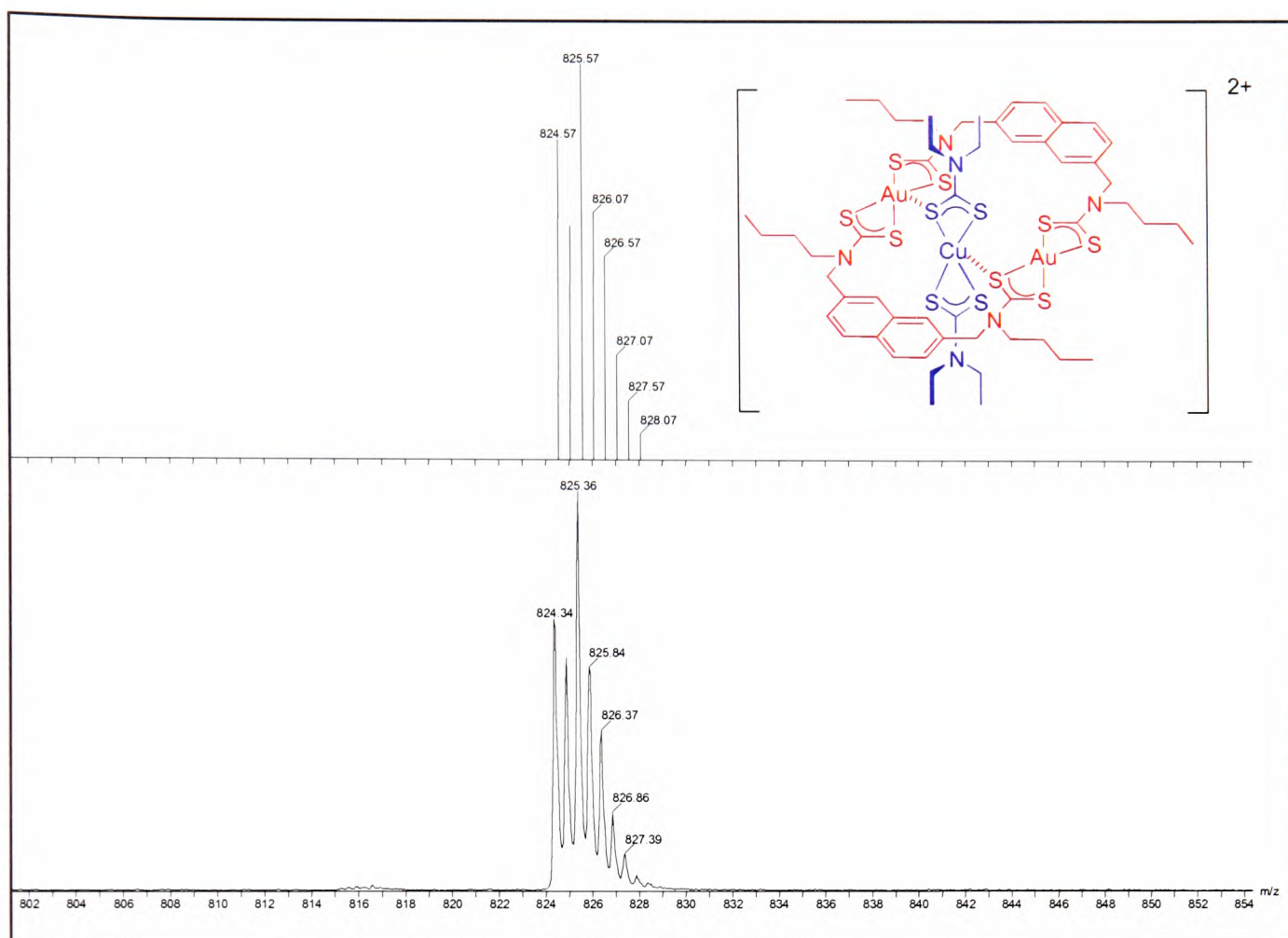


Figure 11 Electrospray mass spectrum of mixed-metal pseudo rotaxane (81) (upper) predicted isotope model for the complex

As can be seen, the spectrum shows two large peaks corresponding to the free doubly-charged gold(III) macrocycle (57) and for the association between the macrocycle and the copper(II) dithiocarbamate thread (81). Both peaks give excellent matches with predicted isotopic models and the relatively high intensity of the second peak suggests a strong interaction between the two components.

This interaction was further studied by electrochemistry. The cyclic and square wave voltammograms of the reversible copper(II/III) oxidation wave of (20) was recorded in a 1:1 acetonitrile/dichloromethane solution containing 0.1M tetra-*n*-butylammonium tetrafluoroborate as a background electrolyte (Figures 12 and 13).

