

# **Ditopic Ligands for the Selective Solvent Extraction of Transition Metal Sulfates**

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**Doctor of Philosophy**

**The University of Edinburgh**

**2004**



## Abstract

The thesis considers the development of new reagents which could transport transition metal *salts* in extractive hydrometallurgy and addresses the ligand design features which are needed to control the strength and selectivity of binding of both a particular metal cation and its attendant anions(s).

Extractive metallurgy of base metals is surveyed in chapter 1 and suggests that more efficient recovery processes are needed. One new approach, which could lead to much better materials balances in many cases, is to use hydrometallurgical techniques which involve co-extraction and transport of metal cations and their attendant anion(s). The problems in obtaining the selective extraction of anions makes the development of such a process very challenging, especially for hydrophilic anions such as sulfate which would be present in many pregnant solutions generated in processing sulfide ores. The rapidly emerging field of anion coordination chemistry and approaches to the development of selective ligands are discussed.

Chapter 2 focuses on the pH dependence of sulfate-loading from an aqueous solution into chloroform solutions of a selection of zwitterionic ditopic ligands containing two 3-dialkylaminomethylsalicylaldimine units. These “salen-type” ligands have quadridentate  $N_2O_2^{2-}$  binding sites for divalent metal cations and the *cis*-coordination of the phenolate aligns the pendant protonated 3-dialkylaminomethyl groups to bind to a sulfate dianion. Studies of the pH dependence of sulfate-loading confirm that sulfate-binding is enhanced significantly by the incorporation of a divalent cation such as  $Cu^{2+}$  in the salen  $N_2O_2^{2-}$  site. Metal dication loading is very dependent on the nature of the bridging group between the two imines in the “salen” unit;  $Cu^{2+}$  loading follows the order *ortho*-phenylene > 1,2-ethane > 2,2'-biphenyl. The 1,2-ethane-bridged ligand, 4,4'-di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(ethylenedinitrilodimethylidyne) diphenol, was found to have a nearly ideal loading profile for  $CuSO_4$ .

Stability to hydrolysis and oxidation is a key requirement for commercial metal solvent extractants. The stability of the imine bond in the “salen-type” extractants investigated in chapter 2 was tested in a two phase chloroform : water system under conditions likely to be used for loading or stripping of metal *salts*. Stability is dependent on the nature of the bridging unit between the two imines varying in this order 2,2'-biphenyl > *ortho*-phenylene > 1,2-ethane. Two new ligands, 4,4'-di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(ethylenedinitrilo-1,1'-phenyldimethylidyne) diphenol and *N,N'*-dimethyl-*N,N'*-bis(2-hydroxy-3-[(*E*)-phenyliminomethyl]-5-*tert*-butylbenzyl)hexane-1,6-diamine, which exhibit improved stabilities at low pH are also discussed.

Anion selectivity in a metal *salt* extractant is difficult to achieve but is vital in order to obtain good materials balances in extractive metallurgy. In chapter 4 a series of zwitterionic ditopic ligands, similar to those developed in chapter 2 but containing amide groups on the pendant arms, were synthesised and it was hoped that the incorporation of additional hydrogen-bond donors would favour the extraction and transport of the hydrophilic sulfate anion. The ligand, 4,4'-di-*tert*-butyl-6,6'-bis([3-benzoylamidopropyl]benzylaminomethyl)-2,2'-(ethylenedinitrilodimethylidyne) diphenol, which contains a propyl bridge, between the amide group and the protonatable ammonium nitrogen atom, shows selectivity for  $\text{Cl}^- > \text{SO}_4^{2-} > \text{H}_2\text{PO}_4^-$ . Selectivity for sulfate over chloride is an important target as the chloride anion is commonly found in solutions generated in hydrometallurgical processes. Two other ligands, with shorter (1,2-ethane) and longer (1,6-hexane) links between the ammonium group and amide unit, were also synthesised and the 1,2-ethane-bridged ligand was found to reduce the chloride to sulfate selectivity. Both ligands were still found to be selective for chloride and this is likely to be a consequence of the well established order of hydrophobicity  $\text{Cl}^- \gg \text{SO}_4^{2-}$  (the Hofmeister order). It was also found that the “strength” of sulfate-extraction was lower than in the ligands developed in chapter 2. UV-Visible spectroscopy was used to monitor the solution behaviour of the extractions.

Zwitterionic macrocyclic metal *salt* extractants were developed to increase the pre-organisation of the anion-binding sites. It was found that the “strength” of sulfate-extraction was notably improved using 10,25-di-nonyl-14,21-dimethyl-3,6,14,21-tetraaza-tricyclo[21.3.1.18,12]octacos-1(27),2,6,8,10,12(28), 23,25-octaene-27,28,diol. This macrocycle is again based on the “salen” unit but contains a hexamethylene strap between the protonatable amine groups. Although the “strength” of extraction (sulfate is bound at a higher pH) was found to be greater than in the related acyclic ligands the macrocycle still showed selectivity for chloride over sulfate. A second macrocycle was synthesised, containing amide-binding units in the strap between the ammonium nitrogens, but, as in chapter 4, the amide hydrogen-bond donor groups were not found to improve the transport of sulfate.

## **Acknowledgements**

I would like to thank a number of people who have helped me through the last three years of studies. Firstly I would like to thank my supervisor Prof. Peter Tasker for supervision throughout my degree. He has always taken time to listen to any problems I've had no matter how busy his own schedule has been and more than often his advice has proved very useful! My postdoctoral supervisor Dr. Paul Plieger has also been extremely helpful throughout my degree especially at the beginning of my PhD when he taught me many important synthetic techniques. I am grateful to the EPSRC and the University of Edinburgh for the funding of my studentship.

I would like to thank Mr. J. Millar, Dr. P. G. Plieger and Mr. W. Kerr for obtaining many of my NMR spectra, Mr H. Mackenzie for mass spectra and Ms S. Djurdjevic for elemental analysis. I also wish to thank Dr. P. G. Plieger for X-Ray structure determinations and Dr. S. Parsons for collecting the data.

My mum and dad have had to put up with me for the last few months while I have been writing this thesis so I would like to thank them for putting up with me! Last but certainly not least I want to thank my girlfriend Jemma who has given me fantastic support throughout the last three years. She has always been there for me and I want to let her know that I couldn't have done it without her!!

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## Abbreviations

Å	Angstrom
Ar	Aryl
b.p.	boiling point
br	broad (spectroscopy)
BuOH	butan-1-ol
°C	degree Centigrade
ca.	approximately
calc.	calculated
CHCl <sub>3</sub>	chloroform
Chpt.	Chapter
cm <sup>-1</sup>	wavenumber (IR)
%Cu	percentage copper
cyclen	tetra-azacyclodecane
d	doublet (NMR)
d-d	d-orbital transitions (UV-Vis)
δ	chemical shift (NMR)
Δ	change in
DCM	dichloromethane
D2EHPA	di(2-ethyl hexyl)phosphoric acid
ε	extinction coefficient (UV-Vis)
ed.	editor(s)
en	ethylenediamine
ES	electrospray (MS)
EtO	ethoxy
FAB	fast atom bombardment (MS)
g	gram
h	hour
ICP-OES	inductively coupled plasma optical emission spectroscopy
IR	infrared

$\lambda$	wavelength
$J$	coupling constant (NMR)
$K_a$	association constant
m	multiplet (NMR), metre
M	molar
$M^+$	positively charged parent molecular ion (MS)
$M^-$	negatively charged parent molecular ion (MS)
mm Hg	pressure
MHz	frequency (NMR)
MeOH	methanol
$\mu\text{L}$	microlitre
mg	milligram
ml	millilitre
$\overline{\text{ML}}_2$	— symbol indicates that the compound is solvated in the organic phase
mmol	millimole
$\text{mmol dm}^{-3}$	millimole per litre
mol	mole
$\text{mol dm}^{-3}$	mole per litre
MS	mass spectroscopy
$m/z$	mass to charge ratio
nm	nanometres ( $10^{-9}$ m)
NMR	nuclear magnetic resonance
obs.	observed
pH	$-\log_{10}[\text{H}^+]$
$\text{pK}_a$	$-\log_{10}K_a$
pp.	inclusive pages
ppm	parts per million
q	quartet (NMR)
s	singlet (NMR); strong (IR)
salen	<i>N,N'</i> -ethylenebis(salicyldeneaminato)
%S	percentage sulfur

SX	solvent extraction
t	triplet (NMR)
T	temperature
trien	triethylenediamine
UV-Vis	ultraviolet-visible
Vol.	volume
vs.	versus
v	wavenumber

### Abbreviations of Journal Titles

Acc. Chem. Res.	Accounts of Chemical Research
Acta Crystallogr., Sect. A	Acta Crystallographic, Section A
Acta Crystallogr., Sect. C	Acta Crystallographic, Section C
Angew. Chem., Int. Ed. Engl.	Angewandte Chemie, International Edition in English
Angew. Chem.	Angewandte Chemie
Annu. Rev. Biochem.	Annual Reviews of Biochemistry
Arch Exp Pathol Pharmacol	Archiv for Experimentelle Pathologie und Pharmakologie
Chem. Commun.	Chemical Communications
Chem. Rev.	Chemical Reviews
Coord. Chem. Rev.	Coordination Chemistry Reviews
Dalton Trans.	Dalton Transactions
Inorg. Chem.	Inorganic Chemistry
J. Am. Chem. Soc.	Journal of the American Chemical Society
J. Biol. Chem.	Journal of Biological Chemistry
J. Chem. Soc., Dalton Trans.	Journal of the Chemical Society, Dalton Transactions
J. Chem. Soc., Perkin Trans. 1 / 2	Journal of the Chemical Society, Perkin Transactions 1 / 2



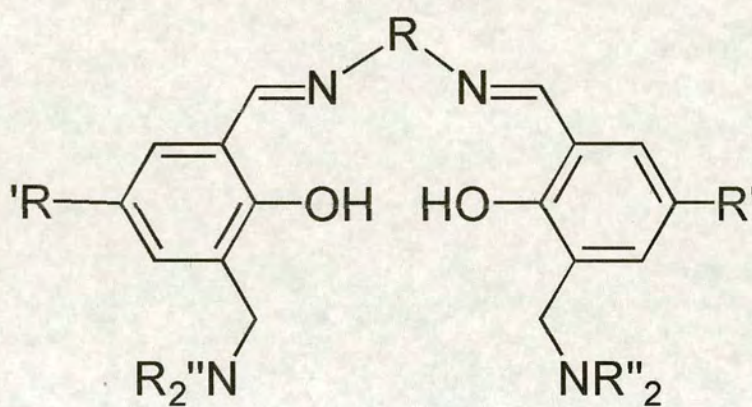
J. Heterocycl. Chem.	Journal of Heterocyclic Chemistry
J. Inclusion Phenom. Mol. Recognit. Chem.	Journal of Inclusion Phenomena and Molecular Recognition in Chemistry
J. Miner. Met. Mater. Soc.	Journal of the Minerals Metals and Materials Society
J. Org. Chem.	Journal of Organic Chemistry
J. Prakt. Chem.	Journal fuer Praktische Chemie
J. Radioanal. Nucl. Chem.	Journal of Radioanalytical and Nuclear Chemistry
New J. Chem.	New Journal of Chemistry
Philos. Trans. R. Soc. London, Ser. B	Philosophical Transactions of the Royal Society of London, Series B
PhysChemComm	Physical Chemistry Communications
Pure Appl. Chem.	Pure and Applied Chemistry
Quart. Rev. Biophys.	Quarterly Reviews of Biophysics
Solvent Extr. Ion Exch.	Solvent Extraction and Ion Exchange
Spectrochim. Acta	Spectrochimica Acta
Supramol. Chem.	Supramolecular Chemistry
Tetrahedron Lett.	Tetrahedron Letters

## Thesis Format

Each chapter in this thesis is written as a separate entity, such that the numbering of compounds, figures, tables, and references is individual to each chapter. The compound numbering for chapters 2 – 5 is summarised in the following section.

## Index of Compounds

### Chapter 2



Ligands	R	R'	NR'' <sub>2</sub>
1	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>
2	2,2'-biphenyl	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>
3	(±)- <i>trans</i> -1,2-cyclohexane	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>
4	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>
5	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	piperidine
6*	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	piperidine

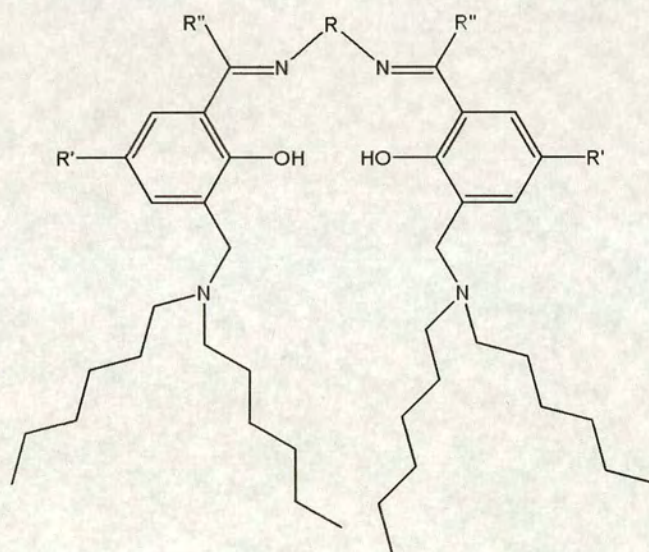
\*Ligand 6 was not isolated, Cu(6)SO<sub>4</sub> was made directly from 2-hydroxy-3-(piperidin-4-ylmethyl)-5-*tert*-butylbenzaldehyde and phenylene-1,2-diamine.

## Metal Complexes

7	[Cu(1-2H)]
8	[Cu(2-2H)]
9	[Cu(3-2H)]
10	[Cu(4-2H)]
11	[Zn(1-2H)]
12	[Ni(4-2H)]
13	[Cu(5)SO <sub>4</sub> ]
14	[Cu(6)SO <sub>4</sub> ]

## Chapter 3

### (i) "Top-down" Ligands



Ligands	R	R'	R''
1	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	H
2	2,2'-biphenyl	Bu <sup>t</sup>	H
3	(±)- <i>trans</i> -1,2-cyclohexane	Bu <sup>t</sup>	H
4	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	H
5	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	-C <sub>6</sub> H <sub>5</sub>

## Metal Complexes

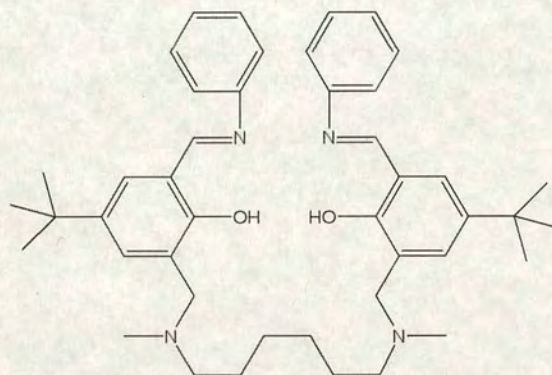
6 [Cu(5-2H)]

7 [Cu(1-2H)]

### Note

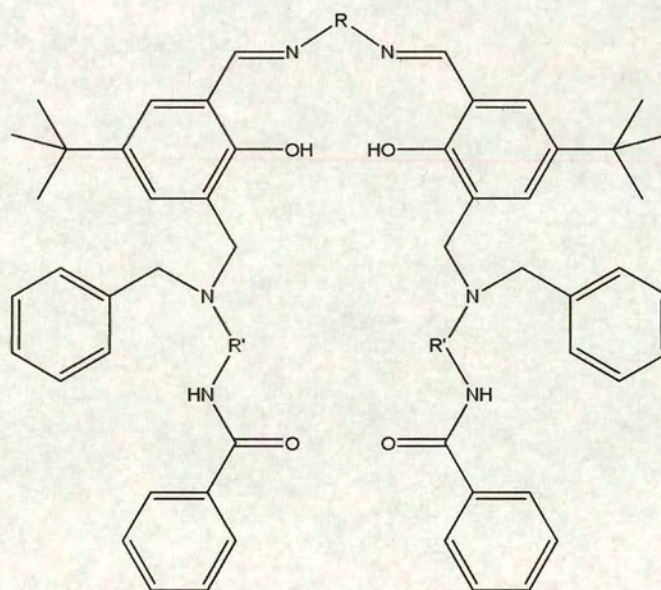
Ligands 1 – 4 and “copper-only” complex 7 are numbered in the same way as in chapter 2.

### (ii) “bottom-up” ligand



Ligand 8

## Chapter 4

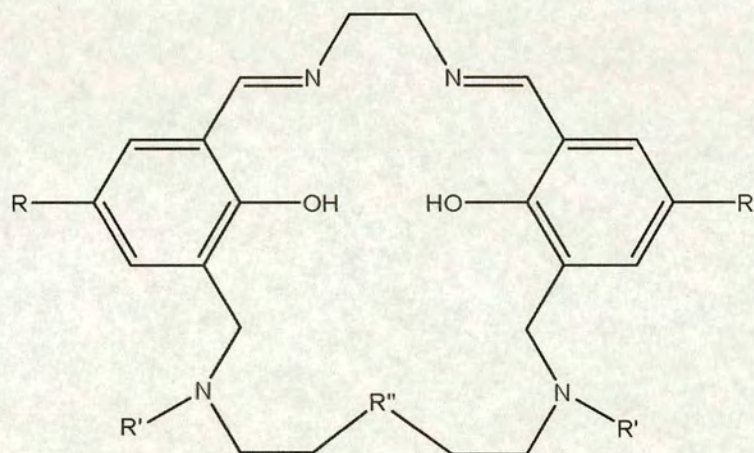


Ligands	R	R'
1	$-(\text{CH}_2)_2-$	$-(\text{CH}_2)_3-$
2	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	$-(\text{CH}_2)_3-$
3	$-(\text{CH}_2)_2-$	$-(\text{CH}_2)_2-$
4	$-(\text{CH}_2)_2-$	$-(\text{CH}_2)_6-$

### Metal Complexes

5	[Cu(1-2H)]
6	[Cu(2-2H)]
7	[Cu(3-2H)]
8	[Cu(4-2H)]

## Chapter 5



Ligands	R	R'	R''
1	Bu <sup>t</sup>	Me	$-(\text{CH}_2)_2-$
2	C <sub>9</sub> H <sub>19</sub>	Me	$-(\text{CH}_2)_2-$
3	Bu <sup>t</sup>	-CH <sub>2</sub> Ph	-CH <sub>2</sub> NHCO(CH <sub>2</sub> ) <sub>3</sub> CONHCH <sub>2</sub> -

### Metal Complexes

4	[Cu(1)SO <sub>4</sub> ]
5	[Cu(2-2H)]
6	[Cu(3-2H)]

# **Chapter 1 : Introduction**

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## 1. Introduction

The aim of the research described in this thesis is to design ditopic ligands for the solvent extraction of transition metal *salts*, which show high selectivity particularly with respect to the binding and co-transport of specific anions. This chapter introduces the main metal recovery processes used by industry and reports a potential new approach for the processing of metal sulfide ores by using ligands which can extract both metal cations and sulfate anions. It describes the key design requirements of these ligands with particular attention given to the rapidly emerging field of anion coordination chemistry and the development of successful sulfate receptors.

### 1.1 Metallurgy

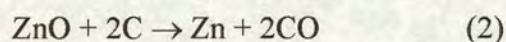
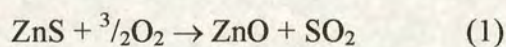
Metallurgy encompasses the extraction of metals from their ores and the purification or modification of the metals for a more useful purpose. The term in practice is more often used to refer to an industrial process than a laboratory technique. Metallurgy is a technology which dates back to 4000 BC<sup>1</sup> or earlier and deals with the principles whereby metals are combined to form alloys such as brass or bronze. The main techniques currently used in industry to process metal ores are pyrometallurgy, hydrometallurgy and gravity and froth flotation methods.

### 1.2 Pyrometallurgy

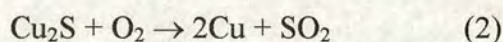
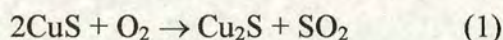
Initially the earth's atmosphere was mainly composed of SO<sub>2</sub> and CO<sub>2</sub> which meant that the metal ores formed were metal sulfide ores. As plants emerged and began the process of photosynthesis, oxygen started to become a major component of the atmosphere. Exposed layers of metal sulfide ores were therefore subject to oxidation to produce oxidic ores. Consequently metal ore deposits commonly contain a sulfidic lower layer, a mixed sulfidic/oxidic (“transition ore”) middle layer and a superficial oxidic layer.<sup>1</sup>



Pyrometallurgy is used to extract metals from their ores<sup>2</sup> by heating the latter to high temperatures, often with a reducing agent such as carbon, to produce the metal. A reductant is used when the reduction product is thermodynamically stable as this favours the production of the metal. For example if carbon is used in the process of extraction from an oxidic metal ore then carbon monoxide is formed. This method is not applicable to sulfidic ores because the carbon disulfide produced is barely thermodynamically stable and the analogue of carbon monoxide, carbon sulfide, is highly unstable.<sup>3</sup> Therefore, before the reduction process, metal sulfides are often roasted in air to convert them to metal oxides. This occurs because the oxidation produces sulfur dioxide which is highly thermodynamically favourable, e.g.



A reducing agent is not required in some cases where heating the ore to high temperatures can be sufficient to extract the metal. An example of this is copper smelting in which copper can be recovered from its sulfidic ore, at temperatures of around 1300°C, by a two-stage process in air.<sup>3</sup> This can be represented, with respect to copper, as



This is again favoured thermodynamically by the formation of sulfur dioxide.

The smelting of copper ores<sup>1</sup> has been used for metal extraction since as early as 4000 BC. This gives the method a significant advantage over many other techniques as the process has been refined and improved for many years and new installations can easily be constructed by a number of specialised companies. Pyrometallurgy can also be carried out on extremely large scales and is very economical making it much more profitable than other extraction techniques.<sup>4</sup> These methods were later adapted and applied to the recovery of other metals such as iron, nickel and zinc.<sup>2</sup> However some of the metals produced by industry need complex recovery processes.

Titanium, for example, is made by the *Kroll* process which converts  $\text{TiO}_2$  to  $\text{TiCl}_4$  by coke production in the presence of  $\text{Cl}_2$ . The titanium tetrachloride produced is then reduced with molten magnesium in an inert argon atmosphere to give titanium metal.<sup>3</sup>

Pyrometallurgical extraction does have some major disadvantages, for example, the emission of pollutants and toxic gases<sup>2</sup> such as  $\text{SO}_2$  and intensely toxic heavy metals.<sup>4</sup> This problem is becoming increasingly significant as environmental regulations get stricter and more difficult to meet. Fossil fuels that are used during the extraction can also form gaseous pollutants. The “off-gases” can contain fine dusts that need to be recovered to further reduce pollution.<sup>2</sup> Also when applied to low-grade ores pyrometallurgical techniques are often not cost effective.

Pyrometallurgy is an important metal extraction technique but other methods are needed which can process the large stocks of low grade ores and meet new environmental regulations.

### 1.3 Gravity and Froth Flotation Methods

Gravity provides the simplest technique for metal ion concentration. Dense metal or ore particles can be separated in swirling water from significantly less dense silicate and other rock-based minerals, as the latter form a suspension and the metal/ore particles sink to the bottom.<sup>3</sup>

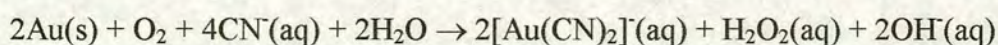
Another technique used in metallurgy is froth flotation and this is typically used to obtain ore “concentrates” and remove impurities. Metal sulfides are the ores most commonly treated in this way but a number of other examples can be found such as the separation of  $\text{KCl}$  from  $\text{NaCl}$ .<sup>3</sup> The process is heavily dependent on converting the desired hydrophilic solids into hydrophobic ones and subsequently removing them as an oil-based froth. The unwanted materials (silicates, aluminosilicates) are removed as an aqueous slurry from the bottom of the separator.

Flotation agents are used which can be selectively attached to the surfaces of the metal ore particles.<sup>5</sup> For example in the treatment of metal sulfide ores, suitable agents for the metal sulfide particles have polar “head groups” which contain sulfur atoms. These tend to absorb on a metal sulfide surface but not onto silicate or aluminosilicate surfaces. The attached long alkyl tails of these collectors render the complexed ore particle hydrophobic,<sup>6</sup> which allows ore concentration by removal of the resultant hydrophobic froth.

## 1.4 Hydrometallurgy

Hydrometallurgical techniques have fewer environmental problems than the foregoing. Since the world supplies of high-grade ores are decreasing, techniques are required for the recovery of metals from low grade ores, transition ores, dumpstocks, mixed metals and residues.<sup>2</sup> Hydrometallurgy is being developed as a more environmentally sound and diverse technique.<sup>4</sup> In addition, it has some economic benefits, since it avoids the high temperatures of pyrometallurgy. Transport costs can be reduced since plants can be situated near the ore bodies.<sup>3</sup>

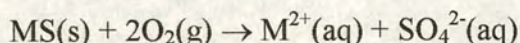
Hydrometallurgical methods use reactions in aqueous solutions to extract selectively (this can involve metal complex formation) and/or concentrate targeted metal ions. The hydrometallurgical process often involves leaching of the ore as the initial step. For example gold particles in crushed rock can be recovered by cyanide leaching with aerated sodium cyanide solution to allow  $[\text{Au}(\text{CN})_2]^-$  to be brought into solution. The undesired impurities (aluminosilicates) do not dissolve which gives:



The reaction can take several days after which the gold can be obtained by electrolysis.<sup>7</sup> Ammoniacal leaching can be used to separate base metal ions. The Sherritt Gordon process utilises the power of aqueous ammonia to complex  $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ , and  $\text{Co}^{3+}$  but not  $\text{Mn}$ ,  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ . After leaching, the individual  $\text{Cu}^{2+}$ ,  $\text{Ni}^{2+}$ , and  $\text{Co}^{3+}$  can be separated by complicated aqueous chemistry. The ions are then

reduced to the base metals using hydrogen under conditions of high pressure and temperature.<sup>3</sup>

Other leaching processes can use very different methods, for example bacteria for the oxidation of insoluble mineral sulfides to the commonly water soluble metal sulfates. Thus *Thiobacillus ferrooxidans* can use the sulfide-sulfate redox cycle to drive its own metabolic processes.<sup>3</sup> This type of reaction requires oxygen:

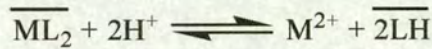


The metal can then be recovered by a hydrometallurgical process. This has the very significant advantage, over the roasting in air of sulfidic ores performed in pyrometallurgy, that  $\text{SO}_2$ , an air pollutant, is not released to the atmosphere.

Liquid-liquid solvent extraction is an important technique in hydrometallurgy. It is capable of dealing with very difficult metal ion separations and generally involves the selective transport of metal ions from an aqueous phase into an immiscible organic phase. This technology has a number of possible applications and one of the most important is the extraction of transition metals from low-grade ores. There are four steps in this form of metal recovery, which consist of leaching, extraction, stripping and electrowinning.<sup>4</sup> The first part of the process, leaching, is the selective dissolution of the metal and this is often done with sulfuric acid. There are two ways that leaching is carried out: simple leaching (at atmospheric temperature and pressure) and pressure leaching (pressure and temperature are increased to quicken the process).<sup>2</sup> Extraction is the next stage in the process and involves the selective transport of metal ion into a non-polar organic phase by means of a hydrophobic ligand, often an organic acid, dissolved in the organic solvent, eg. as in

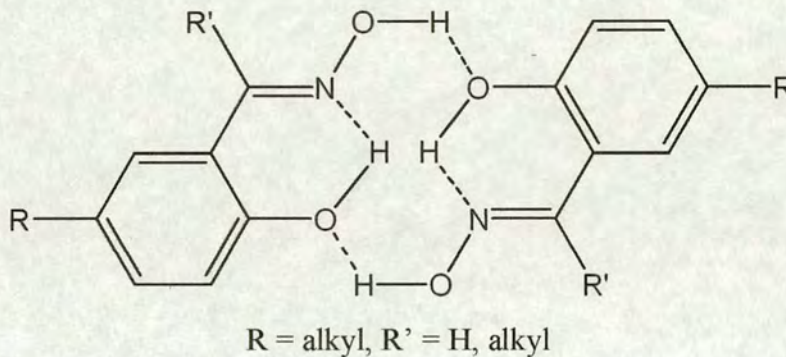


The stripping stage involves the removal of metal ion from the ligand, e.g. by contacting the loaded organic phase with an aqueous phase at lower pH than the leaching solution,



This produces a pure metal salt solution<sup>2</sup> which can be used in the electrowinning stage to give pure metal.

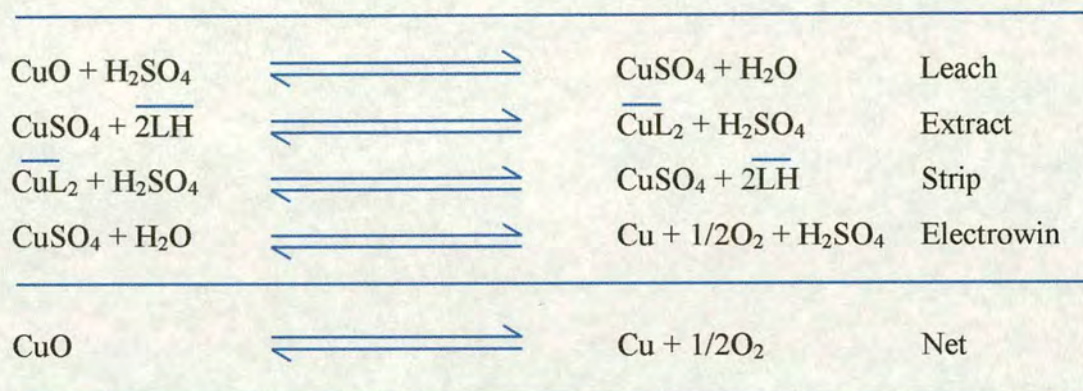
An example of such a process, which is used in industry, is the solvent extraction of copper by selective phenolic oxime ligands (Figure 1.1).<sup>2</sup>



**Figure 1.1** The commercial phenolic oxime copper extractants<sup>2</sup>

In this process the copper oxide is leached from its ore using sulfuric acid to give a pregnant leach solution containing a number of metal sulfates. The leached Cu(II) ions can be extracted into the organic phase by the hydrophobic ligand. The metal ion displaces two protons from two ligand molecules which are released into the aqueous phase, regenerating the sulfuric acid used to leach the ore. The copper is stripped from the loaded organic phase back into an aqueous phase, of lower pH than the pregnant leach solution, to give a pure copper sulfate solution. The ligand is simultaneously re-protonated in the organic phase and is recycled. The pure copper sulfate solution then undergoes electrolysis to produce pure copper metal (product) and sulfuric acid (spent electrolyte) which is fed back into the stripping stage (Figure 1.2).

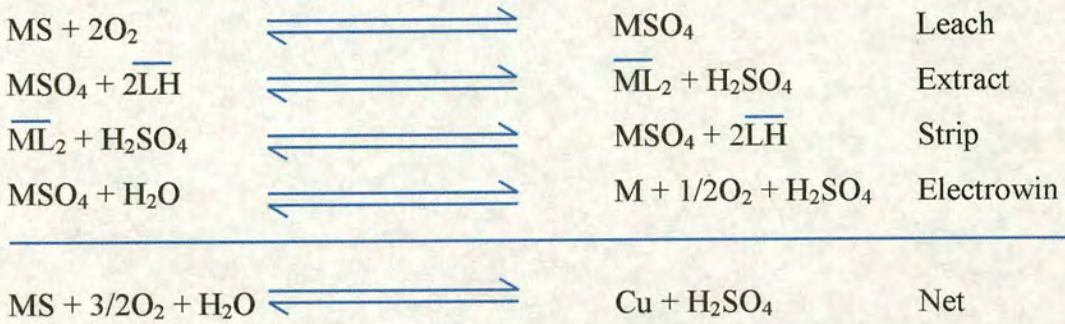
The pH gradient is the driving force for the transport of the copper ion across the circuit. The success of the process is based on the excellent overall materials balance (Figure 1.2) and the charge neutrality of the copper ligand complex which provides organic solubility. The copper produced is also of a very high quality and the reagent can be recycled.



**Figure 1.2** Materials balance for solvent extraction recovery of copper based upon the industrially developed process involving phenolic oxime extractants

Although there are many advantages to this method of recovery there are also some disadvantages, namely the slow kinetics in leaching the ores and the large mass of extractant required per unit mass of copper.

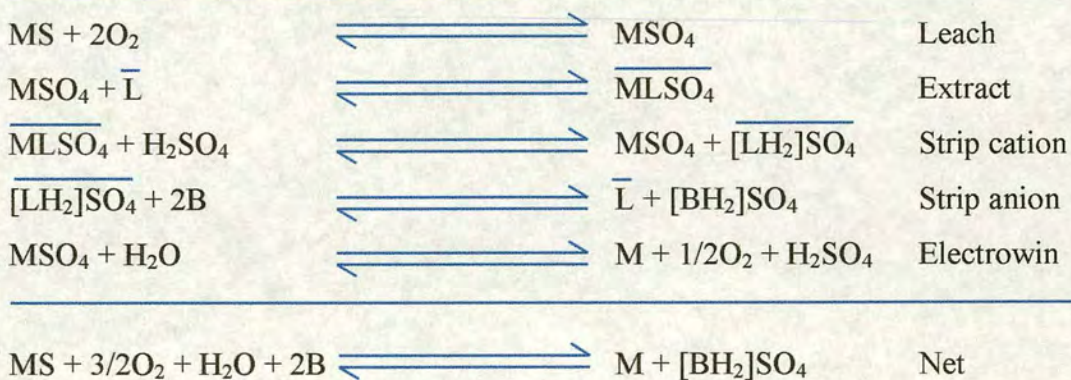
The leaching of metal sulfide ores requires different reactions and this causes problems in the materials balance of the process if the conventional extractants such as the phenolic oximes are used. The dilemma occurs because sulfidic ores cannot be leached efficiently with sulfuric acid and conversion to the oxidic ores by roasting in air releases  $\text{SO}_2$  which must be recovered.<sup>3</sup> Oxidative leaching can be performed by roasting the sulfidic ore at a lower temperature in a limited air supply to produce the metal sulfate which can subsequently be dissolved in water for extraction.<sup>3</sup> The problem with this type of leaching, when used in conjunction with commercial organic acid solvent extractants, LH, is caused by the release of two protons into the aqueous phase (Figure 1.3) creating a build-up of acid. This presents no problem in the metal recovery from oxidic ores because the acid is reused in the leaching step.



**Figure 1.3** Sulfuric acid build-up

However, for sulfidic ores acid is not consumed in leaching and therefore builds up at the front end of the circuit. This results in either acid recovery or neutralisation with a base to maintain pH control. Acid recovery is very expensive and neutralisation is not favoured because a salt waste is generated which has to be removed from solution.

One way to avoid such problems is by preventing the release of the sulfuric acid, during extraction, by using a ditopic ligand that can extract both a metal cation and a sulfate anion (see extract step, Figure 1.4). The stripping of the cation and anion from the ligand can be done in two steps. First the cation can be stripped, as in previous procedures, by using sulfuric acid, of low pH, to produce a pure metal sulfate

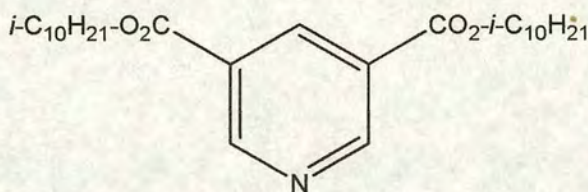


**Figure 1.4** Materials balance for metal recovery via metal sulfate solvent extraction

solution. Secondly the anion can be removed by subsequent stripping with an aqueous base, B, to recycle the ligand (Figure 1.4). With careful planning the salt formed could be a saleable product. The pure metal sulfate solution can be used in the electrowinning stage to give pure metal and also regenerate the sulfuric acid used in stripping the metal.

Extraction of metals by this method has potential applications for treating acid mine drainage and other effluent streams. This could be done by a “subtractive approach” whereby a metal sulfate is selectively removed without the pH being affected. A strategy such as this is useful since the current extractants used in solvent extraction processes, e.g the phenolic oximes, will release protons from the ligand into the aqueous phase upon complexing the metal cation. This in turn lowers the pH and therefore reduces the efficiency of the ligand’s ability to load metal ions (competition with protons).

There are already some examples of extractants which transport metal *salts* in hydrometallurgical processes but most of these use chloride as the accompanying anion, for example in the CUPREX process.<sup>8</sup> This uses oxidative leaching of sulfidic ores with ferric chloride to produce pregnant leach solutions (containing mainly  $\text{CuCl}_2$ ,  $\text{FeCl}_2$ ,  $\text{FeCl}_3$ ) liberating elemental sulfur. In the extract step a neutral ligand such as CLX50 (Figure 1.5) transports  $\text{CuCl}_2$  with a good materials balance (see Figure 1.6).

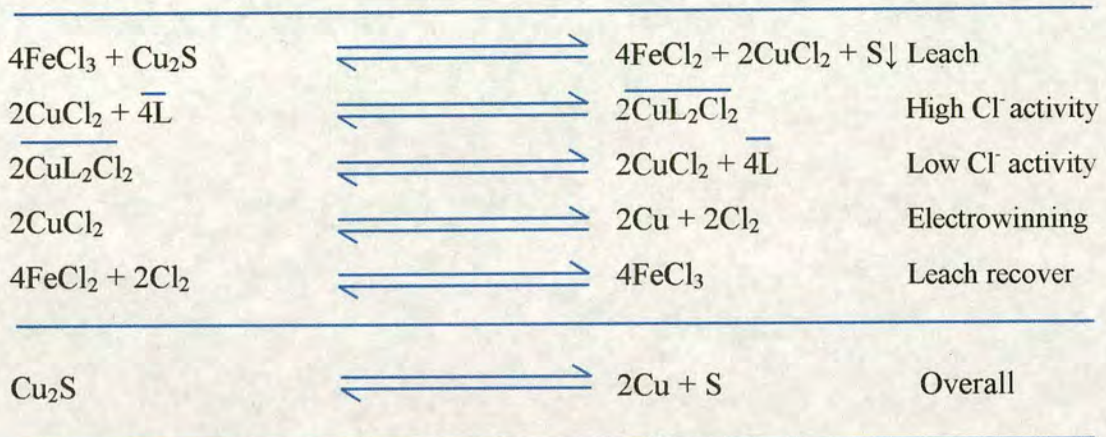


**Figure 1.5** The commercial copper extractant CLX50 used in the CUPREX process.<sup>8</sup>

The extraction equilibrium in the process is highly dependent on the activity of the  $\text{Cl}^-$  anion in the feed solutions. This in turn is highly dependent on the stability of



chlorometallate complexes  $[MCl_x]^{2-x}$  and  $[MCl_x]^{3-x}$  for the metals present,<sup>9,10</sup> and the equations in Figure 1.6 are a simplified representation of the solution speciation.



**Figure 1.6** A simplified flowsheet and materials balance for the recovery of copper from sulfidic ores by oxidative chloride leaching, solvent extraction and electrowinning.<sup>5</sup>

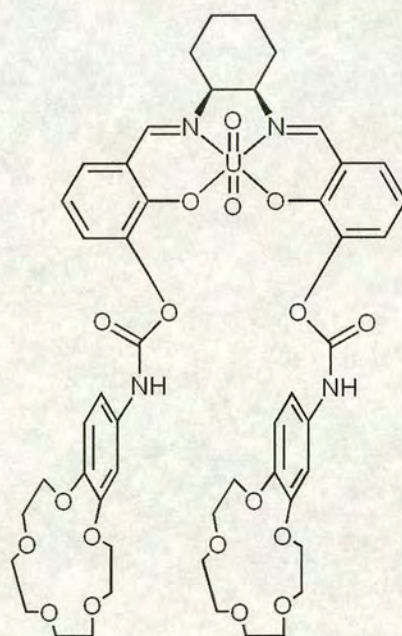
There are problems associated with this process as the  $Cl_2$  generated during electrowinning causes engineering problems and is a safety hazard. Also the hydrochloric acid medium from which the  $CuCl_2$  is extracted is highly corrosive and this again creates engineering difficulties. The transport of  $SO_4^{2-}$  instead of  $Cl^-$  in a solvent extraction process reduces these problems as the electrowinning of metal sulfates is well defined and sulfuric acid is less corrosive.

Hydrometallurgical methods can therefore be used to effectively recover metals in a variety of different ways. The increasing number of environmental regulations makes research into these types of processes of key importance. This is particularly apparent in the processing of metal sulfide ores as although pyrometallurgical methods are efficient they release toxic gases such as  $SO_2$ . Also commercial organic acid reagents, used in the hydrometallurgical processing of metal oxide ores, generate an unwanted acid build-up at the front end of the circuit if used with metal sulfides. This problem could be addressed by the design of ditopic ligands which can extract selectively both metal cations and their attendant anion(s) as the acid could be transported, with the targeted metal ion, across the circuit.

## 1.5 Ligand Design for Metal Salt Solvent Extraction

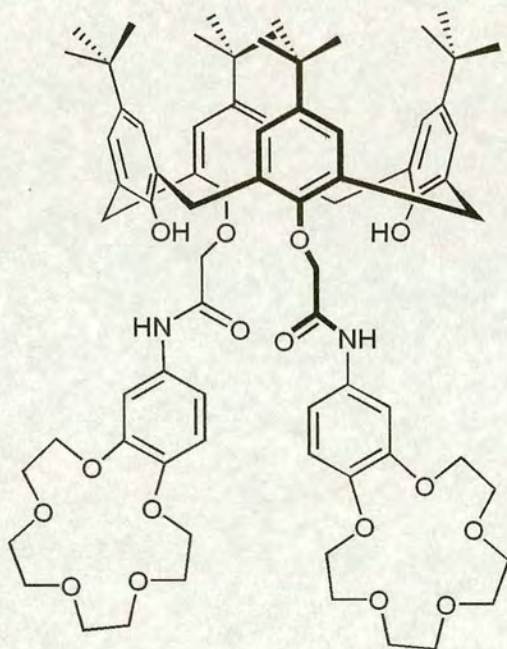
To make metal salt solvent extraction viable, highly selective ligands that can complex both the metal cation and the attendant anion are required. Design of these ligands can focus on producing separate cation and anion binding sites or the anion can be bound directly to the metal centre.

Anion co-ordination chemistry is a growing area but selective extraction is still very difficult to achieve. Initial attempts to design a receptor were focused on first being able to separately bind a metal cation and its attendant anion simultaneously. There are some successful examples of these types of ditopic ligands in the literature. Reinhoudt and co-workers constructed a ligand which contained two cation binding crown ether groups and two anion binding amide moieties which were aided in their role by a Lewis acidic  $\text{UO}^{2+}$  group in relatively close proximity<sup>11</sup> (Figure 1.7). The receptor successfully complexed both potassium and dihydrogenphosphate ions.



**Figure 1.7** Ditopic ligand developed by Reinhoudt and workers<sup>11</sup> to bind  $\text{K}^+/\text{H}_2\text{PO}_4^-$

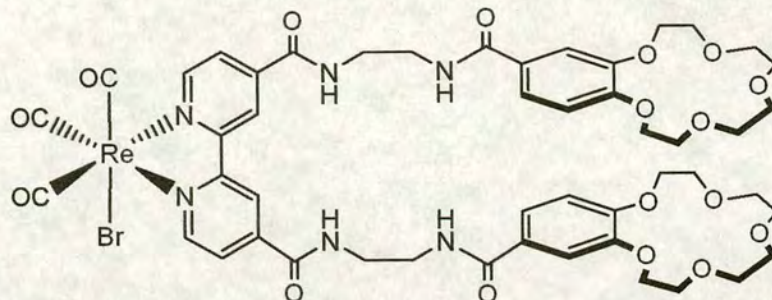
Another example of this type was reported by Beer and co-workers in which the receptor contained two benzo[15]crown-5 moieties attached to the lower rim of calix[4]arene through an amide linker<sup>12</sup> (Figure 1.8). In the absence of alkali metal cations, the amide groups bound no anions but on addition of potassium ions a sandwich complex was formed between the two crown ether units. This templated the formation of an anion binding site by bringing the amide moieties closer together. The system showed particular selectivity for the dihydrogenphosphate anion. This system demonstrates the benefit of using ditopic ligands with separate binding sites. Cooperative binding can be achieved by using cation complexation to facilitate anion binding.