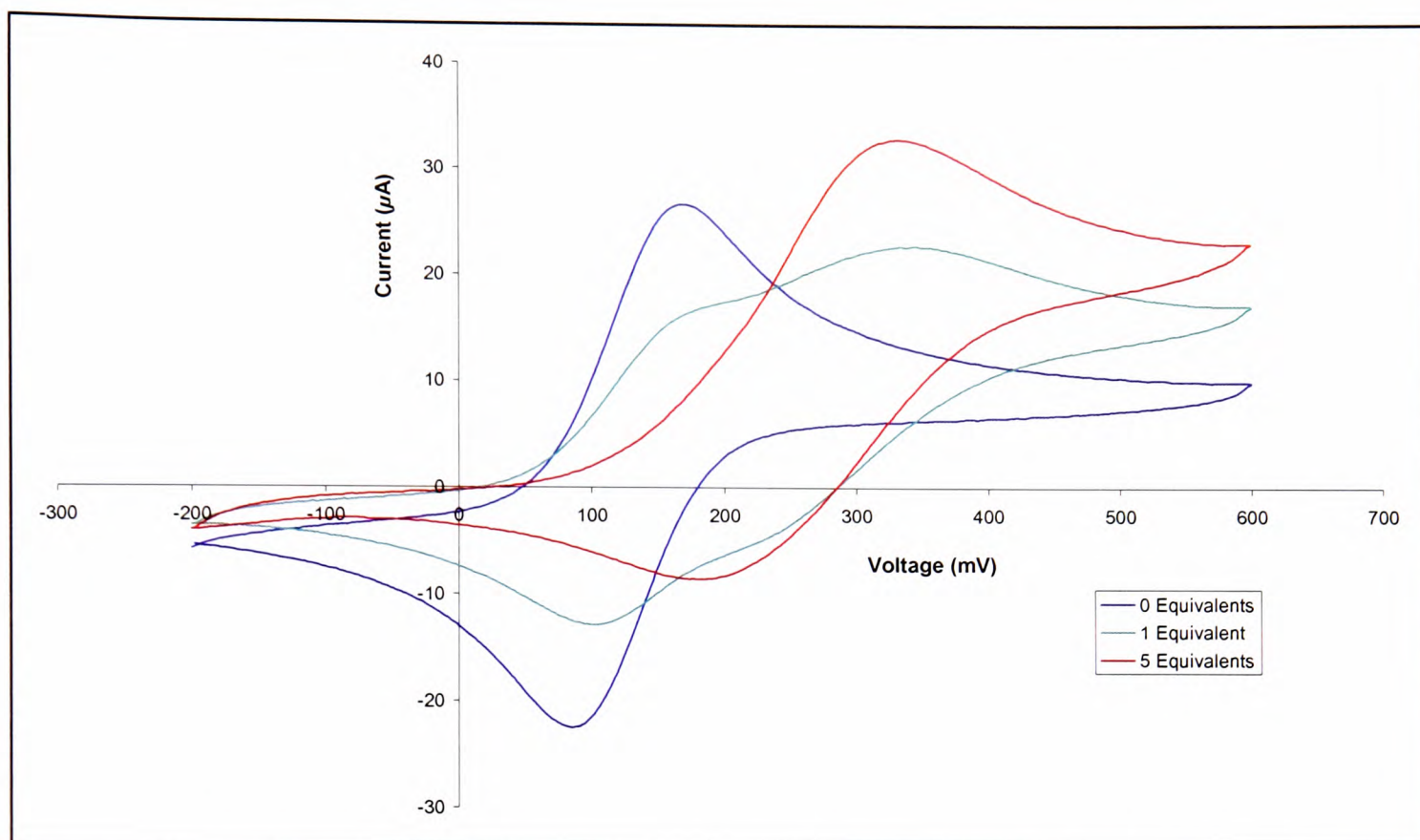


Figure 12 Cyclic voltammogram of (20) upon the addition of various equivalents of (57) in forming the pseudo-rotaxane (81) (1:1 $\text{CH}_2\text{Cl}_2/\text{MeCN}$ containing 0.1M TBABF_4) Scan rate 100 mVs^{-1} {Ag/AgNO₃ reference electrode, glassy carbon working electrode}

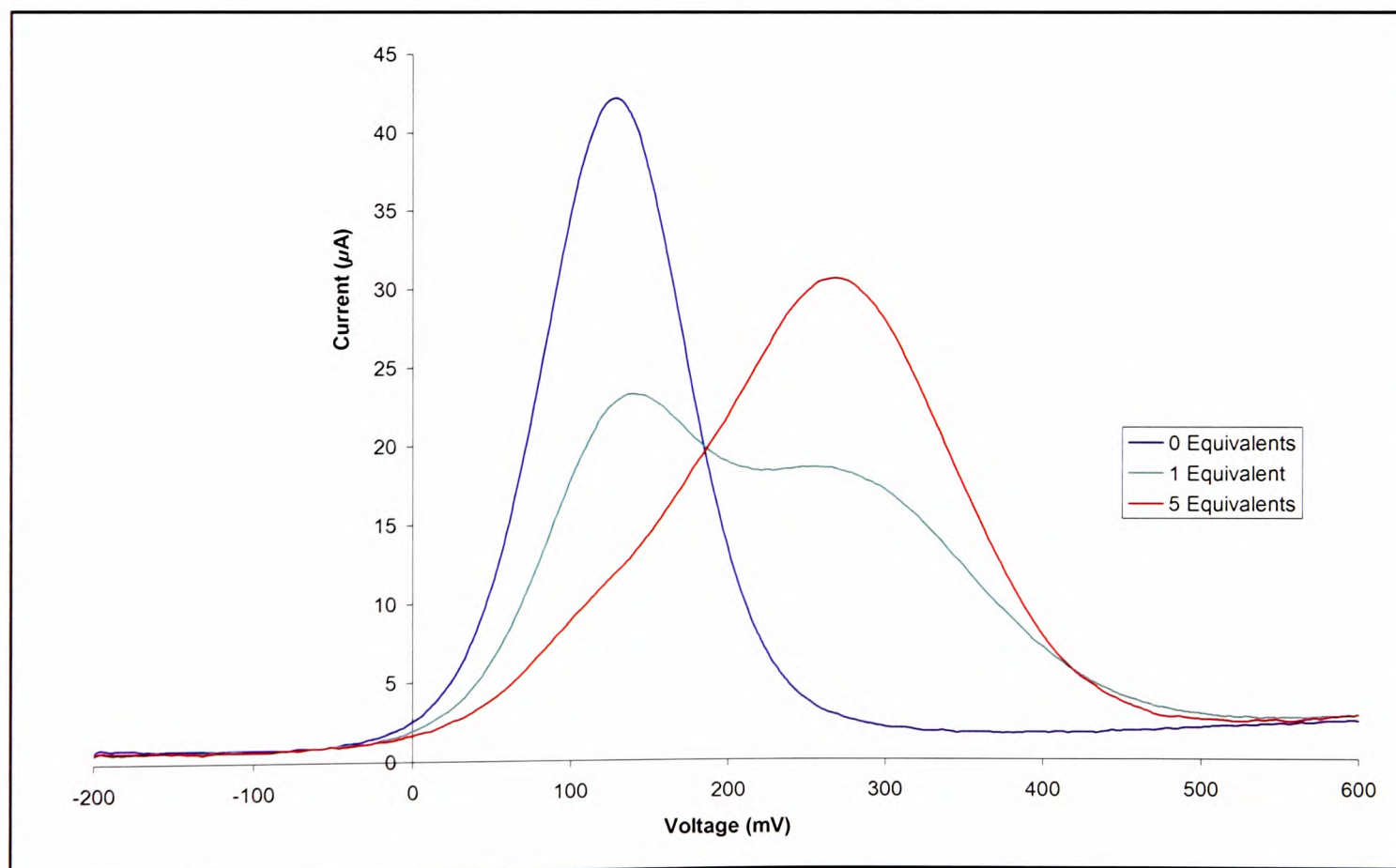


Figure 13 Square wave voltammogram of (20) upon the addition of various equivalents of (57) in forming the pseudo-rotaxane (81) (1:1 $\text{CH}_2\text{Cl}_2/\text{MeCN}$ containing 0.1M TBABF_4) Frequency = 5 Hz, {Ag/AgNO₃ reference electrode, glassy carbon working electrode}

In the absence of (57) a single wave is observed in the voltammograms of (20) corresponding to the copper(II/III) oxidation process. However, addition of the electron-deficient macrocycle results in the evolution of a new wave at more positive potential. After the addition of five equivalents of (57) the first peak is no longer visible within the voltammogram. The electrochemical data for the copper(II) dithiocarbamate thread in the presence and absence of five equivalents of (57) is displayed in Table 1.