**Figure 1.8** Calixarene-based ditopic receptor developed by Beer and co-workers<sup>12</sup>

In other work in this area Beer and co-workers also showed that cation-binding can change the anion selectivity of a ligand. They developed a heteroditopic rhenium(I) bipyridyl receptor (Figure 1.9) which again used amide groups for anion-binding.<sup>13</sup> The ligand, when no  $K^+$  ions were present, was found to bind  $H_2PO_4^-$  over  $Cl^-$  as 1:1 complexes ( $K_{H_2PO_4} = 205 M^{-1}$  and  $K_{Cl} = 55 M^{-1}$  in  $DMSO-d_6$ ). However after  $K^+$  binding an intra-molecular sandwich complex forms and the association constant

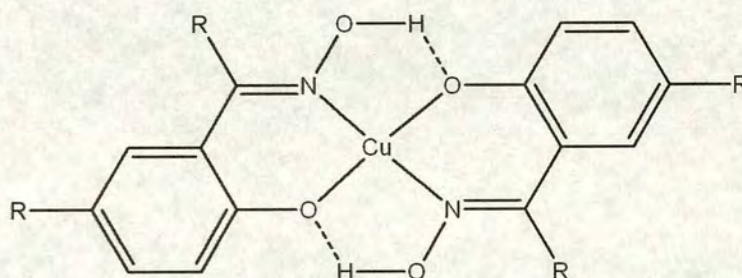
decreases for  $\text{H}_2\text{PO}_4^-$  and significantly increases for  $\text{Cl}^-$  ( $K_{\text{H}_2\text{PO}_4} = 35 \text{ M}^{-1}$  and  $K_{\text{Cl}} = 300 \text{ M}^{-1}$  in  $\text{DMSO-}d_6$ ). This demonstrates how careful ditopic ligand design can tune anion selectivity as the smaller  $\text{Cl}^-$  anion shows a greater affinity for the more compact binding cavity formed upon  $\text{K}^+$  complexation.



**Figure 1.9** Ditopic receptor developed by Beer and co-workers<sup>13</sup>

Designing a ditopic ligand which will show efficient metal sulfate transport and selectivity in a solvent extraction process is a difficult challenge. Separated cation and anion binding sites were targeted because the sulfate ion is a very weak ligand for base metal cations.<sup>5</sup> However the behaviour of ligands in the non-polar solvents used in industrial solvent extraction is also an important point to consider when designing extractants. Intra-molecular and inter-molecular interactions such as hydrogen-bonds become increasingly significant and can be instrumental in controlling the efficiency of complexation and extraction.

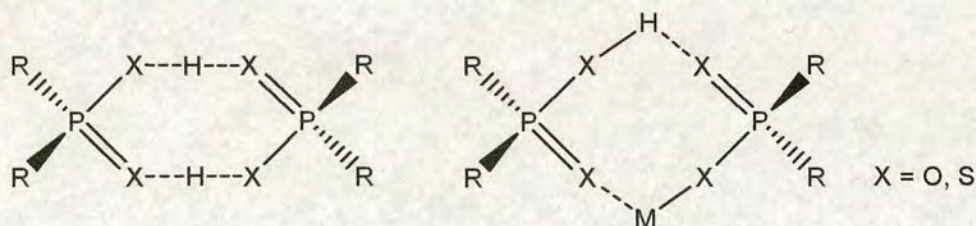
An example of this uses the well-known hydroxy-oxime extractants.<sup>4</sup> These are used in hydrocarbon solvents for the recovery of copper. Inter-molecular hydrogen-bonds



**Figure 1.10** Hydroxy-oxime *pseudo*-macrocyclic copper complex<sup>14</sup>

between the oxime OH groups and the phenolate oxygen atoms lead to the formation of *pseudo*-macrocyclic copper complexes<sup>14</sup> (Figure 1.10) of high stability which contribute to the efficiency of the process.

In another example, the organophosphorus acid metal extractants show very strong inter-ligand hydrogen bonds causing the formation of dimers in hydrocarbon solvents.<sup>6</sup> The eight-membered rings in the dimers are retained upon metal complexation, in the presence of excess extractant (Figure 1.11). This has important consequences as the bite angle defined by the *pseudo*-chelate rings favours tetrahedral coordination and allows the selective extraction of metals such as zinc. For example, D2EHPA extracts  $Zn^{2+}$  more strongly than other first transition series metal ions.<sup>5,6</sup>

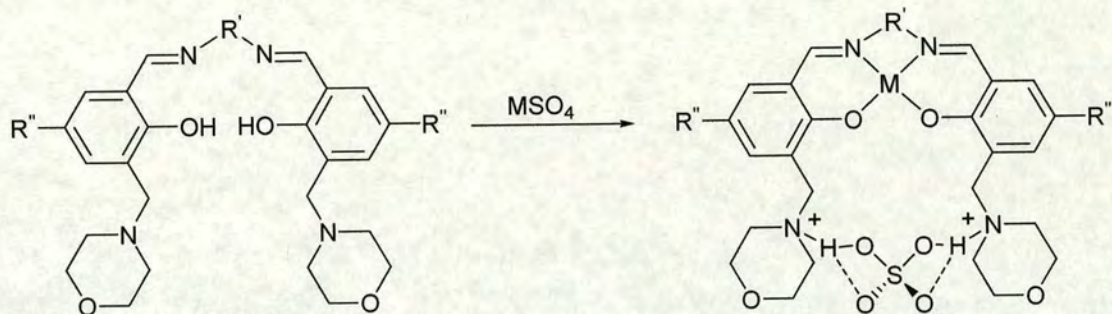


**Figure 1.11** Organophosphorus acid extractants and their mode of metal binding.<sup>5</sup>

Ditopic ligands have been designed in the Tasker group<sup>15</sup> to transport metal salts. The metals that were targeted for extraction were copper and nickel and the anion chosen was sulfate, the anion of choice in a typical aqueous leaching solution. A “salen”-based binding site (salen = *N,N'*-(salicylidene)ethylenediamine dianion) was used as a coordination site for the metal (Figure 1.12) as it is known to bind to nickel and copper.<sup>16,17</sup>

The prototype ligands<sup>15</sup> (Figure 1.12) also have two pendant tertiary amines which are capable of capturing the protons released from the phenolic oxygen atoms upon metal complexation giving the ligand a zwitterionic form (positive and negative sites present but the molecule is overall charge-neutral). These arms create a dicationic binding site for the anions, which has the ability to hydrogen-bond to the captured

anion. These types of interactions are frequently seen in biological systems<sup>18-20</sup> and are important to the efficiency of transport in solvent extraction processes.

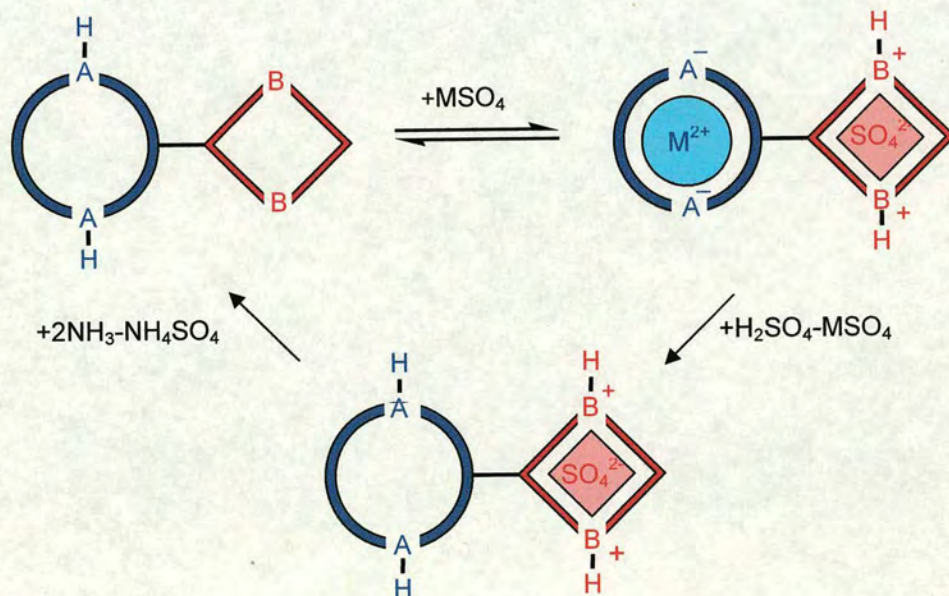


$R'$  =  $-(CH_2)_2-$  (A),  $o-C_6H_4$  (B),  $(\pm)$ -*trans*-1,2-cyclohexane (C)

$R''$  =  $Bu^t$ , nonyl (used for solvent extraction to increase organic solubility)

**Figure 1.12** Prototype ditopic ligands for the transport of metal sulfates.<sup>15</sup>

An advantage of the ligand's zwitterionic form is that no acid is lost to the aqueous phase upon formation of a complex with a metal salt so a pH balance is maintained.



**Figure 1.13** Application of zwitterionic ditopic ligands with dicationic/dianionic sites for the transport of metal sulfates.

The overall charge neutrality of the complex is also important for solubility in hydrocarbons or other solvents of low polarity. These design features open up the possibility for the ligand to be used in hydrometallurgical operations in sulfate media (Figure 1.13). The scheme detailed in Figure 1.13 can be related to the stripping procedure detailed in Figure 1.4 with removal of the metal being followed by recovery of the anion as ammonium sulfate, a saleable product.

In simple solvent extraction tests it was found that copper sulfate was loaded nearly 100% by ligand B (Figure 1.12, nonyl side-arm) in  $\text{CHCl}_3$ , from an aqueous 1M solution of copper sulfate<sup>15</sup> (pH 3.8). The analogous results for the extraction of nickel sulfate were poor and this was been attributed to the slow kinetics of the nickel complexation.<sup>15</sup>

Following these initial results a more detailed study of the extraction processes is required. Anions such as sulfate are protonatable and their extraction is therefore pH dependent. The ligands used are in their zwitterionic form, so the protonation of the amines will change with pH. A pH dependence study of the extraction of metal sulfates is therefore very important. A key aim of such a study is to define the pH region in which co-extraction of metal and sulfate is maximised. A further target is a method of assessing the selectivity of these systems for sulfate compared to other anions (such as chloride) used in hydrometallurgical processes.

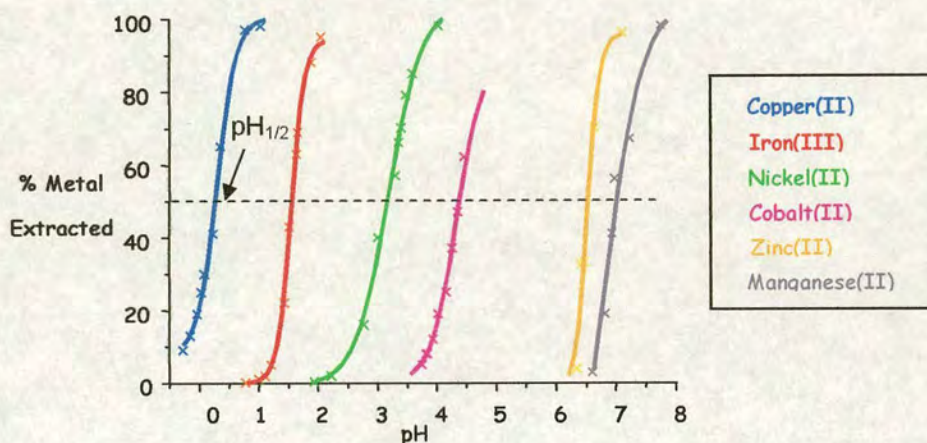
## 1.6 Metal and Anion Detection Methods for Assessing Selectivity

Reliable analytical techniques are required to get accurate data for the amount of metal and anion extracted or the relative strength of their binding. Metal ions can be detected by a variety of methods<sup>21</sup> (eg. ICP-OES, atomic absorption spectroscopy, UV-Vis) which can be used to determine the selectivity of their extraction. Inductively coupled plasma optical emission spectroscopy (ICP-OES) is very good for accurately analysing samples for metal content (less than 10 ppb detection limits)<sup>21</sup> and in a solvent extraction experiment it can be used to analyse both the organic and aqueous phase to check for materials balances.

In hydrometallurgy a common way of assessing the “strength” of an organic acid (LH) extractant is by measuring the  $pH_{1/2}$ , the pH associated with 50% loading of the extractant at a stated concentration and for a defined composition of aqueous feed.<sup>5</sup> Conventionally for,



the lower the  $pH_{1/2}$  the “stronger” the metal complexation. If the metal content of the organic phase is determined over a range of pH then  $pH_{1/2}$  values can be obtained and selectivities assigned (Figure 1.14).



**Figure 1.14** The  $pH_{1/2}$  of a number of metals with P50-oxime (a phenolic oxime) copper extractant.<sup>4</sup>

The stability of anion complexation is examined in a number of different ways in the literature but most of the techniques involve assessing anion selectivity in a single phase system. One popular method is based on potentiometry or more specifically pH-metry.<sup>22,23</sup> This technique is nearly always carried out using a glass pH electrode and to be effective it needs to relate the consumption or liberation of protons in the complexation process to the concentration of the anion-receptor complex formed. However as ligands and anions can often capture protons independently the first step in the procedure is usually to determine the basicity constants of the ligand and anion separately. Once these are known an alkali, or mineral acid is titrated into a solution of the ligand, anion and protons and the variation in the free hydrogen ion concentration is monitored. The stability constants of anion complexation can then



be determined by computer programs.<sup>24</sup> This technique has been used to successfully generate anion selectivity data but to date most of the studies have been carried out in water alone.

NMR is probably the most widely used technique for the determination of anion binding constants in non-aqueous solvents.<sup>25</sup> It has also provided some of the most important structural information on the solution behaviour of anion receptors. The experimentally measurable parameters (chemical shifts, coupling constants etc.) in NMR can be used to determine complex stability constants. These parameters depend on the NMR sensitive nuclei present and their chemical environments as well as the reaction rates of the exchange occurring between them. Slow or fast exchange give different information: in the case of slow exchange the amount of free and complexed species present in equilibrium can be determined from integration of signal area which allows an estimate of the stability constants. Under fast exchange averaged signals of chemical shift are obtained and these can be used to calculate equilibrium constants. NMR can also give information on solution structure as the NMR sensitive nuclei most heavily involved in anion binding will exhibit the largest changes in chemical shift and relaxation times. The disadvantages of NMR are that it can suffer from low sensitivity resulting from the high association and relatively high concentrations ( $10^{-2}$ - $10^{-3}$  M) of both host and guest are required in order to obtain appreciable NMR signals.<sup>26</sup> It also may not be used in the presence of some paramagnetic nuclei.

Anion coordination can also affect the electromagnetic spectrum of the anion and/or the receptor in the  $10^{-8}$ - $10^{-4}$  m wavelength region which allows the use of UV-Vis spectrophotometry and IR spectroscopy. Both of these techniques use the Beer-Lambert-Bouguer Law,

$$A_p = \sum \varepsilon_{ip} \cdot l \cdot C_i,$$

where  $A_p$  and  $\varepsilon_{ip}$  are the absorbance of the solution and molar absorption coefficient of the  $i$ th species at the wavelength denoted by the index  $p$ ,  $C_i$  is the concentration of the  $i$ th species, and  $l$  is the optical path length.<sup>24</sup> This relates the absorption data

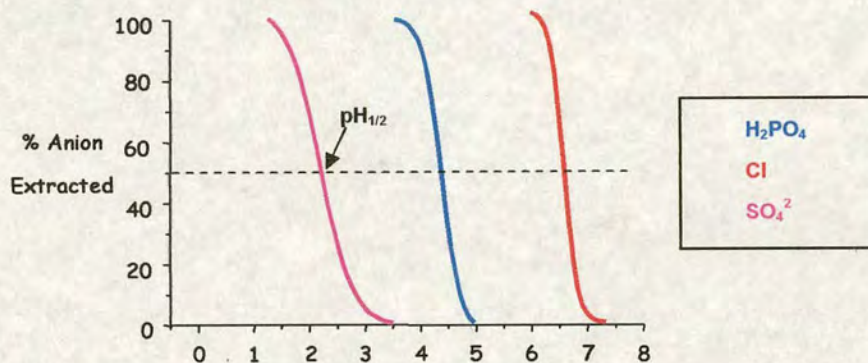
obtained to concentrations which can subsequently be used to calculate equilibrium constants for anion-binding. These techniques are normally used to complement other methods,<sup>27</sup> as they are less accurate, but they have also been utilised as the dominant technique in some cases.<sup>26, 28</sup> This is mainly due to their advantages, as studies can take place at low and high pH and there is no restriction to aqueous solution. Where  $\epsilon_{ip}$  is high, they are applicable to low concentrations. Also, as in NMR, structural information about the anion-receptor complexes can be discovered.<sup>27</sup>

A rapidly growing and popular way of monitoring anion concentrations is the use of anion selective electrodes.<sup>24</sup> There are a number of different metal ion selective electrodes available but the variety of anion selective electrodes is still relatively small. However halide-selective electrodes are now widely available and successfully used. They can conveniently measure anion concentrations and are often used in combination with a glass electrode to give information on the free concentration of the anion under study and the hydrogen ion concentration. Halide-selective electrodes can operate in water and in polar solvents such as acetonitrile.

For analysis by ICP-OES, elements generally require one or more atomic or ionic emission lines in the 160 to 900 nm region to be accurately detected. This technique is not as effective for non-metallic elements as their emission lines either don't fall in the correct range (eg. carbon, halogens)<sup>21</sup> or they have poor detection limits (10 – 100 ppb). Sulfur is an exception as it has emission lines at low wavelengths (180-190 nm) capable of giving results of reliable accuracy. The sulfate anion can therefore be analysed by ICP-OES. In metal *salt* extraction this allows the amount of metal and sulfate extracted by a ligand to be analysed simultaneously as the ICP-OES can perform multi-element analysis.

The selectivity of metal ion complexation can be assessed by  $\text{pH}_{1/2}$  values (Figure 1.14)<sup>4</sup> as a low  $\text{pH}_{1/2}$  value indicates a high “strength” of binding (competition with protons). If  $\text{pH}_{1/2}$  values of sulfate complexation can be obtained by monitoring the extraction of sulfate, over a range of pH, then they could be used to assess the

“strength” of sulfate-binding in a two-phase solvent extraction experiment. However, in this case the higher the  $\text{pH}_{1/2}$  the “stronger” the binding as complexation will only occur when protonation of the anion-binding site (eg. tertiary amine groups) is favourable. If the concentrations of other anions in the organic phase can also be determined, over a range of pH, by using some of the anion analysis techniques used in the literature then anion selectivity in a solvent extraction experiment could be determined using the same principles as metal selectivity. For example, in Figure 1.15,  $\text{Cl}^-$  is extracted at a higher pH than  $\text{H}_2\text{PO}_4^-$  and  $\text{SO}_4^{2-}$  so the “strength” of  $\text{Cl}^-$  binding is greater.



**Figure 1.15** Example of how anion selectivity could be measured in a SX experiment.

This novel approach to assessing anion selectivity should allow quick and efficient determinations of the “strength” of complexation in a two-phase solvent extraction system and is described in chapters 4 and 5.

## 1.7 Developing Sulfate Selective Anion Receptors


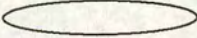
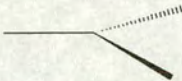
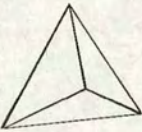
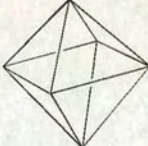
The first aim of the work described in this thesis was to design ligands capable of transporting a metal cation and a sulfate anion from an aqueous to organic phase. This necessitates the design of ligand systems that are selective for the cation and anion targeted. The more challenging of these aims is to design sulfate-selective anion receptors.

Anion coordination chemistry is an emerging area of supramolecular chemistry. Cation recognition is already very well developed and it has taken time for the coordination chemistry of anions to receive a significant level of interest.<sup>24</sup> This is highly surprising when the important part anions play in biology, medicine, catalysis and the environment is considered. For example, in biological systems anions carry genetic information (as DNA is a polyanion) and most of the enzyme substrates and cofactors are anionic in nature.<sup>29</sup> The main reason that less attention has been given to the design of anion receptors is its challenging nature. Anions are much larger than their isoelectronic cations (Table 1.1) and they therefore have a much lower charge to radius ratio.<sup>30</sup> This means that they are more difficult to bind electrostatically (cations are much smaller so their charge is more concentrated). Another difficulty associated with anions is that they are subject to protonation as the pH is lowered. Receptors must therefore be designed to work in a specific pH range as the anion's charge will decrease with pH.

**Table 1.1** radius of selected isoelectronic cations and anions<sup>30</sup>

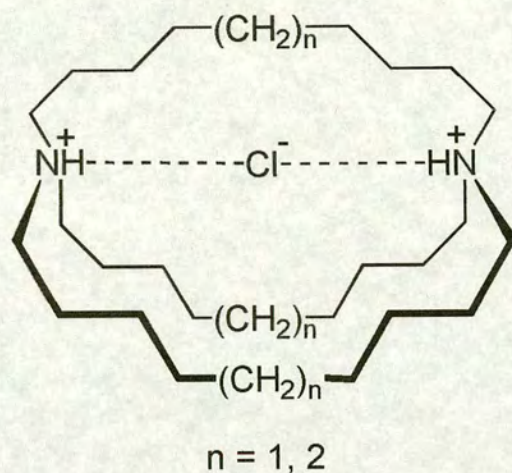
Cation	r[Å]	Anion	r[Å]
Na <sup>+</sup>	1.16	F <sup>-</sup>	1.19
K <sup>+</sup>	1.52	Cl <sup>-</sup>	1.67
Rb <sup>+</sup>	1.66	Br <sup>-</sup>	1.82
Cs <sup>+</sup>	1.81	I <sup>-</sup>	2.06

Anionic species also have a variety of different structures (some common ones are shown in Figure 1.16). The design of receptors is therefore specific for the anion's particular geometry and is far more complicated than for the inherently spherical cations.

Anion Structure	Shape	Anions
	Spherical	$F^-$ , $Cl^-$ , $Br^-$ , $I^-$
	Linear	$N_3^-$ , $SCN^-$ , $OH^-$
	Trigonal Planar	$CO_3^{2-}$ , $NO_3^-$
	Tetrahedral	$PO_4^{3-}$ , $VO_4^{3-}$ , $SO_4^{2-}$
	Octahedral	$[Fe(CN)_6]^{4-}$ , $[Co(CN)_6]^{3-}$

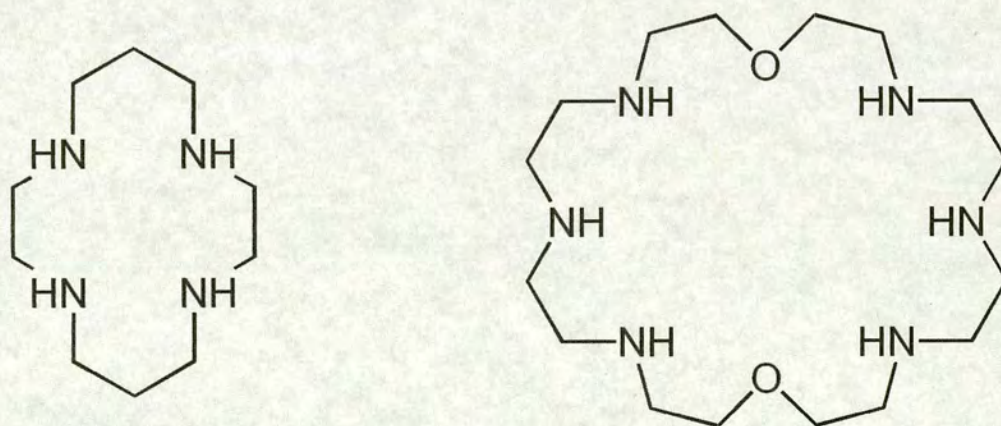
**Figure 1.16** The different structures of anions<sup>31</sup>

The first example of a synthetic anion inclusion complex was reported, in 1968, by Park and Simmons.<sup>32</sup> They discovered a new type of ion-pairing in which a halide guest could occupy the cavity of an organic cage. These complexes became known as the ‘halide katapinates’ (Figure 1.17) and were the basis for most of the early work on anion complexation.