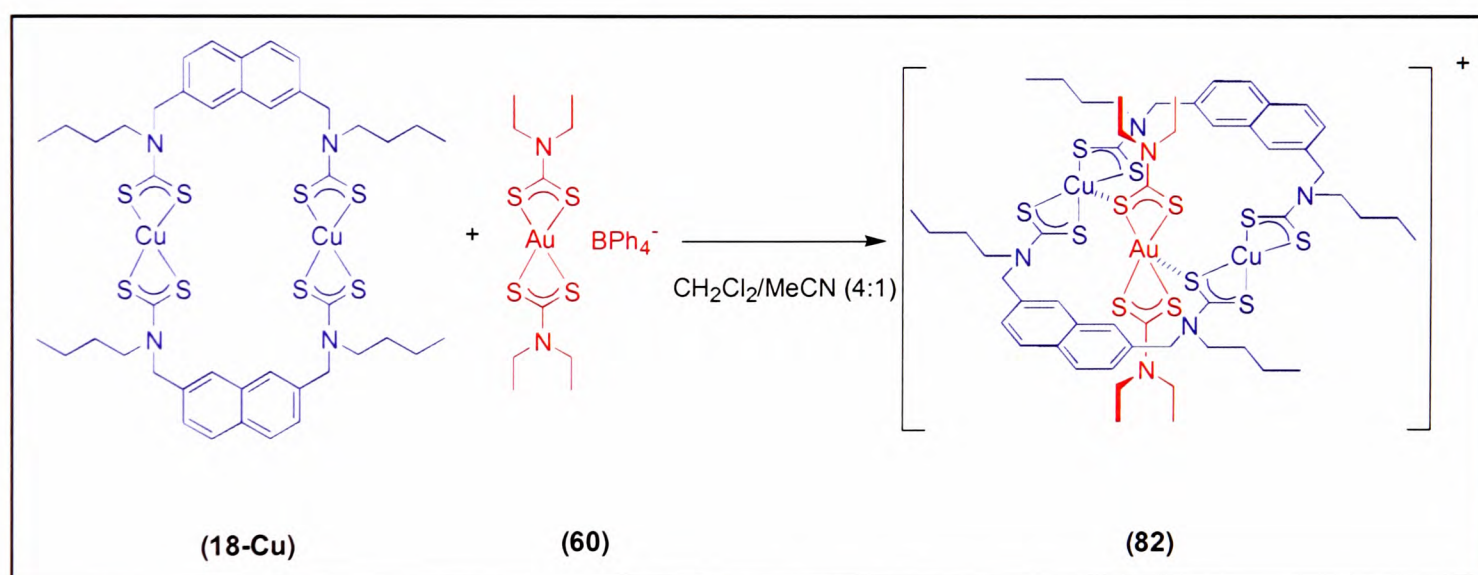
	$E_{1/2}$ (V)	E_{pa} (V)	E_{pc} (V)
(20)	0.13	0.17	0.09
(20) plus 5 equiv of (57)	0.27	0.33	0.18

Table 1 Electrochemical data for the copper(II) thread (20) in the presence and absence of (57) in forming the pseudo-rotaxane (81) in CH₂Cl₂/MeCN (1:1) with 0.1M TBABF₄ as the supporting electrolyte, using glassy carbon as the working electrode and Ag/AgNO₃ reference electrode, sample 1x10⁻³M. Scan rate 100 mVs⁻¹, frequency 5 Hz, T=293K (Errors ±5mV)

The appearance in the voltammograms of a second wave is consistent with the electron-rich copper(II) dithiocarbamate thread interacting with the electron-deficient gold(III)-based macrocycle. The large anodic shift observed (140mV) in the second wave is a result of the copper(II) centre being harder to oxidise, a fact suggesting the thread is bound within the electron-deficient centre of the positively charged dinuclear gold(III) macrocycle. The observation that only a 1:1 complex, and not any higher oligomers, was observed in the electrospray mass spectrum also suggests that the electrochemical shift is a result of the formation of the desired pseudo-rotaxane (81). Unfortunately, attempts to crystallise the complex have to date proved unsuccessful. In addition, UV-vis titration experiments surprisingly failed to provide evidence for the formation of the desired pseudo-rotaxane (81).

Addition of the electron-deficient (**57**) to a dichloromethane solution of (**20**) did not result in any significant perturbations of the electronic spectra. Despite this, it is clear that there is a significant interaction between the electron-rich copper(II) dithiocarbamate thread and the electron-deficient macrocycle, which following the precedent of the [2]catenanes (**78**) and (**79**), is likely to be a result of the copper(II) dithiocarbamate thread forming favourable axial sulphur-metal interactions with the host.

The generation of pseudo-rotaxanes by the addition of electron-deficient guests to electron-rich dithiocarbamate macrocyclic receptors has also been undertaken²⁴. The addition of the electron-deficient gold(III) bis-(*N,N'*-diethyldithiocarbamate) tetraphenylborate (**60**) to the electron-rich copper(II) macrocyclic complex (**18-Cu**) was examined (Scheme 5).