**Figure 1.17** Example of chloride katapinates<sup>32</sup>

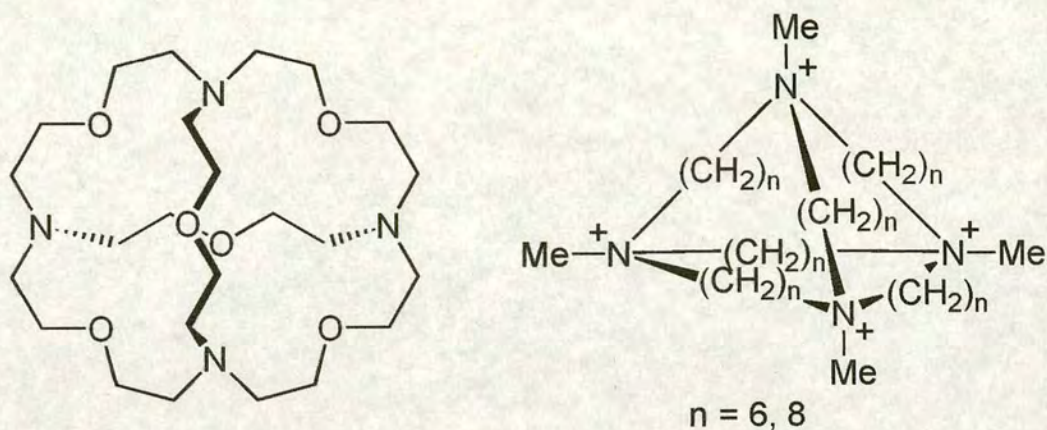
This work mainly consisted of synthesis of a large number of macrocyclic oligoamines (some are shown on Figure 1.18). The designs utilised ammonium groups to facilitate anion-binding.



**Figure 1.18** Early macrocyclic anion receptors<sup>33,34</sup>

Work was also done on the synthesis of a variety of macro-oligocyclic ligands (Figure 1.19). These created a more three dimensional cavity for the anion. The tetrahedral ligand (shown on the right of Figure 1.19) employs purely electrostatic

anion-binding in contrast to ammonium groups which have a combination of electrostatic and hydrogen-bonding.



**Figure 1.19** Early anion receptors with 3-dimensional cavities.<sup>35,36</sup>

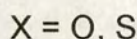
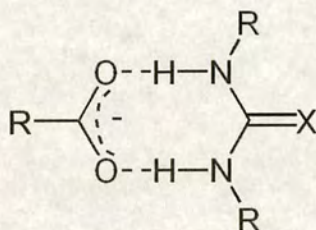
A number of anions, with very different shapes (spherical, tetrahedral etc.) and charges, were found to bind to these macrocyclic ligands with a range of selectivities dependent on cavity size and protonation state.

Anion coordination chemistry developed slowly after these findings and most of the focus remained with cation complexation. Recently however, the supramolecular chemistry of anions has received a lot more attention<sup>24</sup> and there are now many different types of anion receptors in the literature.<sup>37</sup>

Many recent attempts to bind anions have involved the use of amides due to their ability to function as hydrogen-bond donors to anions. The hydrogen-bonding is directional and is therefore very useful when designing receptors for anions of specific shapes and geometries. The first purely amide-based anion receptor was developed in 1986 by Pascal<sup>38</sup> and it was found to bind fluoride anions in deuterated DMSO. In 1993 Reinhoudt and co-workers developed the design possibilities further by synthesising a variety of acyclic tripodal anion receptors containing amide

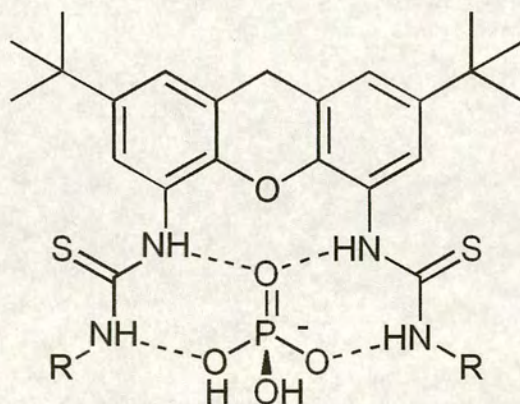
groups.<sup>39</sup> The ligands were all C<sub>3</sub> symmetric and therefore set up to bind tetrahedral anions.

Urea and thiourea are also very good hydrogen-bond donors and are particularly effective due to their excellent directed hydrogen-bonding (Figure 1.20) which facilitates the binding of bidentate anions with high stability constants. Y-shaped anions such as carboxylate are especially strongly bound.<sup>37</sup>



**Figure 1.20** The ideal two-point interaction between (thio)urea and carboxylate anions<sup>37</sup>

Derivatives of simple (thio)urea receptors were developed by Umezama and co-workers<sup>40</sup> to take advantage of this ability to bind more complex anions selectively. In one of the ligands two thiourea groups were used to create a rigid structure in which dihydrogen phosphate could be bound. High stability constants were obtained and this was credited to the preorganisation in the receptor (Figure 1.21).

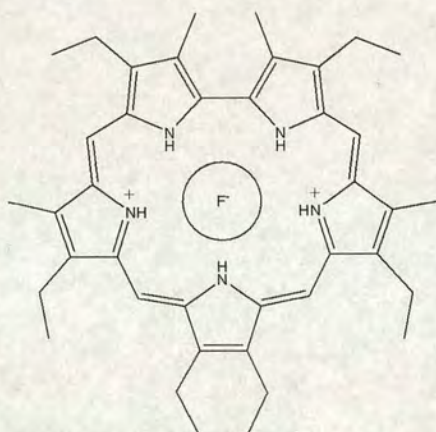


**Figure 1.21** Preorganised thiourea receptor for complex anions<sup>40</sup>



Pyrrole NH groups have been used<sup>41</sup> and have emerged to become one of the most useful anion binding motifs as, unlike amides, they contain no hydrogen-bond acceptors which can often cause intra- or inter-molecular hydrogen-bonding. This is important as this type of interaction weakens a receptor and inhibits its ability to bind anions efficiently as anion-binding competes with self-association. Another advantage is that pyrroles are neither very basic nor acidic so they can sustain an anion-receptor complex under a number of conditions.<sup>41</sup> They are also very versatile as they can be easily functionalised and incorporated into other structures.<sup>41</sup>

They were first discovered to be useful in the area of anion recognition in 1990 when a diprotonated pentapyrrolic macrocycle (Figure 1.22), known as a sapphyrin, was found, by chance, to bind a fluoride anion within hydrogen-bonding distance of all five NH groups in the solid state.<sup>42</sup>



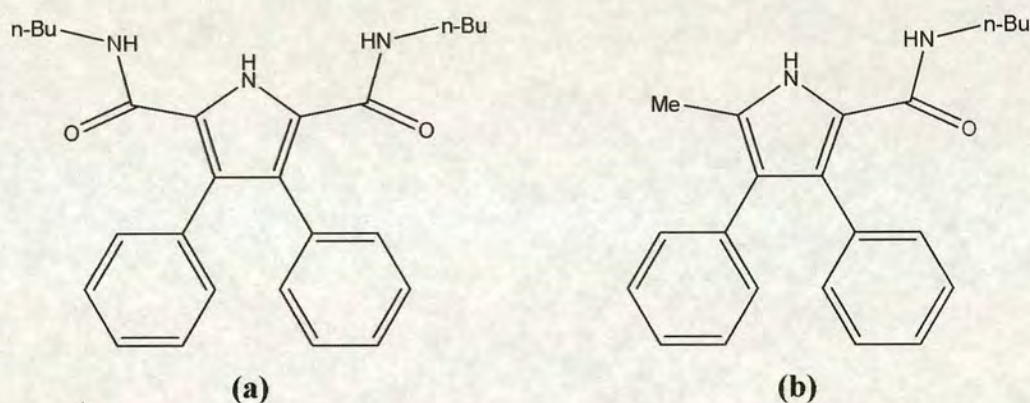
**Figure 1.22** Diprotonated pentapyrrolic macrocycle with coordinated fluoride.<sup>42</sup>

A crystal structure was later obtained of the same macrocycle binding chloride by hydrogen-bonds, however this time one chloride was bound above the cavity and the other was bound below. This suggested that fluoride would be more strongly bound in solution as it fitted better into the cavity and this was confirmed by fluorescence titration experiments which showed a selectivity of three orders of magnitude for fluoride over chloride.<sup>43</sup>

Pyrrole itself has recently been found to stabilise an anion complex in the solid state, but these interactions were not found to persist significantly in solution<sup>44</sup> and

highlighted that pyrrole may work most efficiently as an important component of a larger anion receptor.

This concept has recently been developed by Gale and co-workers<sup>45-47</sup> who have synthesised a series of 2,5-diamidopyrroles. Many of those developed have shown particular selectivity for oxo-anions. The receptor **(a)** in Figure 1.23 was found to bind benzoate with an association constant of  $2.5 \times 10^3 \text{ M}^{-1}$  in contrast to the mono-functionalised receptor **(b)** which has an association constant of only  $202 \text{ M}^{-1}$  for the oxo-anion. The higher affinity was attributed to the ability of the 2,5-diamidopyrrole to form three hydrogen-bonds to the anion<sup>48</sup> rather than just the two possible in **(b)**. This was later confirmed by a crystal structure of the complex showing how well positioned anion-binding groups can be used in combination to create a more effective receptor framework.

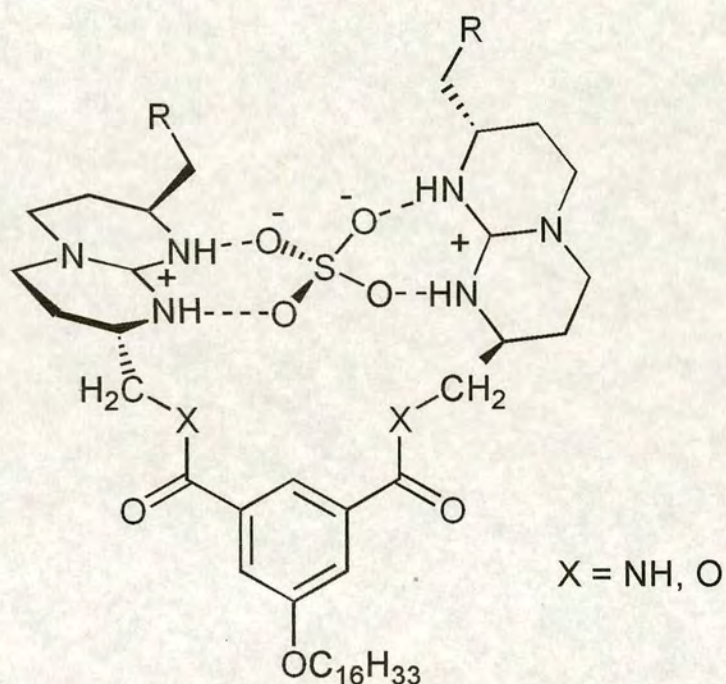


**Figure 1.23** A 2,5-diamidopyrrole and a 2-amido-5-methylpyrrole for anion binding.<sup>47</sup>

The aim of this project is to design an anion-binding site that is preferentially selective for sulfate over other anions. The literature has been severely lacking in sulfate-selective receptors and only a handful of examples had been published until very recently.

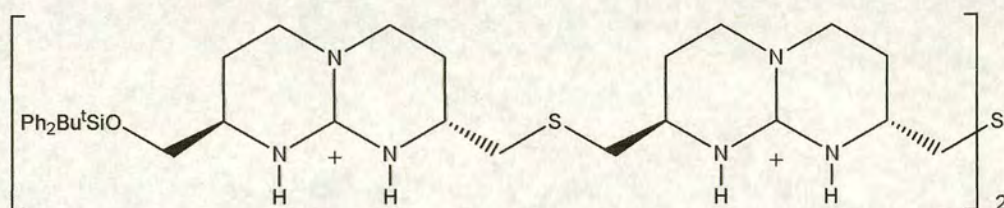
One of the most successful designs has involved the use of guanidinium groups.<sup>49</sup> The guanidinium moiety is an interesting case and it is set up very much like ureas in that it can form two hydrogen-bonds to anions such as carboxylate. However it is also positively charged resulting in the formation of more strongly bound complexes

with anions. It is protonated over a wide pH range ( $pK_a \sim 13.5$ ) and this obviously aids anion-binding. In the example, in Figure 1.24, bicyclic guanidine units are used to induce the selectivity.<sup>49</sup> The acyclic receptor is designed for tetrahedral anions as the two bicyclic guanidines align perpendicular to each other. The two units are connected via an aromatic spacer unit and the system shows a remarkable selectivity for sulfate over hydrogen phosphate indicating that the particular geometry of this receptor is favoured by the sulfate anion.



**Figure 1.24** Ditopic guanidinium receptors for sulfate extraction<sup>49</sup>

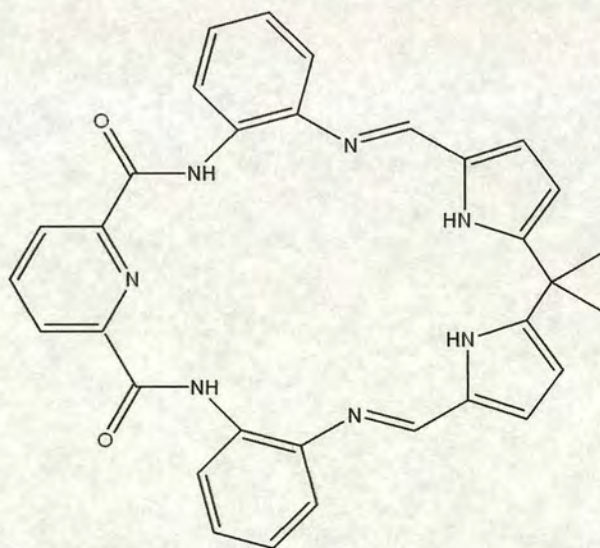
The ability of guanidinium units to bind sulfate was also shown by De Mendoza and co-workers<sup>50</sup> who demonstrated how two strands of a guanidinium-based compound (Figure 1.25) could fold in a double helical structure around a sulfate anion.



**Figure 1.25** A guanidinium receptor for sulfate encapsulation<sup>50</sup>

Unfortunately guanidinium groups would not be suitable components of reagents for most hydrometallurgical processes as they are very difficult to synthesise, therefore expensive, and the high  $pK_a$  of the unit would make it very hard to strip out the sulfate and recycle the ligand.

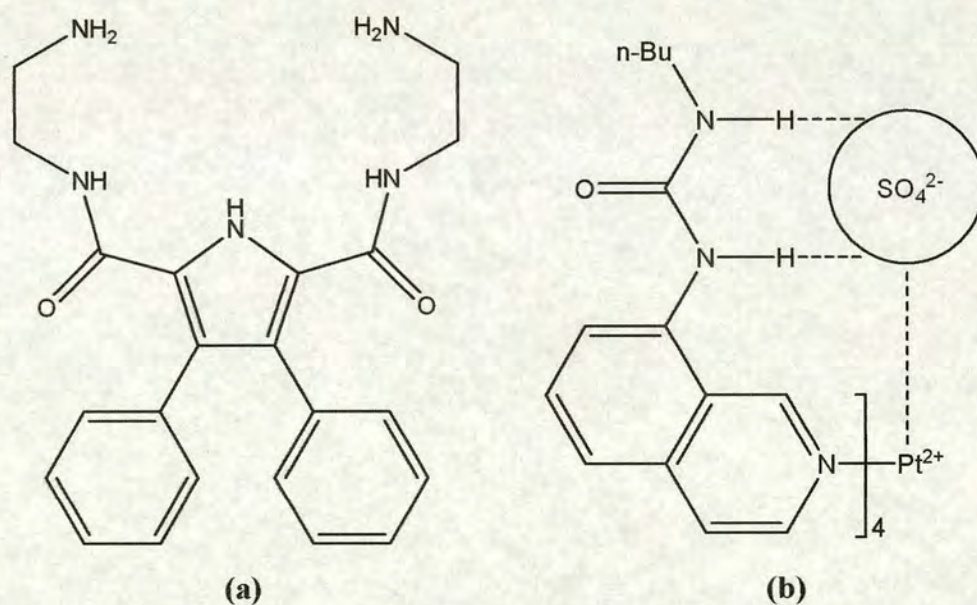
A number of sulfate-receptors have been developed very recently with a variety of different designs. Sessler and co-workers have synthesised a diamidodipyrromethane macrocycle which shows an extraordinarily high sulfate over nitrate selectivity (Figure 1.26).<sup>51</sup> This selectivity is particularly significant because of the need for efficient removal of the sulfate anion from nitrate-rich radioactive waste streams.<sup>52</sup> This is required as, unlike nitrate anions, they can adversely affect the treatment process. The macrocycle is a hybrid of the well known anion-binding motif pyridine-2,6-dicarboxamide<sup>53</sup> and dipyrromethane fragments which are key anion-binding components in calixpyrroles (see Figure 1.30).<sup>44</sup> This therefore effectively demonstrates how anion-binding units can be combined in novel ways to alter selectivity patterns.



**Figure 1.26** A new diamidodipyrromethane macrocycle with high  $SO_4^{2-}$  vs  $NO_3^-$  selectivity.<sup>51</sup>

Gale and co-workers have recently synthesised two very different but very successful receptors for sulfate. The first utilises his well developed 2,5-diamidopyrrole backbone which has been used to create a number of anion receptors with varying properties.<sup>45-47</sup> In this case amine pendant arms were attached to the 2,5-

diamidopyrrole unit (Figure 1.27 (a)) and the resultant receptor showed a particularly high affinity for the  $\text{HSO}_4^-$  anion.<sup>54</sup> This was attributed to a proton transfer from the  $\text{HSO}_4^-$  anion to the receptor to produce a more highly charged receptor and anion ( $\text{SO}_4^{2-}$ ). Indeed when the analogous ammonium receptor was prepared only a very weak association was observed, probably due to the absence of proton exchange. This demonstrates how the nature of a receptor's pendant groups can have a profound effect on its anion-binding properties. The second design is based on a Pt(II) complex of four urea functionalised *iso*-quinoline ligands (Figure 1.27 (b)) which shows selectivity for sulfate over chloride, bromide and iodide.<sup>55</sup> The complex selectively encapsulates sulfate in a “cone” formation in both solution and the solid state by a combination of electrostatic attraction from the Pt centre and hydrogen-bonding from the ureas. In fact the urea groups contribute a total of eight hydrogen-bonds to three of the four sulfate oxygens and this is made possible by the flexibility of the receptor.

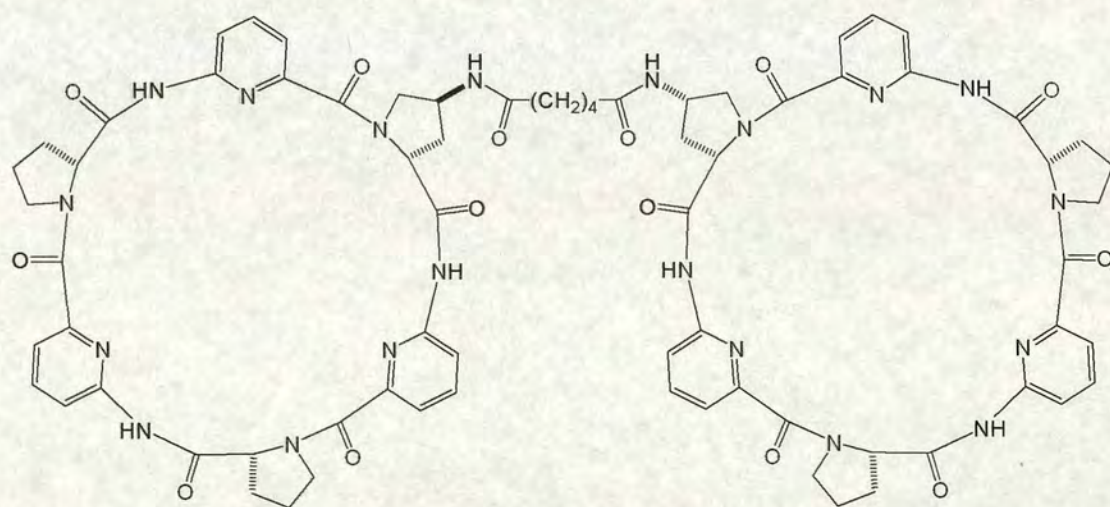


**Figure 1.27** Two different but effective sulfate receptors developed by Gale and co-workers.<sup>54, 55</sup>

A similar number of hydrogen-bond donors are used in the sulfate-binding protein, SBP, which has been developed by nature for the selective transport of the sulfate anion.<sup>56</sup> This natural anion receptor is a specialised protein which binds sulfate in a

solvent-inaccessible cavity by means of seven hydrogen-bonds. These are received from the peptide backbone NH, serine OH and tryptophane NH groups. The SBP, in contrast, to the phosphate-binding protein, PBP, only binds fully deprotonated anions and this is facilitated by the absence of any of the hydrogen-bond acceptors which are important to the operation and selectivity of the PBP.<sup>24</sup> This illustrates how very small differences in receptor design can profoundly affect its selectivity.

Hydrogen-bonds are very important for selective anion encapsulation and an electrostatic interaction is not always necessary. This has been especially well proven by Kubik and co-workers who have developed a neutral anion receptor which uses only hydrogen-bonds for recognition but still shows appreciable anion selectivity in water/methanol solution.<sup>57</sup> This is particularly notable because neutral receptors often fail to function in aqueous media due its competitive nature.<sup>57</sup> The compound consists of two cyclohexapeptide subunits containing L-proline and 6-aminopyridine acid subunits in an alternating sequence, which are connected by an adipic acid spacer (Figure 1.28).