Scheme 5 Formation of pseudo-rotaxane (82**)**

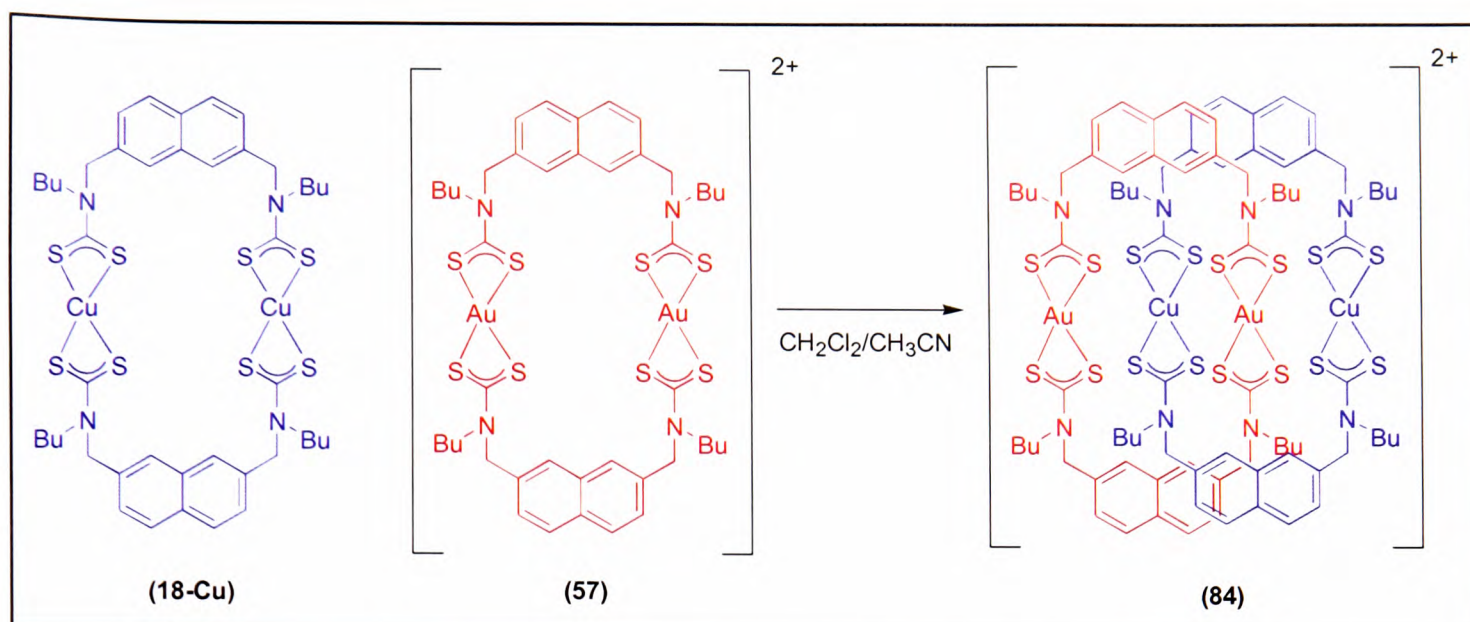
Analysis of the solution via electrospray mass spectrometry revealed the formation of the desired pseudo-rotaxane (**82**). In addition, examination of the cyclic and square wave voltammograms of (**18-Cu**) in the presence of five equivalents of the electron-deficient gold(III) dithiocarbamate thread (**60**) revealed a significant 30mV anodic shift in the copper(II/III) redox couple of (**18-Cu**). This means that it is harder to oxidise the copper(II) centre in the presence of (**60**). This suggests the gold(III) dithiocarbamate unit is being bound within the cavity of the electron-rich dinuclear copper(II) dithiocarbamate macrocyclic complex. This observation is consistent with the formation of a pseudo-rotaxane architecture

via the formation of favourable axial metal-sulphur interactions between the components.

4.2 Mixed-Metal Catenanes

Encouragingly, the interaction between electron-deficient guests and electron-rich copper(II) dithiocarbamate complexes have suggested the formation of pseudo-rotaxane structures. In light of these results attempts were made to extend this methodology to generate a mixed-metal catenane. Although mixed-metal catenanes have recently been generated²⁵, this has been through a stepwise approach, not in the one pot method used here. In addition, gold(I) has also been used on numerous occasions to generate interlocked structures; however, this usually relies on the use of gold(I) and the strong templating aurophilic interactions that they produce²⁶.

The strategy employed to generate a mixed-metal catenane was to combine one equivalent of the gold(III) dithiocarbamate-based complex **(57)** with the analogous copper(II) dithiocarbamate-based macrocycle **(18-Cu)** in an acetonitrile/dichloromethane (1:1) solution (Scheme 5). It was hoped that the electron-deficient gold(III) centres would interpenetrate the electron-rich copper(II)-based macrocycle, through the lability of the copper-dithiocarbamate bonds. The naphthyl spacers of the two macrocycles should hold the metal centres at the optimal distance in order to generate analogues of the [2]catenanes **(78)** and **(79)**. However, in the case of the mixed metal-catenanes, the presence of an oxidant should not be required in order for the interlocked heteropolymetallic [2]catenane complex to form.



Scheme 6 Synthesis of mixed-metal catenane (84)

A 1:1 mixture of **(18-Cu)** and **(57)** was prepared and the golden solution allowed to stir at room temperature for ten minutes. After this time, a sample was taken and analysed by electrospray mass spectrometry. The resulting spectrum is displayed in Figure 14.

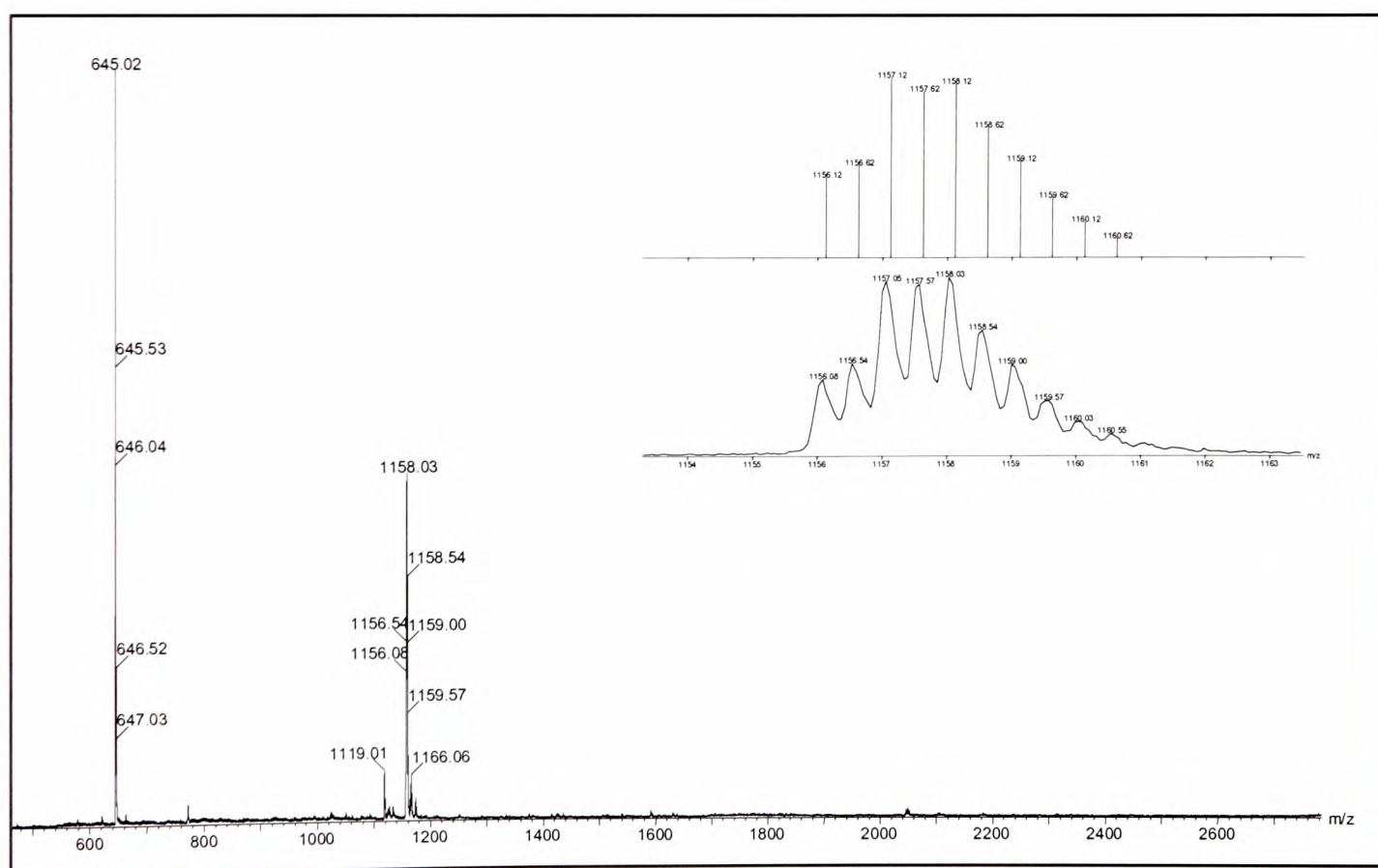


Figure 14 Electrospray mass spectrum of **(84)** inset: peak at m/z 1158 (upper) predicted isotope pattern

The spectrum clearly shows a peak at m/z 1158.0 which corresponds to the desired interlocked mixed-metal [2]catenane structure. Examination of this peak reveals an excellent

correlation between the predicted and the actual isotope models of the desired dicationic pseudo-rotaxane structure (Figure 14(inset)).

The interaction between the two complexes was further studied by electrochemistry. The copper(II/III) oxidation couple of **(18-Cu)** was observed in the absence of the gold(III) dithiocarbamate macrocycle **(57)** in a 1:1 dichloromethane/acetonitrile solution. One equivalent of the electron-deficient macrocycle was then added to the solution and the cyclic and square wave voltammograms were re-recorded after ten minutes. The resultant voltammograms are shown in Figures 15 and 16 and the electrochemical data is displayed in Table 2.

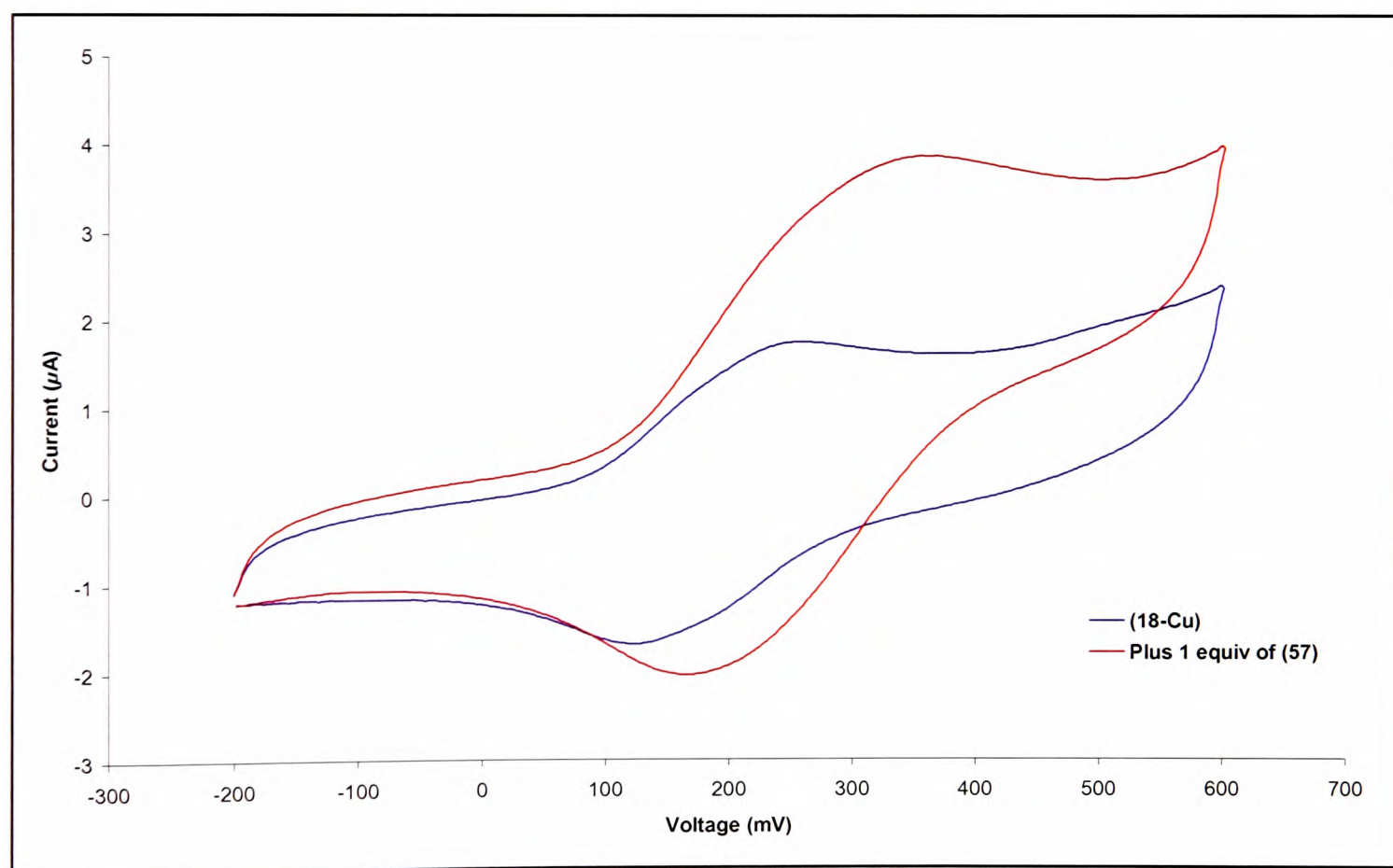


Figure 15 Cyclic voltammogram for the Cu(II) dithiocarbamate-based macrocycle **(18-Cu)** in the presence and absence of **(57)** in $\text{CH}_2\text{Cl}_2/\text{MeCN}$ (1:1) with 0.1M TBABF₄ as the supporting electrolyte, sample $1 \times 10^{-3}\text{M}$. Scan rate 100 mVs^{-1} , $T = 293\text{K}$ { : Ag/AgNO₃ reference electrodes, glassy carbon working electrode }