**Figure 1.28** A neutral receptor with a remarkable sulfate affinity in aqueous solution.<sup>57</sup>

The receptor shows a particularly high affinity and selectivity for sulfate in aqueous solution, forming 1:1 complexes. The encapsulation of the anion is likened to the

storage of a pearl in an oyster as the two cyclohexapeptide subunits operate as two “shells” which enclose the sulfate anion (“pearl”) by means of an adipic acid spacer or “hinge”. This has led to the use of the term “molecular oyster”. The anion is bound exclusively by hydrogen-bonds in the cavity, sufficiently strongly to prevent aqueous solvation, and is therefore a useful model for the sulfate-binding protein.

The design of a selective sulfate-receptor is clearly a challenging target as there are only a few literature examples. However the successful systems have very varied structures opening up a number of design possibilities. It has also been shown that very subtle changes to the receptor framework can have a significant affect on the selectivity.

## 1.8 The Hofmeister Series

The limited number of selective sulfate-receptors reported in the literature is surprising considering the important role the sulfate anion plays in biology<sup>56</sup> and the problems it causes in radioactive waste treatment processes.<sup>52</sup>

The difficulties associated with generating an efficient sulfate-receptor are strongly linked to a phenomenon known as the Hofmeister series which was first noted in 1888 when Franz Hofmeister was conducting experiments to rank the ability of various ions to precipitate a mixture of hen egg white proteins (Figure 1.29).<sup>58</sup>

strongly hydrated anions	weakly hydrated anions
Citrate <sup>3-</sup> > SO <sub>4</sub> <sup>2-</sup> = tartrate <sup>2-</sup> > HPO <sub>4</sub> <sup>2-</sup> > CrO <sub>4</sub> <sup>-</sup> > acetate <sup>-</sup> > HCO <sub>3</sub> <sup>-</sup> > Cl <sup>-</sup> > NO <sub>3</sub> <sup>-</sup> > ClO <sub>4</sub> <sup>-</sup>	

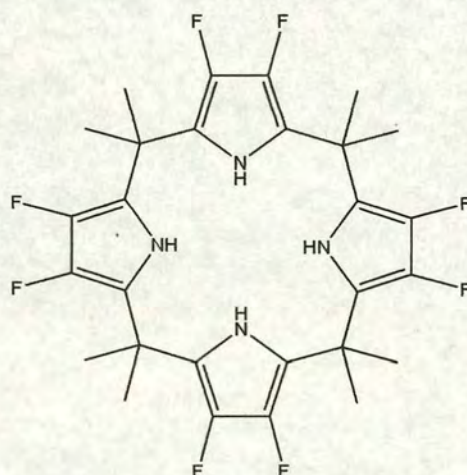
**Figure 1.29** The original Hofmeister series<sup>58</sup>

The series was found to have many applications and has been used to explain a body of data on the behaviour of water at interfaces and a number of associated phenomena.<sup>59</sup>

The Hofmeister order has also been found to be important when developing anion extractants, for use in liquid-liquid systems, because it can be used to predict why an anion such as  $\text{ClO}_4^-$  will generally be extracted, from aqueous media into a water immiscible solvent, over an anion like  $\text{SO}_4^{2-}$ . The reason is that  $\text{SO}_4^{2-}$  is much more heavily hydrated than  $\text{ClO}_4^-$ , and therefore more hydrophilic, so it prefers to stay in an aqueous environment. In general, anion-extraction is more favourable for large, charge-diffuse anions.

In order to reverse the Hofmeister effect an anion-binding solvent extractant is required to bind sufficiently strongly to compensate for dehydration associated with transfer to the organic phase. This is often done by using hydrogen-bond donors<sup>60</sup> or Lewis acid groups.<sup>24</sup> Numerous attempts have been made but as yet only limited success has been achieved in reducing or reversing the Hofmeister effect.

The selective solvation of hydrophilic phosphate anions is achieved in nature by the phosphate-binding protein by means of twelve H-bonds.<sup>24</sup> This level of specificity is very difficult to achieve when designing receptors but some systems, such as the fluorinated calixpyrroles developed by Moyer and co-workers<sup>61</sup>, have had some success. The neutral receptors were found to extract caesium salts of smaller anions as effectively as the large charge-diffuse iodide. For example,  $\beta$ -octafluoro-*meso*-octamethylcalix[4]pyrrole (Figure 1.30) extracts chloride as effectively as iodide into nitrobenzene.



**Figure 1.30** A  $\beta$ -fluorinated calix[4]pyrrole which extracts  $\text{Cl}^-$  and  $\text{Br}^-$  as effectively as  $\text{I}^-$ .<sup>61</sup>



The design of receptors, which can reverse the Hofmeister bias, is an important future target for effecting the separation of hydrophilic anions in radioactive waste remediation and various other applications such as new metal recovery processes, based on metal sulfate extraction.

## **1.9 Ligand Requirements**

Selectivity, as previously discussed, is a particularly important requirement of any extractant. However there are also a number of other criteria which need to be fulfilled in order for the ligand to be usable in a commercial metal recovery process and some of these will be discussed in this report.

**Strength** – This is required as if the ligand does not show a sufficient strength of extraction then the selectivity becomes irrelevant.

**Speed** – The extraction needs to take place quickly as slow kinetics of either complex formation or phase transfer reduces the efficiency of the process.

**Separation** – The two-phase system needs to settle and reach equilibrium rapidly after the extraction.

**Solubility** – The ligand and the resultant complex need to be soluble in water-immiscible solvents and to have negligible solubility in the aqueous phase.

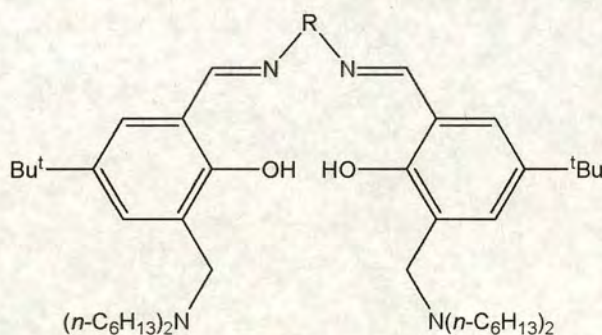
**Stability** – The ligand needs to show both hydrolytic stability and resistance to oxidation.

**Safety** – The ligand needs to satisfy all safety requirements and environmental regulations.

**Synthesis** – The ligand synthesis needs to be simple and inexpensive to make its production industrially viable.

## 1.10 Objectives

In this chapter it has been shown that efficient metal recovery can be facilitated by a number of different techniques such as pyrometallurgy, froth flotation and hydrometallurgy. The pyrometallurgical treatment of metal sulfide ores, while successful, has environmental problems (eg. emission of SO<sub>2</sub> gas) so new methods of recovery are required. The research described in this thesis focuses on designing ditopic ligands for the solvent extraction of transition metal sulfates which could be used in new flowsheets for the hydrometallurgical processing of metal sulfide ores. Prototype ligands have been developed by the Tasker group<sup>15</sup> but detailed studies of their extractive behaviour in a two-phase system, over a range of pH, are required in order to assess their suitability for use in commercial recovery processes. A key aim of such a study is to find a pH region where loading of both metal and sulfate is maximised and this is investigated in chapter 2 by using some simple derivatives of the prototype ligands (Figure 1.31). The role of the metal in “templating” the formation of the anion-binding site is also examined.



L	1	2	3	4
R	-(CH <sub>2</sub> ) <sub>2</sub> -	2,2'-biphenyl	(±)- <i>trans</i> -1,2-cyclohexane	<i>o</i> -C <sub>6</sub> H <sub>4</sub>

**Figure 1.31** Ligands developed for solvent extraction experiments in CHCl<sub>3</sub>/H<sub>2</sub>O (chapter 2).

Extractants used in hydrometallurgical processes must meet a number of different requirements (section 1.9) and one of the most important is that the ligand has

stability. In chapter 3 the hydrolytic stability of the ligands detailed in Figure 1.31 and two new ligands, 4,4'-di-*tert*-butyl-6,6'-bis(di-hexylaminomethyl)-2,2'-(ethylenedinitrilo-1,1'-phenyldimethylidyne) diphenol and *N,N'*-dimethyl-*N,N'*-bis(2-hydroxy-3-[(*E*)-phenyliminomethyl]-5-*tert*-butylbenzyl)hexane-1,6-diamine, which exhibit improved stabilities at low pH are discussed.

Selectivity of extraction, especially with respect to the binding and transport of sulfate, is also an important requirement for a metal sulfate extractant. In chapter 4 the anion selectivity of a series of ligands, containing amide hydrogen-bonding groups, are described. Pre-organisation has been shown, in the literature,<sup>40, 51</sup> to be important to achieve selective anion-binding so in chapter 5 macrocyclic ligands were developed with the aim of improving the “strength” and selectivity of sulfate complexation and the efficiency of transport.

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**Chapter 2 : Metal Salt Extractants Containing  
3-Dialkylaminomethylsalicylaldimine Units**

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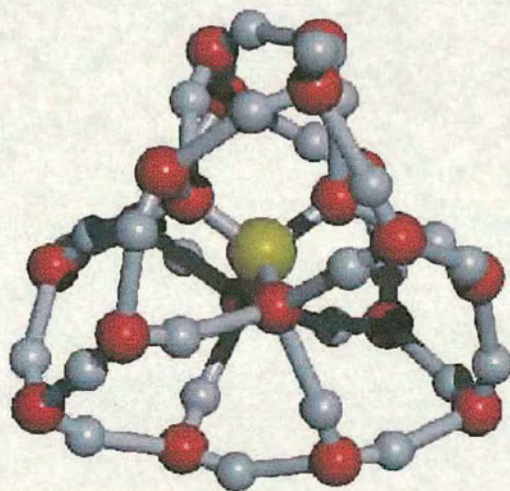
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## 2.1 Introduction

The design of ditopic ligands, for the co-extraction of cations and anions, is a complicated task as the coordination of an ion into one of the binding sites can change the overall configuration of the ligand and hence the arrangement of the other binding site. However, successful design of such a system could take advantage of this and use the coordination of a cation to template the formation of the anion-binding site. Achieving this type of co-operative binding is a key target when designing the metal sulfate extractants discussed in this chapter.

Another difficult challenge when creating a ditopic ligand for the hydrometallurgical processing of metal sulfates (section 1.4) is to be able to achieve efficient sulfate extraction. This problem is intrinsically linked to a phenomenon known as the Hofmeister series<sup>1</sup> (section 1.8) which is related to the levels of hydration of anions. In water it has been shown that sulfate forms a hydration shell from small rings of hydrogen-bonded water (Figure 2.1).<sup>2</sup> This clustering arrangement is thought to contain as many as sixteen water molecules and support for this comes from photoemission spectroscopy as there is an obvious change in properties beyond  $n = 16$  for  $\text{SO}_4^{2-}(\text{H}_2\text{O})_n$  clusters.<sup>3</sup>

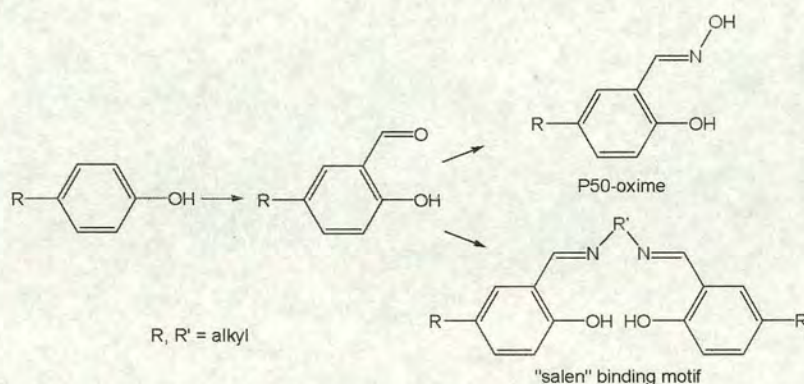


**Figure 2.1** A sulfate anion surrounded by a hydration shell of 16 water molecules.<sup>4</sup>

Such a level of hydrogen-bonding is not seen in anions with similar tetrahedral structures such as  $\text{ClO}_4^-$ . In fact  $\text{ClO}_4^-$  is found at the opposite end of the Hofmeister series and is only weakly hydrated and therefore more easily extracted into a water-immiscible solvent.

Sulfate's high affinity for an aqueous environment makes it very difficult to extract so a strong coordination site must be constructed, within a hydrophobic ligand, before transport into a water-immiscible solvent becomes favourable. Very strong and highly effective anion-binding units are therefore required in the ligand to promote sulfate-extraction. Amine groups, when protonated, can have electrostatic interactions with anions and they also have the ability to hydrogen-bond to them. However for two amine groups to be effective, for the encapsulation of a di-negative anion such as sulfate, they need to be fixed in a suitable arrangement so that they can both interact with the anion.

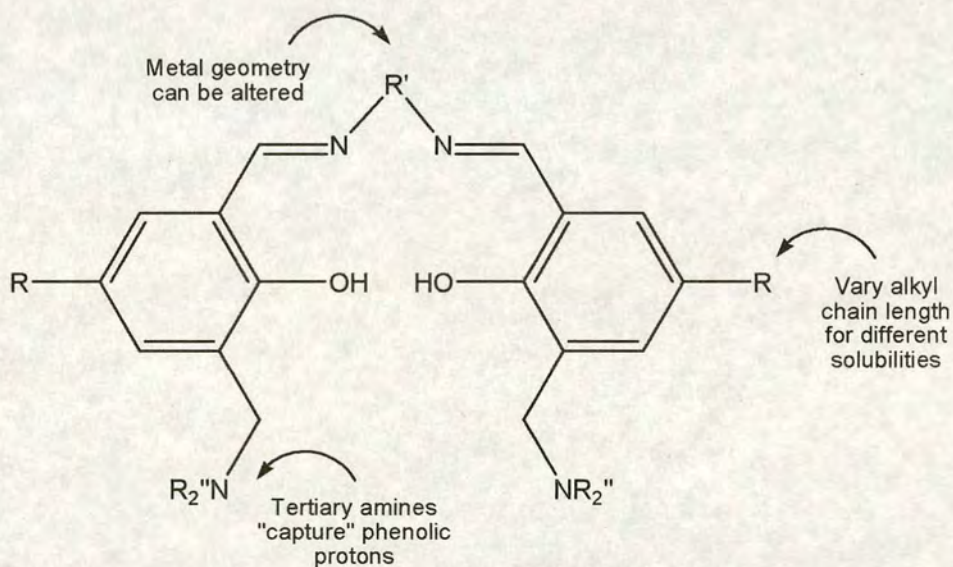
There are a variety of metal-binding sites, used in ligands, which have been designed and utilised for the solvent extraction of metals.<sup>5</sup> One of the most important requirements in industry, especially for the recovery of base metals (eg. Cu, Ni, etc.), is that the cost of the extractant is low. The phenolic oxime extractant, P50, which is used in the hydrometallurgical recovery of copper, is synthesized by a cheap and high yielding route.<sup>6</sup> One of the precursors, the parent salicylaldehyde, can also be used in the synthesis of "salen" [*N,N'*-ethylenebis(salicylideneaminato)] and derivatives (Figure 2.2).



**Figure 2.2** Synthesis of salicylaldoximes and the "salen" binding unit.

The “salen” binding unit has been found to be highly effective in a number of industrial applications. Cationic manganese(III) complexes of the salen ligand have been found to be effective catalysts for the epoxidation of various olefins<sup>7</sup> and cobalt salen complexes have been successfully used as mimics of biological oxygen carriers.<sup>8</sup> The cobalt(II) complexes, when used in combination with a base such as pyridine, react with oxygen in a rapid, reversible reaction and comparisons between this process and the binding of oxygen in hemoglobin have greatly contributed to the understanding of oxygen carrier proteins.

Salen is known to form stable complexes with nickel and copper<sup>9, 10</sup> by deprotonation of the phenol groups. It can also be conveniently functionalised, in the position *ortho* to the hydroxyl group, with pendant amine arms (Figure 2.3).<sup>11</sup> The advantage of this is that the tertiary amines can then capture the protons liberated upon metal coordination and align in close proximity to generate a dicationic binding site for anions. The ligand can therefore operate in its zwitterionic form to generate charge neutral metal salt complexes.



**Figure 2.3** Prototype metal salt extractant

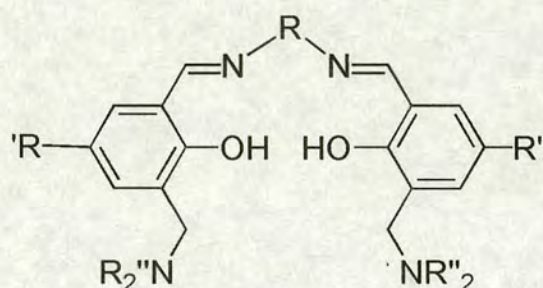
A number of these ligands have been synthesised by the Tasker group<sup>12</sup> and they have been shown to extract CuSO<sub>4</sub>, giving loadings close to the theoretical maximum (1 : 1 : 1, ligand : Cu<sup>2+</sup> : SO<sub>4</sub><sup>2-</sup>), into CHCl<sub>3</sub> at pH 3.8. However knowledge of their

extractive behaviour, over a range of pH, is necessary to assess whether they could be used in commercial metal recovery processes. This chapter will discuss the solution studies of some simple derivatives of the prototype ligands. A key aim of this study is to define the pH region where loading of copper and sulfate is maximised.

## 2.2 Synthesis

### 2.2.1 Ligands and Metal Complexes

The ligands (Figure 2.4) and metal complexes synthesised for this chapter are summarised below (Table 2.1).



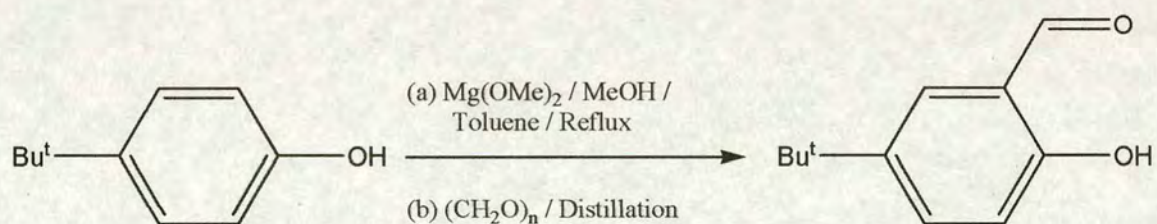
**Figure 2.4** Prototype metal sulfate extractants; R = alkyl, aryl; R' = alkyl; R'' = alkyl.

**Table 2.1** Ligands and metal complexes used and their designated reference numbers. \*The free Ligand 6 was not synthesised, [Cu(6)SO<sub>4</sub>] was made directly from the aldehyde (section 2.8.4.2).

Ligands	R	R'	NR'' <sub>2</sub>	Metal Complexes	
1	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>	7	[Cu(1-2H)]
2	2,2'-biphenyl	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>	8	[Cu(2-2H)]
3	± <i>trans</i> -1,2-cyclohexane	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>	9	[Cu(3-2H)]
4	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	N( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>2</sub>	10	[Cu(4-2H)]
5	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	piperidine	11	[Zn(1-2H)]
6*	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	piperidine	12	[Ni(4-2H)]
				13	[Cu(5)SO <sub>4</sub> ]
				14	[Cu(6)SO <sub>4</sub> ]

## 2.2.1.1 Synthesis of Free Ligands

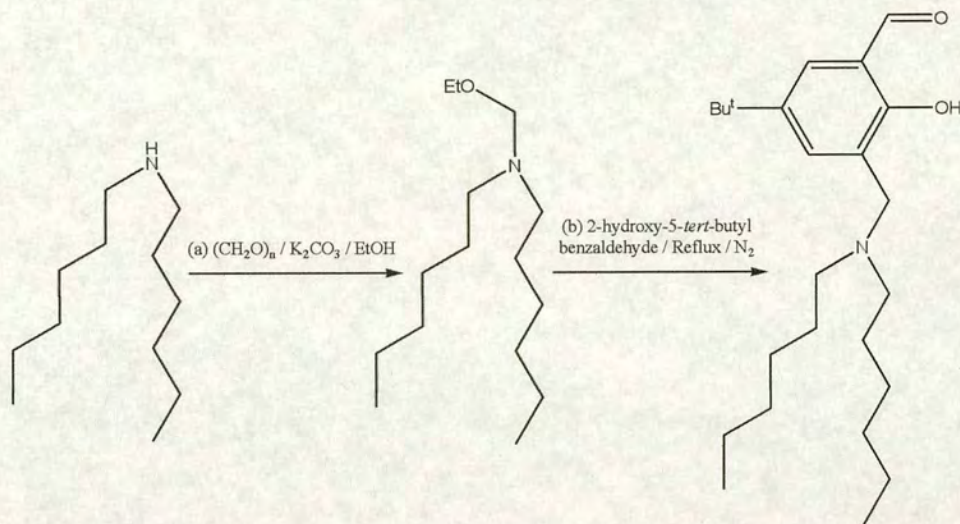
Ligand **5** with piperidine substituents was prepared as described previously.<sup>13</sup> The initial intention was to use this in detailed solvent extraction experiments. However, when metal salt complexes of ligand **5** were formed they were found to have an appreciable solubility in both the aqueous and organic phases. Ligands **1-4** with longer alkyl chains, two *n*-hexyl groups attached to the pendant amines, were prepared to minimise bleeding of ligands and complexes to the aqueous phase. These were readily synthesised by a four-step convergent synthesis from *tert*-butyl-substituted salicylaldehyde, paraformaldehyde, dihexylamine, and a diamine of choice. The preferred method used in this thesis for preparation of substituted salicylaldehydes was based upon the industrial process developed by Levin and co-workers<sup>14</sup> involving magnesium-mediated formylation (Figure 2.5) using magnesium methoxide and paraformaldehyde.