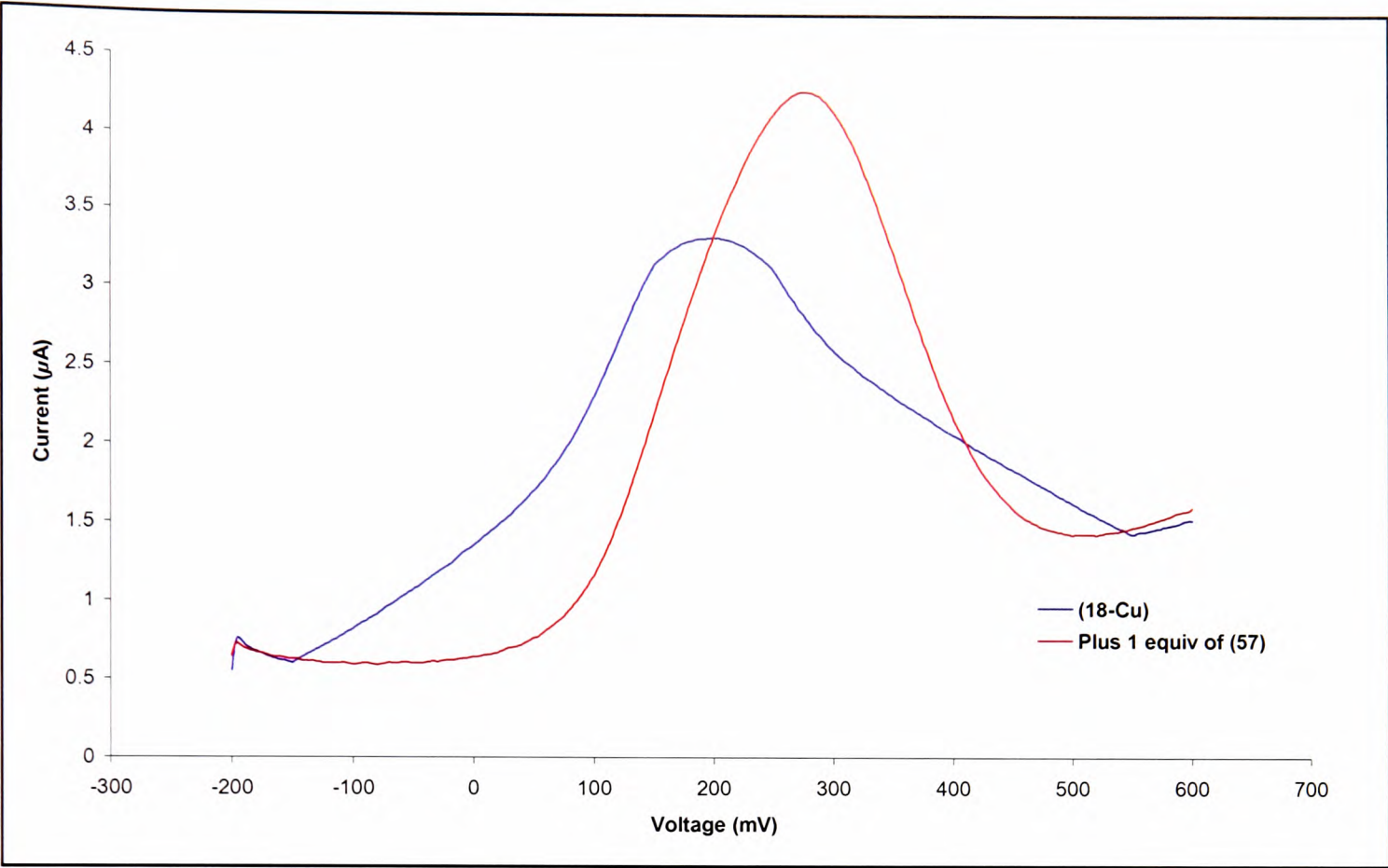


Figure 16 Square wave voltammogram for the Cu(II) dithiocarbamate-based macrocycle (18-Cu) in the presence and absence of (57) in CH₂Cl₂/MeCN (1:1) with 0.1M TBABF₄ as the supporting electrolyte, sample 1x10⁻³M. Frequency = 5 Hz, T = 293K {Ag/AgNO₃ reference electrode, glassy carbon working electrode}

	E _{1/2} (V)	E _{pa} (V)	E _{pc} (V)
(18-Cu)	0.20	0.25	0.11
(18-Cu) plus 1 equiv of (57)	0.28	0.35	0.16

Table 2 Electrochemical data for Cu(II) macrocycle (18-Cu) in the presence and absence of (57) in CH₂Cl₂/MeCN (1:1) with 0.1M TBABF₄ as the supporting electrolyte, sample 1x10⁻³M. Scan rate 100 mVs⁻¹, frequency 5 Hz, T=293K {Ag/AgNO₃ reference electrode, glassy carbon working electrode} (Errors ±5mv)

The addition of one equivalent of the electron-deficient gold(III) dithiocarbamate-based macrocycle (57) results in a significant anodic shift of 80mV in the copper(II/III) redox couple of (18-Cu). This means that it is harder to oxidise the copper(II) centre in the presence of (57). This is consistent with the copper(II) dithiocarbamate unit being held adjacent to the electron-deficient gold(III) centres, such as in the interlocked [2]catenane structure. The

magnitude of the shift resulting in [2]catenane formation (80mV) is, however, less than the shift observed in the copper(II/III) couple upon addition of (20) to (57) (where a 140mV shift is seen in forming the pseudo-rotaxane). This difference may be attributed to the fact that in the pseudo-rotaxane structure (81) the copper(II) dithiocarbamate thread is surrounded on each side by a positive charge of one gold(III) dithiocarbamate unit, whereas this is not the case in the [2]catenane.

Unfortunately, the UV-vis spectrum of the two macrocyclic complexes fails to result in any significant perturbations upon the interlocking of the two rings. However, the prominent peak observed in the electrospray mass spectrum, the large anodic shift in the electrochemical studies and the precedent of forming interpenetrating structures from the similar systems (78) and (79) suggest that the [2]catenane structure is again forming.

4.3 Transmetallation

It has been demonstrated within Chapter Four that the addition of tetrachloroaurate salts to first row transition metal dithiocarbamate complexes results in a transmetallation reaction. This is where the gold(III) preferentially displaces the first row transition metal forming gold(III) dithiocarbamate complexes. This reaction has been shown to generate a variety of structures ranging from mononuclear complexes through to octanuclear resorcinarene architectures.

A similar transmetallation experiment was performed, in which four equivalents of potassium tetrachloroaurate were added to one equivalent of the tetranuclear mixed-valence copper-based catenanes $[\text{Cu}_4\text{L}_4]$ (78) and (79)²⁷ in a dichloromethane/acetonitrile (1:1) solution. The solution was analysed at regular intervals by electrospray mass spectrometry.

In the absence of the gold(III) salt, only peaks corresponding to the $[\text{Cu}_4\text{L}_4]^+$ and $[\text{Cu}_4\text{L}_4]^{2+}$ peaks were observable in both structures. After the addition of the tetrachloroaurate salt to the

[2]catenane, however, a number of new peaks began to appear in the spectra. Pleasingly, over time, gold (III) substituted the copper centres in a transmetalation reaction and the appearance of new mixed-metal species were observed. After five minutes, a peak had appeared in the spectra (m/z 2185.0 and 2408.5 for (78) and (79) respectively) corresponding to the substitution of one copper centre for a gold(III) $[\text{Cu}_3\text{AuL}_4]^+$. After 10 minutes, a further peak in both spectra, corresponding to the $[\text{Cu}_2\text{Au}_2\text{L}_4]^{2+}$ [2]catenane was also clearly visible, and after 15 minutes a small peak was observable for the $[\text{CuAu}_3\text{L}_4]^{3+}$ species. The electrospray mass spectrum of the solution of (79) after 15 minutes is highlighted in Figure 17.

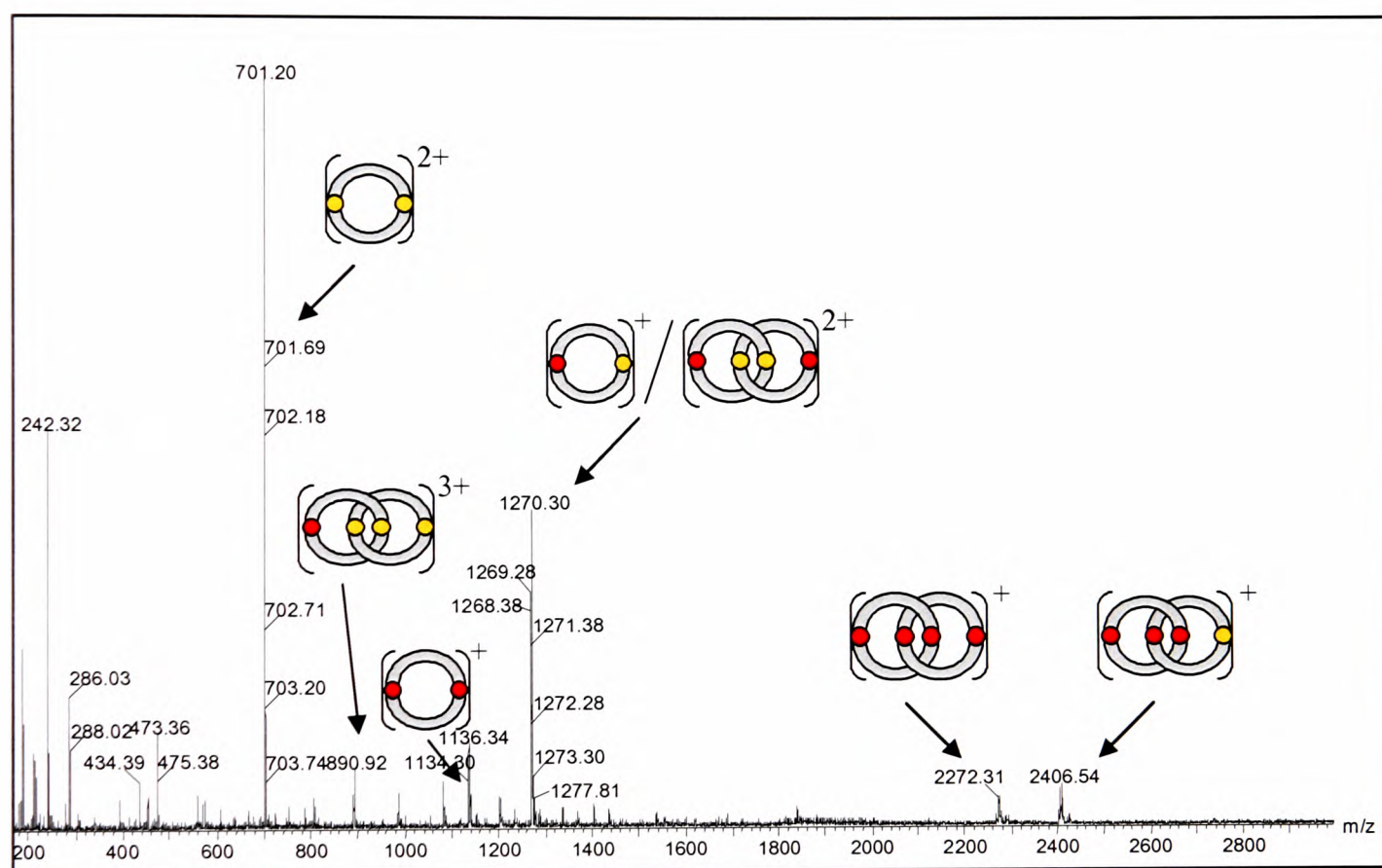


Figure 17 Electrospray mass spectrum of (79) 15 minutes after the addition of 4.0 equivalents of KAuCl_4 (Key: red spheres= Cu centres, gold spheres= Au centres)

The spectrum shows that a number of species are present in the solution after 15 minutes, including the mono-, di- and trisubstituted copper/gold [2]catenanes, in addition to the unsubstituted copper [2]catenane. As well as these interlocked species, peaks corresponding to the dissociation products of the gold and copper macrocyclic complexes were also seen. Further examination reveals the multiple splitting of the species at m/z 1270.3. There appears

to be two species present in fact as closer inspection reveals two sets of peaks; one with integer spacings and another set with half-integer spacings (Figure 18). Examination of the predicted isotopic patterns for the disubstituted catenane $[\text{Au}_2\text{Cu}_2\text{L}_4]^{2+}$ (Figure 18(right inset)) and the mono-substituted dissociation pattern $[\text{AuCuL}_2]^+$ (Figure 18(left inset)) reveal that the observed pattern is a result of the overlaying of these two molecular ions.