**Figure 2.5** The formylation of *tert*-butyl phenol

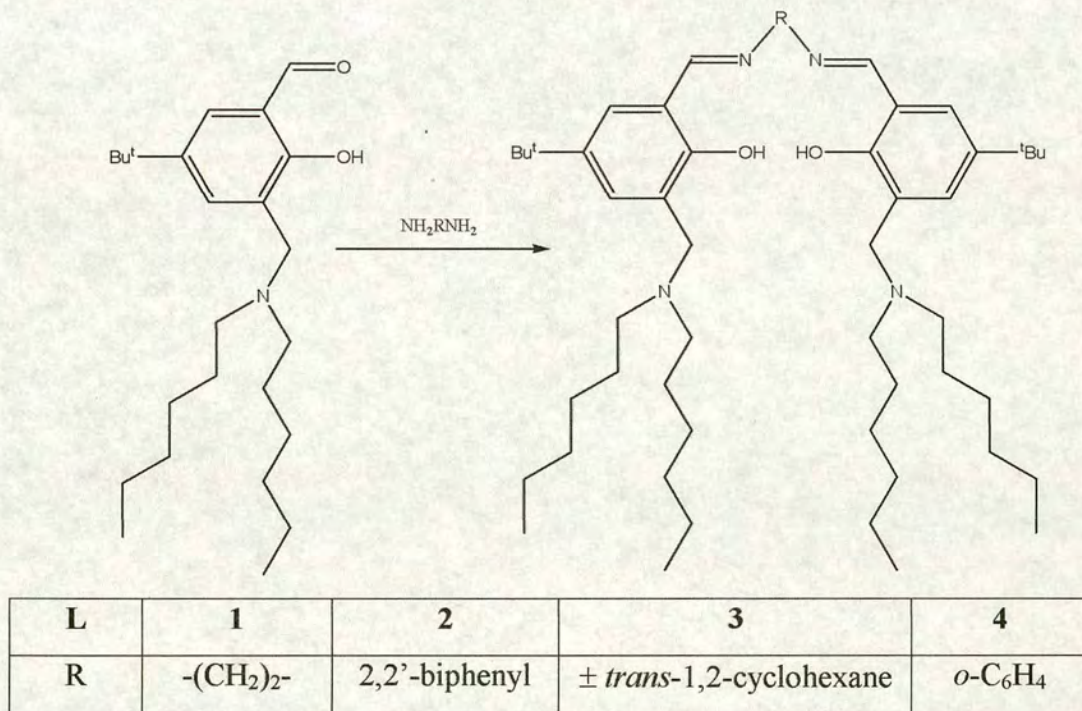
Subsequent substitution in the remaining *ortho* position with the dihexylaminomethyl group was achieved *via* a two-step Mannich reaction under non-aqueous aprotic conditions. Firstly the Mannich base ethoxy-N-dihexylaminomethane was prepared, by an adaptation of the method used by Fenton and co-workers<sup>11</sup>, from dihexylamine and paraformaldehyde in ethanol with potassium carbonate and purified by distillation. Then 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzaldehyde was synthesised by refluxing the Mannich base with the salicylaldehyde in acetonitrile, under a dinitrogen atmosphere (Figure 2.6). The product was obtained in a moderate

yield (~50%) after purification by silica column chromatography (ethyl acetate:hexane, 1:20).



**Figure 2.6** The two-step Mannich reaction used to append a bis-hexylaminomethyl group onto 2-hydroxy-5-*tert*-butylbenzaldehyde.

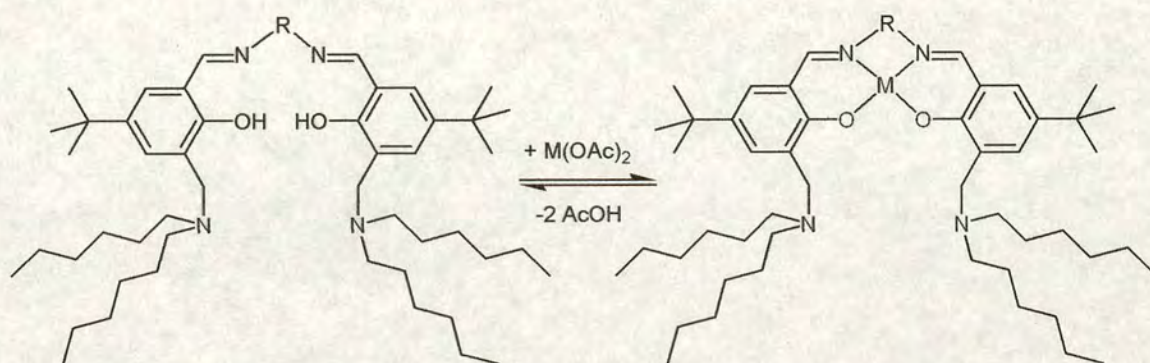
The Schiff base condensations of the substituted salicylaldehydes were carried out with the appropriate diamines (Figure 2.7) at room temperature in non-aqueous solvents, giving the products in high yield (~ 98 %).



**Figure 2.7** Schiff base condensations of substituted salicylaldehydes to give ligands 1 – 4.

## 2.2.1.2 Synthesis of Metal Complexes

Neutral “metal-only” complexes of **1** – **4** were prepared from metal(II) acetates (Figure 2.8). The crude complexes were then washed with pH 9 ammonia solution to remove excess metal acetate and to ensure the amines were free of protons.



**Figure 2.8** The formation of the “metal-only” complexes  $[M(L-2H)]$ ,  $M = Cu, Ni$  or  $Zn$

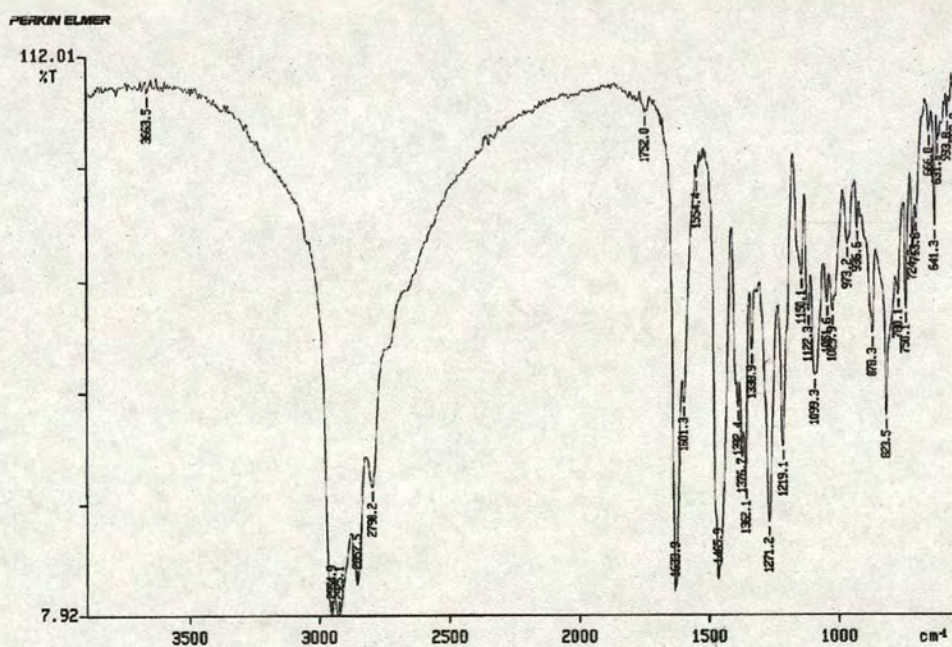
Colour changes, indicating complex formation, were instantaneous in methanol solution except for the zinc(II) complex which has a full set of d-orbitals and hence no colour. The changes were as expected for  $H_2salen$ -type complexes of these metals<sup>12</sup>, for example red-orange for nickel(II) and dark green for copper(II). The “metal-only” complexes **7** – **12** were found to have sufficient solubility in chloroform and very low solubility in water to make them suitable for use in solvent extraction experiments.

The copper sulfate complex, **13**, of ligand **5** was prepared as described previously.<sup>13</sup> The copper sulfate complex **14** was prepared by contacting two equivalents of 2-hydroxy-3-(piperdin-4-ylmethyl)-5-*tert*-butylbenzaldehyde<sup>13</sup> with one equivalent of phenylene-1,2-diamine in methanol. The resulting solution was intimately mixed with one equivalent of copper sulfate in methanol to yield the complex. The ligand was not isolated as the  $CuSO_4$  complex was made solely to prepare crystals suitable for X-Ray diffraction.

## 2.3 Characterisation

### 2.3.1 IR Spectroscopy

All of the ligands and metal complexes have been characterised by FTIR spectroscopy. Stretches can be seen for C-H bonds ( $2920 - 2970 \text{ cm}^{-1}$ ) in each spectrum. The strong imine band (C=N) also appears in all of the spectra of the ligands (eg. Figure 2.9) and complexes ( $1610 - 1640 \text{ cm}^{-1}$ ). The presence of this signal and the absence of a carbonyl stretch ( $1683 \text{ cm}^{-1}$ ), from the aldehyde precursor, confirms that the Schiff base condensation reactions have gone to completion in every case. The imine signal is lowered slightly in energy upon metal complexation (Table 2.2). This indicates that the imine nitrogen is involved in metal binding. This is consistent with various crystal structures which contain the salen



**Figure 2.9** The IR spectrum of **1** showing a strong imine band at  $1634 \text{ cm}^{-1}$  and stretches for C-H bonds between  $2920$  and  $2960 \text{ cm}^{-1}$ .

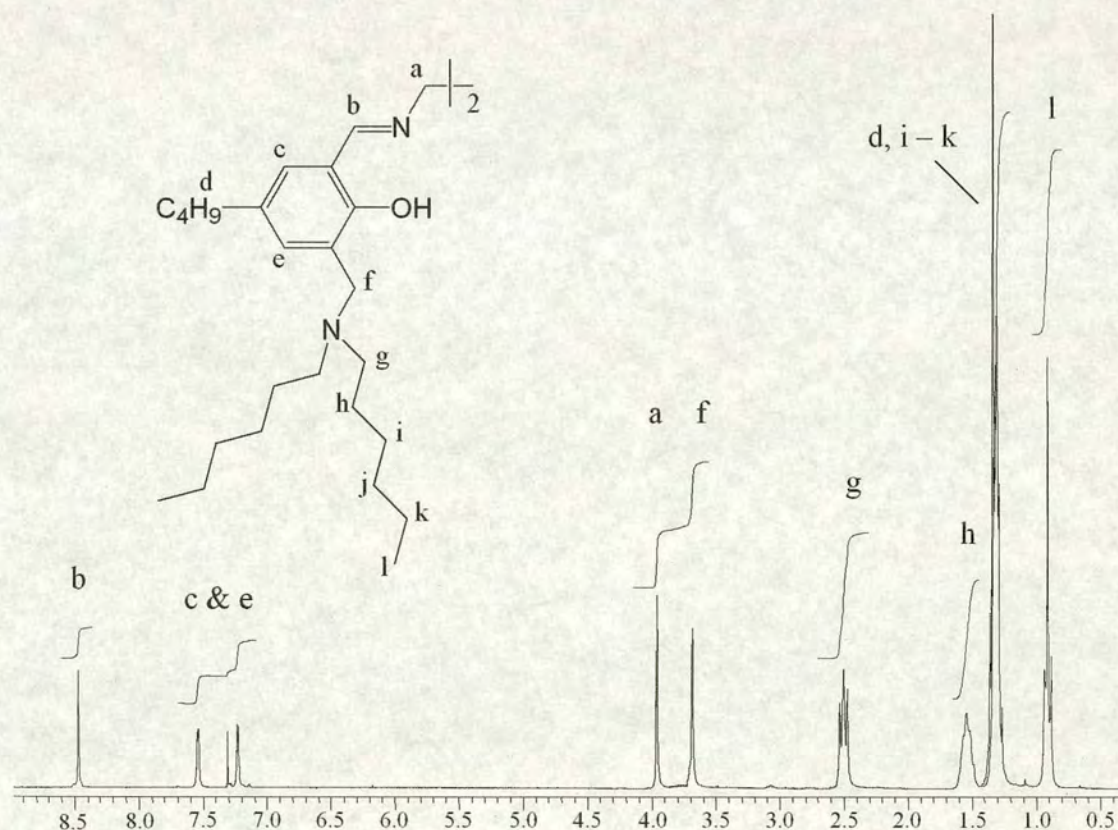


**Table 2.2** The imine stretching frequencies for ligands 1 – 4 and their metal complexes ( $\text{cm}^{-1}$ ).

	Ligand 1	Ligand 2	Ligand 3	Ligand 4
<b>L</b>	1634	1618	1632	1619
<b>Cu</b>	1628	1617	1615	1618
<b>Ni</b>	-	-	-	1618
<b>Zn</b>	1632	-	-	-

### 2.3.2 NMR Spectroscopy

All of the ligands (eg. Figure 2.10) and precursors have been characterised by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy in  $\text{CDCl}_3$ . The diamagnetic zinc(II) and nickel(II) complexes **11** and **12** were both characterised by  $^1\text{H}$  NMR spectroscopy at 250 MHz. There was no evidence of any paramagnetic line broadening in the nickel(II) complex indicating that the metal is coordinated in a square planar geometry in solution.

**Figure 2.10** The  $^1\text{H}$  NMR spectrum of **1** showing a peak for the imine proton at  $8.4 \delta$  ( $\text{CDCl}_3$ ).

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR data provide evidence for the successful completion of the Schiff base condensation reactions as relevant signals for the imine bond ( $-\text{CH}=\text{N}-$ ) appear in both (Table 2.3). Further support comes from the absence of an aldehyde peak in the  $^1\text{H}$  NMR spectra ( $\sim 10.5 \delta$ ) and a carbonyl signal ( $\sim 190 \delta$ ) in the  $^{13}\text{C}$  NMR spectra of all the ligands.

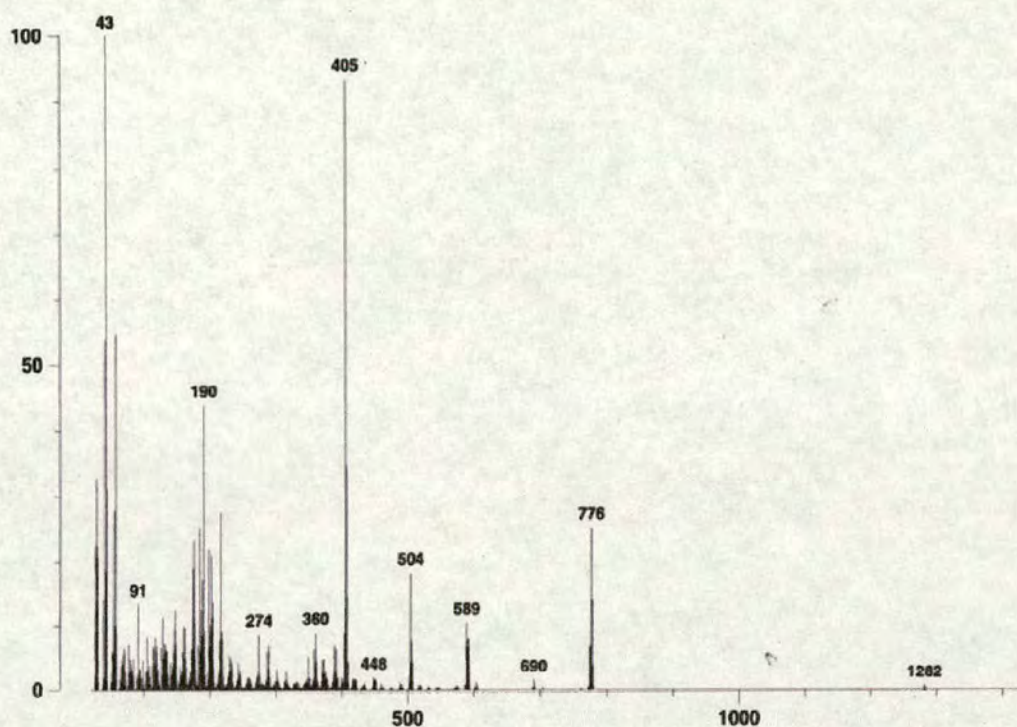
The zinc(II) and nickel(II) complexes **11** and **12** also show peaks for the imine functionality (Table 2.3). The peak for the imine proton, which is situated close to the metal coordination site, is shifted further upfield than in the free ligand in both cases indicating that the metal is shielding the imine. This effect is more prominent in the nickel(II) complex than in the zinc(II) complex. The spectrum of the zinc complex contains some broad peaks and this is possibly due to exchange of the zinc cation between ligands. This could occur as a result of incomplete complexation of zinc(II) (see section 2.3.3).

**Table 2.3** The imine  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shifts for ligands **1** – **4** and metal complexes **11** and **12** ( $\text{CDCl}_3$ ).

	$\delta_{\text{H}}$	$\delta_{\text{C}}$
Ligand <b>1</b>	8.44	166.4
Ligand <b>2</b>	8.53	166.4
Ligand <b>3</b>	8.30	165.4
Ligand <b>4</b>	8.83	161.1
Zn ( <b>1-2H</b> )	8.30	-
Ni ( <b>4-2H</b> )	8.26	-

### 2.3.3 Mass Spectrometry

The FAB mass spectra of the ligands **1** – **4** all show peaks assignable to the free ligands (eg. ligand **1**, Figure 2.11). FAB mass spectrometry of the copper and nickel “metal-only” complexes indicated a metal to ligand ratio of 1:1 in each case. No evidence was seen for any complexes containing more than one metal ion.

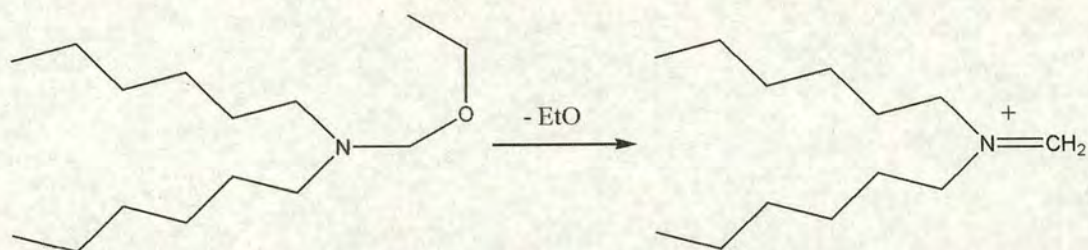


**Figure 2.11** The FAB mass spectrum of **1** showing a peak at  $m/z = 776$  for the free ligand

The zinc(II) complex **11** showed peaks for a 1:1 complex but also a notable peak for the free ligand and this was not seen in the other metal complex spectra. ICP data (section 2.8.4.1) indicated that the metal to ligand ratio in **11** was approximately 5:6 so it is likely that the zinc complexation was incomplete.

The FAB mass spectra of the copper sulfate complexes **13** and **14** indicated a metal to ligand to sulfate ratio of 1:1:1. Therefore the 2:2:2 assemblies seen in the solid state were not observed (section 2.6).

The FAB mass spectrum for the Mannich base ethoxy-*N*-dihexylaminomethane did not give the expected peak. The parent ion ( $M^+$ ) was not found but there was a strong peak at  $m/z = 198$ . This ratio corresponds to the positively charged iminium ion ( $M - EtO$ , Figure 2.12) which is thought to be the active species in the Mannich reaction.<sup>15, 16</sup> The Mannich base is prepared as an intermediate step so it is not surprising that it fragments in this way.



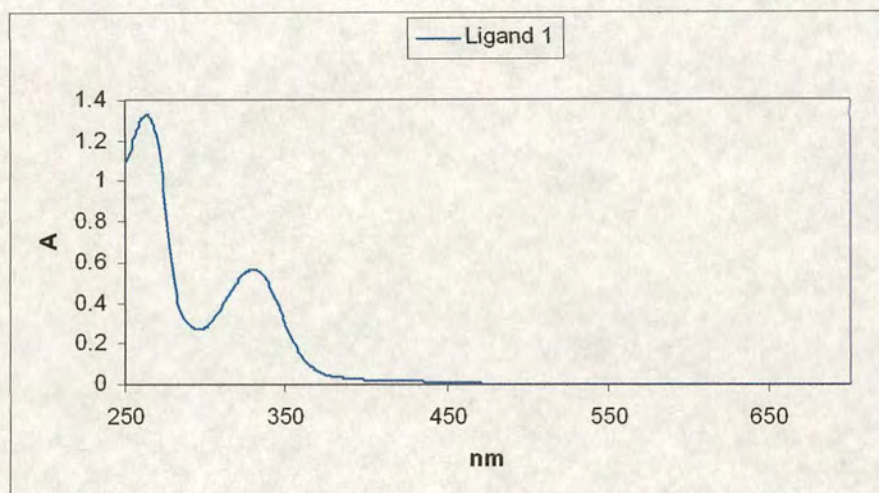
**Figure 2.12** The formation of the iminium ion from the Mannich base.

### 2.3.4 UV-Visible spectroscopy

The electronic absorption spectra were recorded for the metal complexes **7-14**. Metallation with nickel in complex **12** resulted in a broad band at 387 nm, due to intraligand  $\pi \rightarrow \pi^*$  transitions and a band at 495 nm with charge transfer character.<sup>10</sup> The band expected for d-d transitions was not visible probably due to the weakness of this feature and its close proximity to the charge transfer band. The copper “metal-only” complexes **7-10** and the copper sulfate complexes **13-14** spectra show an intense band in the 270-330 nm region, due to intense  $\pi \rightarrow \pi^*$  ligand based transitions, a moderately intense band in the 370-460 nm region, which is charge transfer in character and a weak feature is present around 550-580 nm which is assigned to d-d transitions.<sup>9, 17</sup> The exception to this behaviour is the 2,2'-biphenyl bridged copper complex **8**. The weak d-d transition in this complex is shifted to 640 nm (Table 2.4) from a maximum of 580 nm in the other copper complexes. This suggests that a different coordination geometry is imposed by the rigid and twisted biphenylene bridge. This is not unexpected as the square planar coordination of copper preferred by, for example, the *o*-phenylene bridged complex **10** would be highly unfavourable. The electronic absorption spectrum of the zinc complex **11** shows a band at 354 nm which is due to  $\pi \rightarrow \pi^*$  ligand based transitions. There are no d-d transitions in **11** as the complex has a full set of d-orbitals. The spectrum of free ligand **1** has two bands at 263 and 330 nm which are caused by  $\pi \rightarrow \pi^*$  ligand based transitions (Figure 2.13).

**Table 2.4** Maxima in the UV-Visible spectra of “copper-only”, [Cu(L-2H)], complexes 7–10 (CHCl<sub>3</sub>).

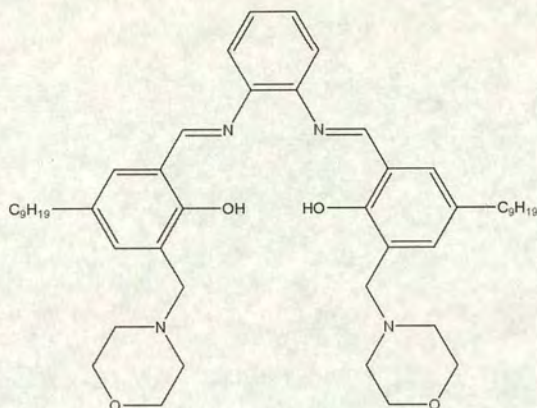
Copper Complex	$\lambda_{\max}$ 1 (nm)	$\lambda_{\max}$ 2 (nm)	$\lambda_{\max}$ 3 (nm)
7	283	382	576
8	286	410	640
9	281	379	560
10	318	446	580

**Figure 2.13** The electronic absorption spectra of 1 showing two  $\pi \rightarrow \pi^*$  ligand based transitions at 263 and 330 nm (CHCl<sub>3</sub>, 0.05 mM).