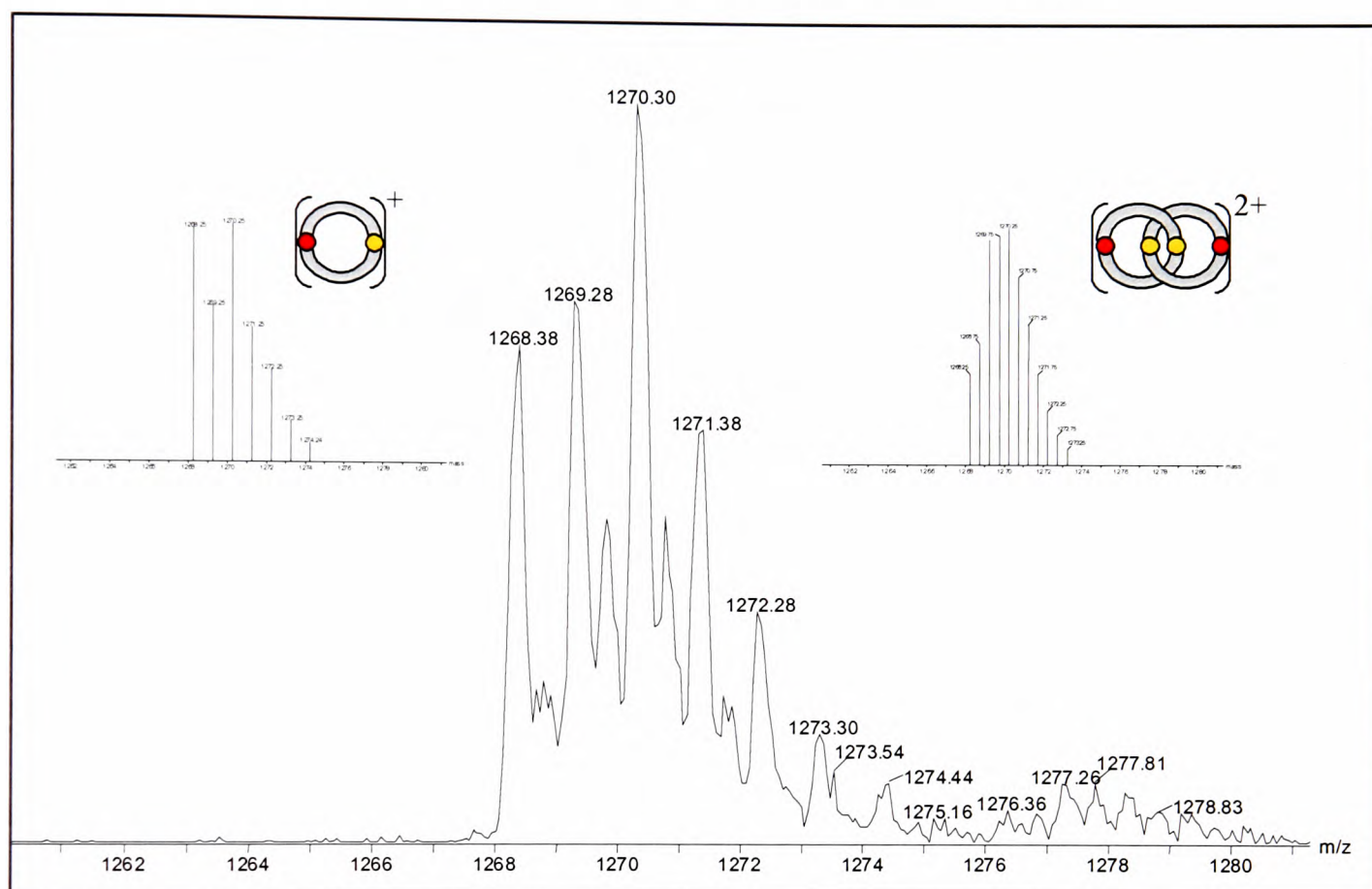


Figure 18 Peak at m/z 1270.3 in the electrospray mass spectrum of the transmetalation of (79) after 15 minutes (inset: isotopic models for (left) the monosubstituted macrocyclic complex and (right) the disubstituted [2]catenane structure)

Further analysis of the solutions does not reveal the growth of the tetrasubstituted $[\text{Au}_4\text{L}_4]^{4+}$ peak, and indeed the $[\text{Au}_3\text{CuL}_4]^{3+}$ also disappears from the spectrum. Analysis of the spectra after 15 minutes reveals the dissociation products of the macrocyclic complexes of $[\text{CuAuL}_2]^+$ and $[\text{Au}_2\text{L}_2]^{2+}$ peaks dominate the spectra. This suggests that the catenane cannot accommodate three or four positive charges in close proximity for any considerable period of time. The unfavourable electrostatic repulsions between the newly formed gold(III) centres force the catenane to dissociate into its constituent bimetallic macrocyclic complexes; hence the multiply-substituted [2]catenanes are no longer seen. The time scale of the experiment,

whereby one copper centre is replaced by a gold(III) atom is approximately every five minutes, which is consistent with the transmetallation of the parent copper(II) macrocycle (**18-Cu**), which was shown to have a half life of fifteen minutes. This shows the interlocking of these macrocycles does not significantly affect the kinetics of the transmetallation reaction. This experiment further demonstrates the stability of the catenane and shows that it is possible to perform transmetallation reactions upon it. The observed stability of the $[\text{Cu}_3\text{AuL}_4]^+$ and $[\text{Cu}_2\text{Au}_2\text{L}_4]^{2+}$ mixed-metal catenane species that were generated during the experiment, also suggests that a donor-acceptor interaction between the electron-rich copper(II) dithiocarbamate donor and the electron-deficient copper(III) dithiocarbamate or gold(III) dithiocarbamate acceptor stabilises the interlocked [2]catenane structure. However, as the electron-rich copper(II) centres are sequentially substituted for gold(III) centres, electrostatic repulsions increase, which ultimately lead to the demise of the interlocked species.

5 Conclusion

It has been shown in this Chapter that the dithiocarbamate-based macrocyclic complexes can be used to generate a range of interpenetrating structures. The partial oxidation of the copper(II) naphthyl-spaced macrocycles (**18-Cu**) and (**74**) using iron(III) chloride results in the formation of a [2]catenane in near-quantitative yield. The generation of this architecture relies on the lability of the copper(II) dithiocarbamate coordinate bond allowing the interlocking of the two rings. The [2]catenane structure is stabilised by favourable axial dithiocarbamate sulphur-copper interactions between adjacent electron-rich copper(II) and electron-deficient copper(III) dithiocarbamate moieties. The spacing between the rigid naphthyl spacer separates these groups to the optimum distance to allow construction. In addition, these interlocked architectures are destroyed by the oxidation of all four copper centres, presumably due to unfavourable electrostatic repulsions between the adjacent metal

centres.

Whilst it has not proved possible to generate similar [2]catenanes using other dinuclear copper(II) dithiocarbamate macrocyclic complexes, a mixed-ligand [2]catenane (**80**) could be identified by electrospray mass spectrometry. This structure was formed from a mixture of macrocyclic complexes which led to the formation of a combinatorial library of both macrocyclic and catenane products.

The use of gold(III) dithiocarbamate-based cations has removed the necessity to oxidise the copper dithiocarbamate complexes to create interpenetrating structures. This methodology has been employed to generate both mixed-metal pseudo-rotaxanes and a [2]catenane. These architectures are held together by the same axial metal-sulphur donor-acceptor interactions as seen in the mixed-valence [2]catenanes (**78**) and (**79**). Both electrospray mass spectrometry and electrochemical studies have indicated the formation of these mixed-metal interlocked structures. The copper(II) for gold(III) transmetallation of a preformed copper(II/III) [2]catenane has also led to the formation of mixed-metal catenane structures. In this case, however, the incorporation of a number of positively-charged gold(III) centres in close proximity, whilst being thermodynamically favourable, is mutually electrostatically unfavourable, leading to the eventual break-up of the interlocked structures.

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