## 2.4 The pH Dependence of Sulfate-loading

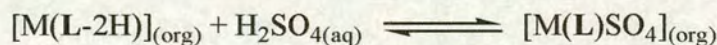
### 2.4.1 Proof of Concept Studies

The ditopic extractant shown in Figure 2.14 has been shown<sup>12</sup> to load CuSO<sub>4</sub> close to levels corresponding to formation of a 1 : 1 : 1 ligand : Cu<sup>2+</sup> : SO<sub>4</sub><sup>2-</sup> assembly. More detailed analysis of the extractive behaviour of such systems, over a range of pH, is needed to define efficient stripping and loading procedures. This type of study is particularly important for the sulfate anion as anion coordination<sup>18</sup> is not as well defined as cation coordination and there is only limited information in the literature on the behaviour of sulfate in a two-phase system.<sup>19</sup>



**Figure 2.14** A ditopic ligand found to load  $\text{CuSO}_4$  close to levels corresponding to formation of a 1 : 1 : 1 ligand :  $\text{Cu}^{2+}$  :  $\text{SO}_4^{2-}$  assembly.<sup>12</sup>

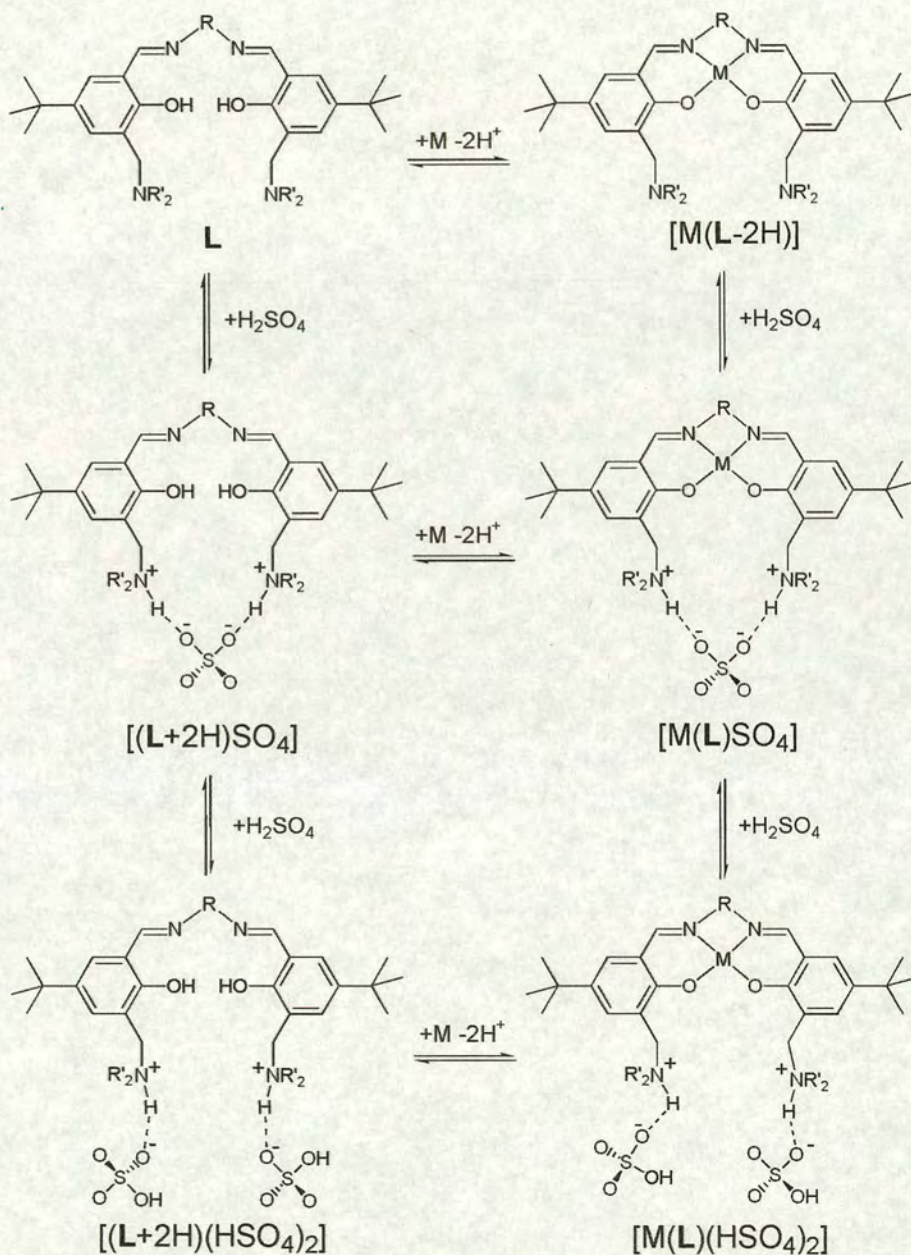
“Metal-only” complexes  $[\text{M}(\text{L}-2\text{H})]$  (Figure 2.15), prepared by the reaction of ligands with their corresponding metal(II) acetates, can be used to examine the pH dependence of sulfate extraction. By monitoring the uptake of sulfuric acid by these systems, at different pH, the relative “strength” of sulfate extraction can be measured, e.g.



One of the advantages of this method is that it focuses the experiment on the sulfate-loading as the metal is already bound to the ligand. This helps simplify the analysis of the extraction process because it reduces the probability of some of the possible solution equilibria taking place (Figure 2.15).

The “metal-only” complexes **10** and **12** and their resultant metal sulfate complexes were found to have sufficient solubility in a  $\text{CHCl}_3/\text{H}_2\text{O}$  system for solvent extraction experiments. The sulfate-binding was investigated from pH 0 – 5 to ascertain the pH range for effective sulfate extraction. The metal present in the organic phase was also monitored to determine the effect of pH on the stability of the metal complex and “strength” of metal-binding.

In all of the sulfate-extraction experiments 100% loading of sulfate corresponds to the formation of a complex with a L : SO<sub>4</sub> ratio of 1 : 1. In the same way, when it is calculated that 100% of the metal is present in the organic phase, this is indicative of a L : M ratio of 1 : 1.

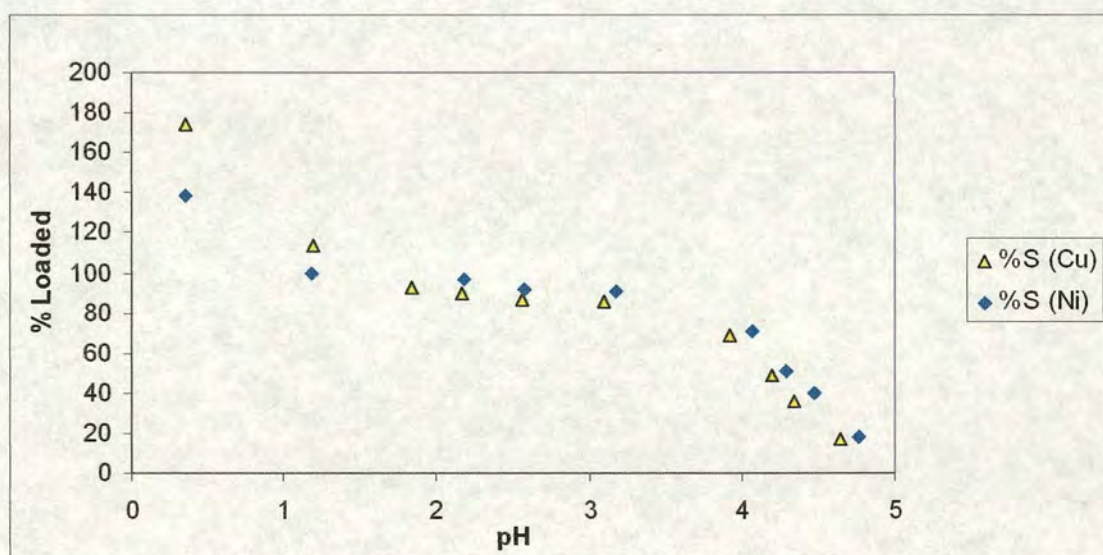


**Figure 2.15** Some of the equilibria associated with metal and sulfate-loading of ligands L. R' = *n*-C<sub>6</sub>H<sub>13</sub> for the CHCl<sub>3</sub>/H<sub>2</sub>O solvent extraction studies, and R = -(CH<sub>2</sub>)<sub>2</sub>-, 2,2'-biphenyl, ± trans-1,2-cyclohexane, *o*-C<sub>6</sub>H<sub>4</sub> for 1, 2, 3, 4 respectively.

The *o*-phenylene-bridged ligand **4** gives a rigid planar  $N_2O_2^{2-}$  donor set in its complexes with Cu(II) and Ni(II) so **10** and **12** were expected to be stable with respect to  $M^{2+}$ -displacement by protons with negligible metal loss even at low pH. This is very significant because using these particular “metal-only” complexes will allow us to study the equilibria associated with  $SO_4^{2-}$  or  $HSO_4^-$  loading (Figure 2.15) in a system where the disposition of the pendant tertiary amine groups is fixed by the metal ion. The sulfate-loading is expected to be pH dependent because only the protonated form of the amine anion-binding site will bind sulfate and this form will not exist at high pH.

There was only negligible loss of copper and nickel from their ligand **4** complexes, in  $CHCl_3$ , after contact with aqueous phases in the pH range 0 – 5. This indicates, as expected, that the metal complexes **10** and **12** are stable to acid, even at low pH.

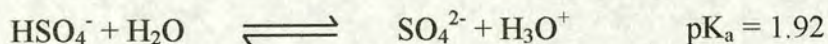
The sulfate-loading of the complexes **10** and **12** (Figure 2.16) was very similar which is not surprising considering that ligand **4** is expected to bind both Cu(II) and Ni(II) in a square planar geometry. An important feature of the loading-behaviour is that the complexes show selectivity for  $SO_4^{2-}$  over  $HSO_4^-$ . This is seen most effectively at



**Figure 2.16** The pH dependence of  $H_2SO_4$  uptake by the “metal-only” complexes **10** and **12**. Sulfur content of the organic phase is plotted as a percentage of the theoretical uptake assuming a  $SO_4^{2-}$  : ligand ratio of 1 : 1 for the nickel complex (diamonds) and the copper complex (triangles).



pH ~ 2 as the first pK<sub>a</sub> of SO<sub>4</sub><sup>2-</sup> occurs<sup>20</sup> at pH = 1.92.



At this pH the ratio of SO<sub>4</sub><sup>2-</sup> to HSO<sub>4</sub><sup>-</sup> in the aqueous phase is 1 : 1 (It is assumed that the pK<sub>a</sub> will remain the same in the aqueous phase when dealing with a biphasic system) but the organic phase contains only the 1 : 1 : 1 complex [M(4)SO<sub>4</sub>]. This conclusion can be drawn as the SO<sub>4</sub><sup>2-</sup> loading is found to be very close to 100% and if the mono-charged HSO<sub>4</sub><sup>-</sup> anion were present then the sulfur to ligand ratio, determined by ICP-OES analysis, would exceed 1 : 1 to maintain charge neutrality. The Ni(II) complex **12** even shows selectivity at pH ~ 1 when the HSO<sub>4</sub><sup>-</sup> anion is in a large excess.

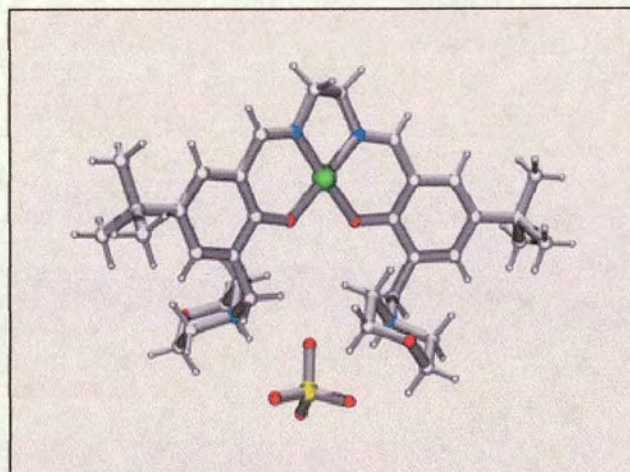
At pH 0.3 the sulfate-loading is greater than 100%. At this pH more than 90% of the sulfur is present as the HSO<sub>4</sub><sup>-</sup> anion in the aqueous phase making the loading of two monocharged HSO<sub>4</sub><sup>-</sup> anions more likely (concentration effect). However as 200% loading is not reached in either metal complex it seems that some SO<sub>4</sub><sup>2-</sup> anions are bound even in a large HSO<sub>4</sub><sup>-</sup> excess.

These experiments showed that SO<sub>4</sub><sup>2-</sup> can be efficiently loaded by the metal complexes **10** and **12** in the pH region 1.5 – 3.5. The SO<sub>4</sub><sup>2-</sup> loading drops off rapidly between pH 4 – 5 because at this point the amine arms are no longer fully protonated in the organic phase (dihexylamine pK<sub>a</sub> ~ 11.3 in water)<sup>21</sup>. Stripping of SO<sub>4</sub><sup>2-</sup> could therefore take place by contacting the loaded ligand with aqueous solutions of pH > 5.

#### 2.4.2 Metal Templatation

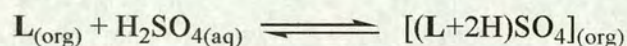
Crystal structures were obtained of some of the metal sulfate complexes of the prototype ditopic ligands and they demonstrated that metal coordination can be used to template the formation of an anion-binding site.<sup>12</sup> For example in the crystal structure of the nickel(II) sulfate complex, shown in Figure 2.17, the coordination of

the Ni(II) cation in a square planar geometry orientates the pendant trialkylammonium arms to create a dicationic binding cavity for the anion. The sulfate is bound in this site by a combination of electrostatic interactions and two bifurcated hydrogen-bonds.



**Figure 2.17** The crystal structure of a NiSO<sub>4</sub> complex of an ethylene-bridged, <sup>t</sup>Bu-substituted ditopic ligand containing pendant morpholine amine arms.<sup>12</sup>

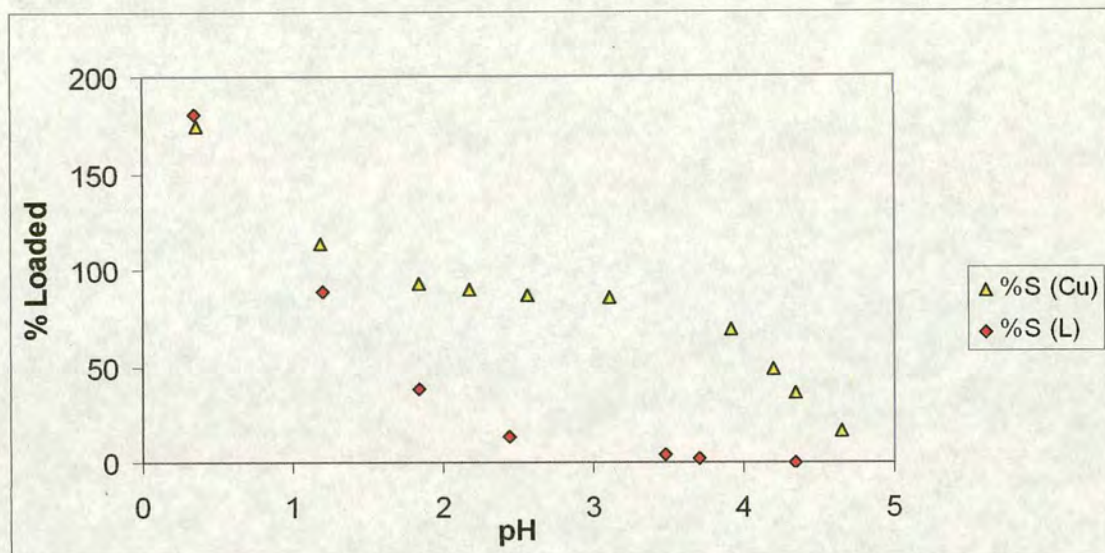
In an attempt to provide evidence, in solution, for the important role metal templating plays in effective anion coordination, sulfate extraction experiments were performed on the free ligand **4**, e.g.



in a similar way to the pH dependence studies on the “metal-only” complexes (Figure 2.15).

The sulfate-uptake by the *o*-phenylene bridged ligand **4** and its copper complex **10** are shown together in Figure 2.18 to allow the comparison of their relative sulfate affinities. For the free ligand very little transfer of sulfate to the organic phase is observed at pH > 2. As the pH is dropped below this value the uptake increases rapidly, approaching 200% at pH < 0.5, which can be attributed to the extraction of two monocharged HSO<sub>4</sub><sup>-</sup> anions which are present in the aqueous phase in an excess

at this pH (section 2.4.1). The  $\text{SO}_4^{2-}$  anion is present in a similar excess at  $\text{pH} > 3$  and no loading is seen in this region.



**Figure 2.18** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by ligand **4** and  $[\text{Cu}(\mathbf{4} - 2\text{H})]$ . Sulfur content of the organic phase is plotted as a percentage of the theoretical uptake assuming a  $\text{SO}_4^{2-}$  : ligand ratio of 1 : 1 for the free ligand (triangles) and the copper complex (diamonds).

In contrast, the previously discussed “copper-only” complex **10** (section 2.4.1) loads  $\text{SO}_4^{2-}$  at pH values below 4.5, and the loading curve suggests that the 1 : 1 : 1 complex  $[\text{Cu}(\mathbf{4})\text{SO}_4]$  predominates in the pH region 1.5 – 3.5. This increase in the apparent basicity of the pendant di-*n*-hexylaminomethyl groups in the copper complex, favouring protonation and transport of sulfate, is consistent with the copper(II) cation templating the pendant tertiary amine groups to assemble a good sulfate-binding site which is dicationic with two hydrogen-bond donors and a hydrophobic exterior.

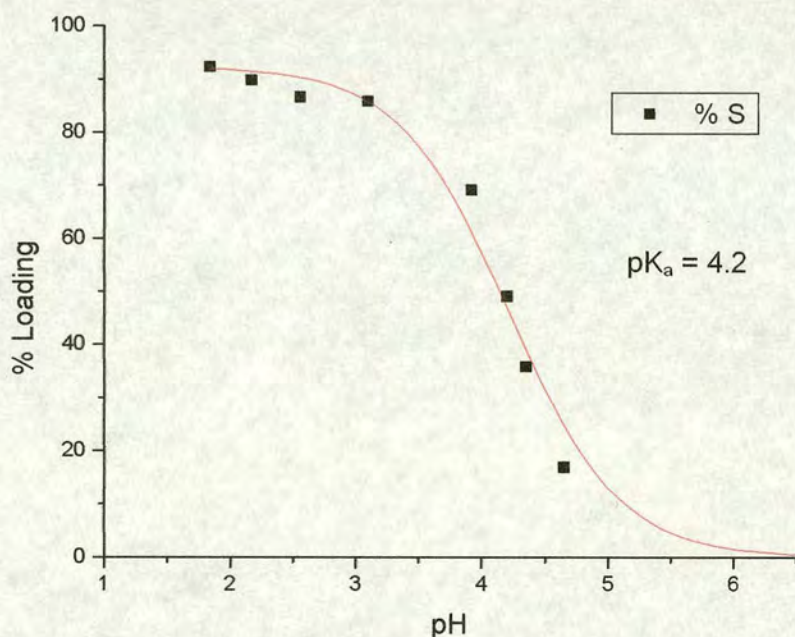
### 2.4.3 The Design of an Extractant for the Efficient Recovery of Metal Sulfate

The pH dependence of the sulfate-loading by the ditopic ligand **4** is close to ideal for base metal recovery from sulfate feeds (Figure 2.19). This is because the  $\text{pH}_{1/2}$  for sulfate extraction is high enough to allow efficient loading of the anion, with the

metal ion, from acidic feeds. However it is also because the  $pH_{1/2}$  value is not too large as this would complicate ligand recovery as very alkaline solutions would then be required to remove the anion. The  $pH_{1/2}$  value for sulfate-loading was determined by calculating the apparent  $pK_a$  of the amine arms in the organic phase ( $CHCl_3$ ) when in contact with sulfuric acid in a two-phase solvent extraction system. This was done by fitting the sulfate extraction data obtained (section 2.4.1) to the equation,

$$y = M + (\Delta C / (1 + 10^{(pK_a - x)})),$$

where  $y$  is the %S loaded onto the complex,  $M$  is the maximum sulfate-loading,  $\Delta C$  is the maximum change in the sulfate-loading and  $x$  is the pH. For the sulfate-loading by “copper-only” complex **10** the value of the  $pK_a$ , which is directly related to the  $pH_{1/2}$  of the sulfate extraction, was calculated as 4.2 (Figure 2.19). Other  $pH_{1/2}$  values used in this chapter were calculated by a similar method.



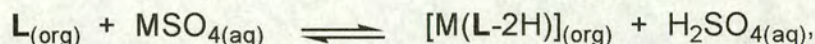
**Figure 2.19** Determination of the apparent  $pK_a$  of the tertiary amine arms in the “copper-only” complex **10** for the extraction of sulfate into  $CHCl_3$  ( $pK_a = 4.2 \pm 0.1$ ).

The overall behaviour of **4** does not fit an ideal profile for the commercial recovery of metal sulfates as the  $pH_{1/2}$  for metal loading is required at a higher pH to facilitate

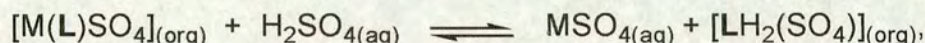
convenient stripping procedures (Figure 2.20). A practicable process would involve > 90% loading of  $\text{MSO}_4$  at  $\text{pH} \approx 3.0$  without pH adjustment.



A very efficient materials balance for the circuit requires the  $\text{pH}_{1/2}$  for the formation of the salen complex,



to be *ca.* 2.0 (as shown in Figure 2.20). Acid stripping could then occur at  $\text{pH} \leq 1.5$ ,



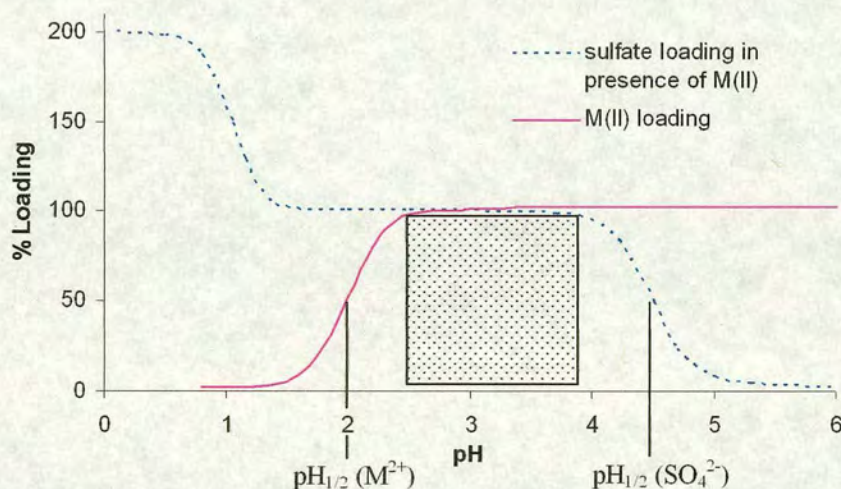
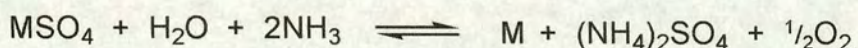
the ligand could be regenerated with base at  $\text{pH} \approx 3.0$ ,



and the metal recovered by electrolysis.



This then regenerates the acid for stripping and gives the overall materials balance,

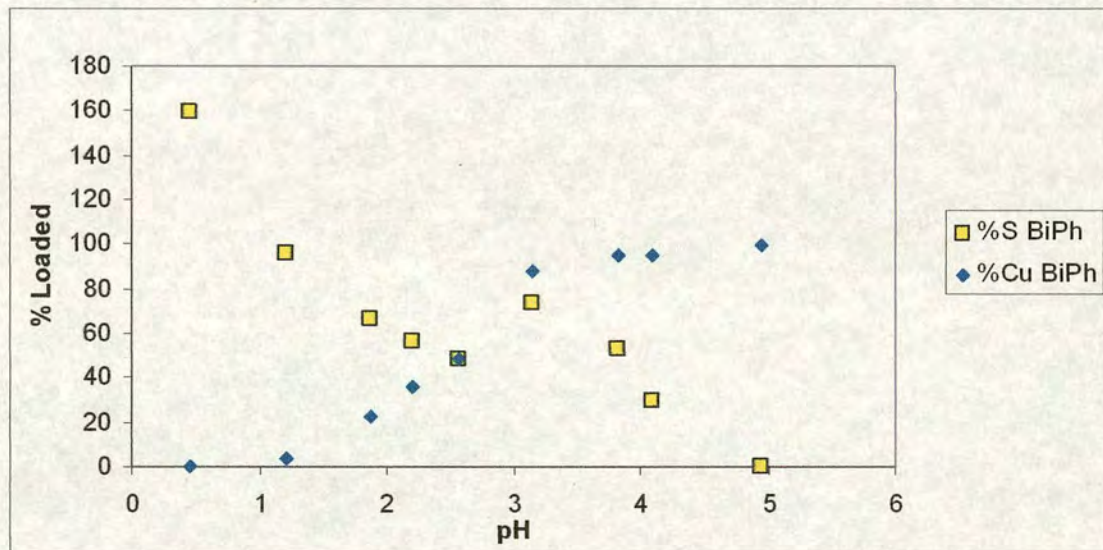


**Figure 2.20** Idealised pH profile for the loading and stripping of  $\text{M}(\text{II})$  and  $\text{SO}_4^{2-}$ .

As already discussed (section 2.4.1) the *o*-phenylene bridging unit in ligand **4** gives rigid planar complexes with Cu(II) and Ni(II) which are very stable with respect to metal displacement by protons. Stripping of the metal would therefore require acid of extremely low pH and this does not fit the ideal pH-profile (Figure 2.20). Consequently the “strength” of the metal-binding site needs to be detuned. This could be done by perturbing the planarity of the  $N_2O_2^{2-}$  donor set by replacing *o*-phenylene with other bridging units. Two such groups are the 2,2'-biphenyl and  $\pm$  *trans*-1,2-cyclohexane used in ligands **2** and **3** respectively.

The metal ion chosen for study was Cu(II) because it forms the most stable complexes of all the divalent 1<sup>st</sup> transition series<sup>22</sup> and more environmentally friendly methods are required for the recovery and processing of copper sulfides.<sup>6</sup>

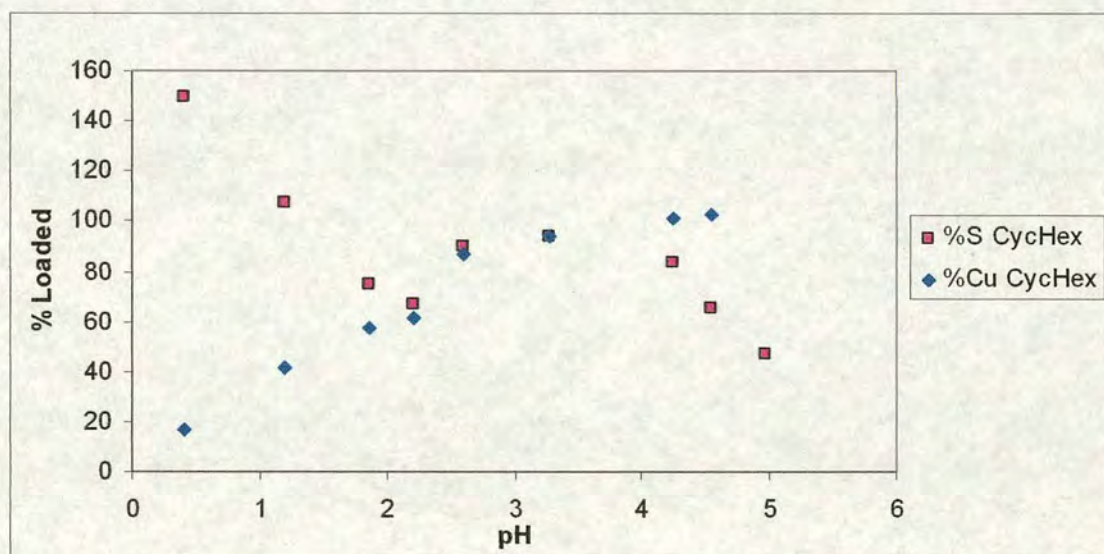
The pH-dependence of sulfate-loading and “strength” of metal complexation by ligand **2** were monitored by using the “copper-only” complex **8**. In this case the metal-binding has been detuned with respect to the “strength” of binding observed for the “copper-only” complex **10**.



**Figure 2.21** The pH dependence of  $H_2SO_4$  uptake by  $[Cu(2 - 2H)]$  and its “strength” of metal binding. Sulfur and copper content (squares and diamonds respectively) of the organic phase are plotted as a percentage of the theoretical uptake assuming a 1 : 1  $SO_4^{2-}$  or  $Cu^{2+}$  : ligand ratio in the complex.

The sulfate-loading has also had its “strength” reduced as the  $\text{pH}_{1/2}$  dropped from 4.2 to 3.9. This could be due to the twisted 2,2'-biphenyl metal coordination geometry templating a less favourable sulfate-binding site in which the pendant amine groups are not as well placed for anion encapsulation. The result of this is that there is no plateau region where the loading of copper and sulfate are maximised because just as copper uptake becomes significant, at around pH 3, the sulfate content of the ligand begins to drop.

The “copper-only” complex **9**, with a  $\pm$ -*trans*-1,2-cyclohexane bridge between the imino-nitrogen donors, was studied in a similar experiment (Figure 2.22). In this case between pH  $\sim$  3 and pH  $\sim$  4 both copper and sulfate loading exceeds 90%. The “strength” of sulfate-loading is greater than for the “copper-only” complexes **8** and **10** as the  $\text{pH}_{1/2}$  has increased to 4.9. However the problem with this ligand is that the “strength” of copper-binding is such that the metal is loaded over a wide pH region. This would reduce the efficiency of metal stripping as acid of low pH would be required. However this ligand is a significant step forward from ligands **2** and **4** as it loads Cu(II) and  $\text{SO}_4^{2-} > 90\%$  in a distinct pH region and both the metal and the anion could be recovered by pH adjustment.



**Figure 2.22** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by  $[\text{Cu}(\mathbf{3} - 2\text{H})]$  and its “strength” of metal binding. Sulfur (squares) and copper (diamonds) content of the organic phase are plotted as a percentage of the theoretical uptake assuming a 1 : 1  $\text{SO}_4^{2-}$  or  $\text{Cu}^{2+}$  : ligand ratio in the complex.

#### 2.4.4 Further Evidence for Metal Templatation of the Anion Binding Site

The graphs used to assess the pH dependence of sulfate-loading and the “strength” of copper-binding by “copper-only” complexes **8** and **9** (section 2.4.3) give further evidence for the important role metal coordination plays in improving sulfate-extraction. The templating of the sulfate-binding site has already been demonstrated in the crystal structure of a nickel(II) sulfate complex (Figure 2.17) and by comparing the pH dependence of sulfate-loading of **4** and [Cu(**4-2H**)] (section 2.4.2).

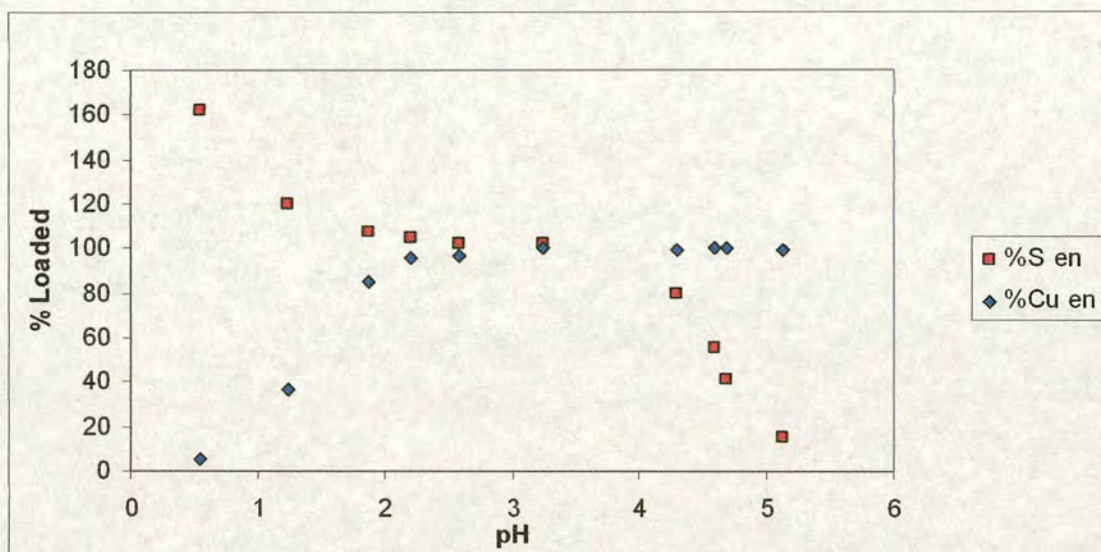
This behaviour is particularly apparent when the pH dependence of  $\text{Cu}^{2+}$  and  $\text{SO}_4^{2-}$  loading shown by ligand **2** are examined in more detail (Figure 2.21). The sulfur loading is  $> 100\%$  at  $\text{pH} \sim 0.5$  due to the uptake of  $\text{HSO}_4^-$  anions but as the pH is increased  $> 1$  the loading of sulfate drops below  $100\%$  indicating that not all of the anion binding sites are occupied. As the copper content begins to increase significantly at  $\text{pH} \sim 3$  the loading of sulfate rises again. At  $\text{pH} > 3$  the sulfate-loading begins to decrease, presumably because above this pH protonation of the pendant amine arms is no longer favourable. However before this drop in sulfate loading the increased copper coordination appears to be responsible for improving sulfate transport indicating that metal templatation is crucial to the formation of an effective anion-binding site. A similar trend is also observed in the sulfate-loading behaviour of “copper-only” complex **9** (Figure 2.22).

#### 2.4.5 The Design of an Extractant with an Ideal Copper and Sulfate Loading Profile

The ideal loading profile for a  $\text{CuSO}_4$  extractant (section 2.4.3) has a pH region in which  $\text{Cu(II)}$  and  $\text{SO}_4^{2-}$  loading are  $> 90\%$  and both the  $\text{Cu(II)}$  cation and  $\text{SO}_4^{2-}$  anion can be recovered by pH adjustment. The most successful extractant described above has been the  $\pm$  *trans*-1,2-cyclohexane-bridged ligand **3** as it met all of these criteria. However although the metal coordination site was twisted, destabilising copper with respect to displacement by protons, the metal stripping was not ideal as it occurred over a wide pH range (Figure 2.22). This could be a consequence of the rigidity of



the 1,2-cyclohexane bridge. Ligand **1** with a 1,2-ethane bridging group should have greater flexibility whilst still showing a preference for a square planar geometry.



**Figure 2.23** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by  $[\text{Cu}(1 - 2\text{H})]$  and its “strength” of metal binding. Sulfur (squares) and copper (diamonds) content of the organic phase are plotted as a percentage of the theoretical uptake assuming a 1 : 1  $\text{SO}_4^{2-}$  or  $\text{Cu}^{2+}$  : ligand ratio in the complex.

The pH dependence of sulfate-loading and “strength” of copper-binding by ligand **1** (Figure 2.23) were found to fit the ideal profile for a  $\text{CuSO}_4$  extractant. The pH region 2 – 4 allows  $\text{CuSO}_4$  to be loaded > 90% and  $\text{Cu}(\text{II})$  and  $\text{SO}_4^{2-}$  could be efficiently recovered by pH adjustment (section 2.4.3). Although this ligand meets the initial requirement for transport of copper(II) sulfate in having an ideal extraction profile, commercial reagents also need to fulfil a number of other important criteria (section 1.9). Some of these will be discussed and addressed in the following chapters.

## 2.5 UV-Visible Spectroscopy of Solvent Extraction Experiments

The solvent extraction experiments detailed in section 2.4 employed analysis by ICP-OES (Inductively Coupled Plasma Optical Emission Spectroscopy) to determine the metal and sulfur content of the organic layers. The samples were prepared by

removing aliquots of the  $\text{CHCl}_3$  layers after extraction, concentrating them *in vacuo*, and subsequently re-dissolving each of the samples in butan-1-ol (10 ml). These solutions can also be analysed by UV-Visible spectroscopy and the results obtained can then be correlated with the corresponding ICP-OES results for metal and sulfur loading. This is useful as information can be gained on how well separated the cation and anion binding sites are, in solution, as at high sulfate concentrations any direct metal-anion interactions should significantly alter the spectrum.

UV-Visible analyses were carried out on the butan-1-ol solutions obtained from the solvent extraction experiments of “copper-only” complexes **7** – **9**. The copper content has been shown to be close to 100% in all of the solutions analysed. The changes in the wavelength of the absorption band at  $\sim 360 - 410$  nm, at different sulfate concentrations, were recorded for each complex (Table 2.5).

Only very small differences were seen between the spectra of the “copper-only” complexes **7** and **9** in butan-1-ol in the absence of any sulfate ion and those of the corresponding complexes containing high concentrations of sulfate (Table 2.5), indicating that sulfate-binding has little effect on the wavelengths of the electronic absorption bands. This provides evidence that the cation and anion binding sites in ligands **1** and **3** are well separated in solution and the anions do not interact strongly with the metal-based chromophore.

However there are slightly more significant differences between the spectrum of the “copper-only” complex **8** and those of its partially loaded sulfate complexes. The changes are small but suggest that the sulfate anion may interact weakly with the copper cation. This is not unreasonable as the twisted metal coordination geometry of the 2,2'-biphenyl ligand will open up the space between the phenolate donor atoms and provide the opportunity for the sulfate ion to be closely associated with at least one of the pendant trialkylammoniums whilst approaching the coordination sphere of the metal. In the crystal structure<sup>12</sup> of a  $\text{NiSO}_4$  complex of a related ligand the sulfate anion acts as a bidentate ligand for the Ni(II) ion. Such an arrangement for Cu(II) is

less likely but it does at least show that direct metal-anion interactions can occur in ligands containing a 2,2'-biphenyl-bridge.

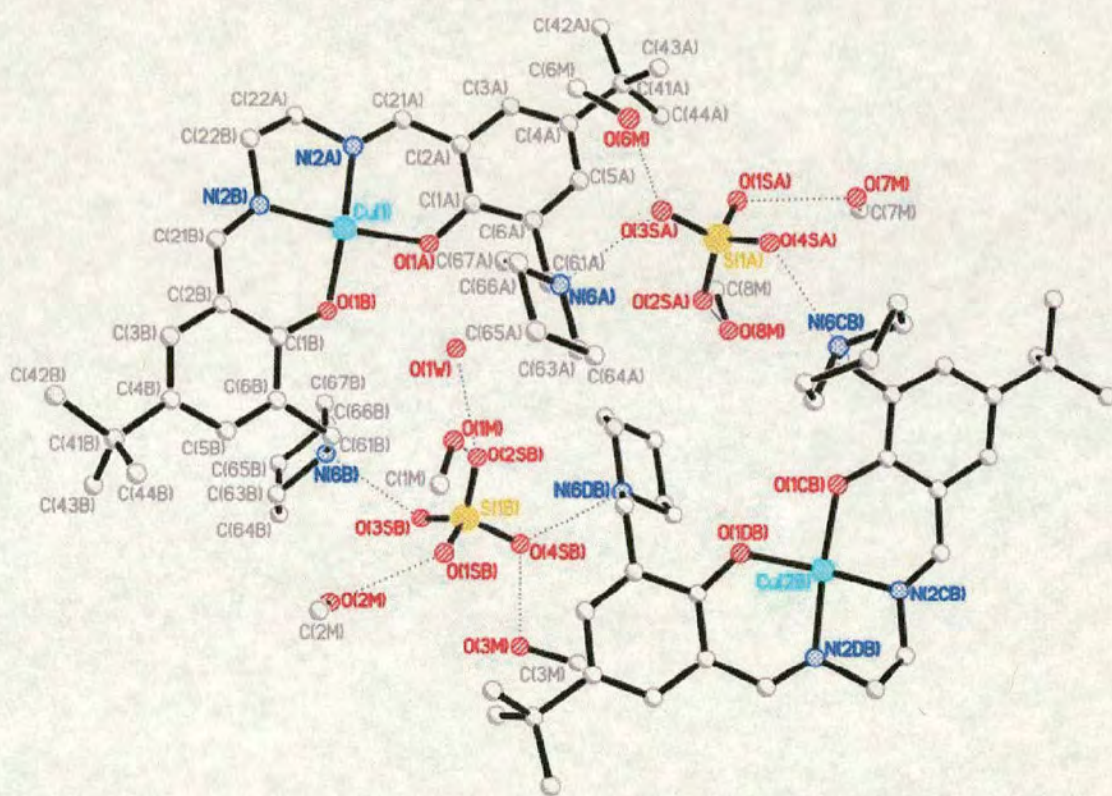
**Table 2.5** The changes in wavelength of the charge transfer band in the visible spectra of complexes 7 – 9, in butan-1-ol, at different concentrations of sulfate. %S corresponds to the sulfate-loading in the organic phase, recorded by ICP-OES (section 2.4), for the sample. <sup>a</sup> Spectrum of the “copper-only” complex [Cu(L-2H)] in butan-1-ol which has had no contact with aqueous sulfate solutions.

“Copper-only” Complex 7						
<b>pH</b>	4.30	4.60	4.69	4.94	(7) <sup>a</sup>	$\Delta\lambda = -3$
<b><math>\lambda</math> / nm</b>	372	372	372	371	369	
<b>% S</b>	80	55	42	15	0	
“Copper-only” Complex 8						
<b>pH</b>	3.15	3.82	4.1	4.95	(8) <sup>a</sup>	$\Delta\lambda = 9$
<b><math>\lambda</math> / nm</b>	397	400	401	406	406	
<b>% S</b>	74	53	30	0	0	
“Copper-only” Complex 9						
<b>pH</b>	3.28	4.25	4.97	5.32	(9) <sup>a</sup>	$\Delta\lambda = -3$
<b><math>\lambda</math> / nm</b>	371	370	369	369	368	
<b>% S</b>	94	84	47	41	0	

## 2.6 X-Ray Crystallography

The solvent extraction studies detailed in this chapter demonstrate that coordination of a metal cation into ditopic ligands containing “salen-type” metal-binding units can template the formation of a more effective sulfate-binding site (section 2.4.2). In

these studies it was assumed that this involves the formation of a complex with a metal to ligand to sulfate ratio of 1 : 1 : 1, as has been seen in previous crystal structures.<sup>12</sup> However the structure of the CuSO<sub>4</sub> complex (13) of ligand 5 (Figure 2.24), which is closely related to ligand 1, having pendant piperidino groups rather than pendant dihexyl groups, exists as a 2 : 2 : 2 dimer in the solid state.<sup>23</sup> Two copper complexes of ligand 5 are linked into a *pseudo*-macrocycle by two bridging sulfate anions via a combination of electrostatic interactions and intermolecular N–H···O hydrogen bonds (Table 2.6). Metal templation may also be important for efficient organisation of such extended structures.



**Figure 2.24** Assembly of [Cu(5)SO<sub>4</sub>] complexes in the solid state structure [Cu(5)SO<sub>4</sub>]<sub>2</sub>·H<sub>2</sub>O·8CH<sub>3</sub>OH.<sup>23</sup> H-atoms attached to C-atoms have been removed for clarity.

Cu(1)-O(1B)	1.882(3)	Cu(2)-O(1D)	1.894(3)
Cu(1)-O(1A)	1.917(3)	Cu(2)-O(1C)	1.896(3)
Cu(1)-N(2A)	1.930(4)	Cu(2)-N(2C)	1.923(4)
Cu(1)-N(2B)	1.944(4)	Cu(2)-N(2D)	1.934(4)
N(6A)···O(3SA)	2.709(5)	N(6B)···O(3SB)	2.664(5)
O(1B)-Cu(1)-O(1A)	91.06(13)	O(1D)-Cu(2)-O(1C)	88.84(13)
O(1B)-Cu(1)-N(2A)	166.78(17)	O(1D)-Cu(2)-N(2C)	172.00(18)
O(1A)-Cu(1)-N(2A)	93.63(14)	O(1C)-Cu(2)-N(2C)	94.45(15)
O(1B)-Cu(1)-N(2B)	93.28(14)	O(1D)-Cu(2)-N(2D)	92.81(14)
O(1A)-Cu(1)-N(2B)	166.59(16)	O(1C)-Cu(2)-N(2D)	169.13(17)
N(2A)-Cu(1)-N(2B)	84.95(15)	N(2C)-Cu(2)-N(2D)	85.33(16)
$\sum$ <i>cis</i> -angles	362.9(6)	$\sum$ <i>cis</i> -angles	361.4(6)
N(6A)-S(1A)-N(6C)_ $\$1$	119.59 (0.09)		
N(6B)-S(1B)-N(6D)_ $\$1$	145.79 (0.10)		

Symmetry equivalent  $\$1 = 1+x, y, z.$

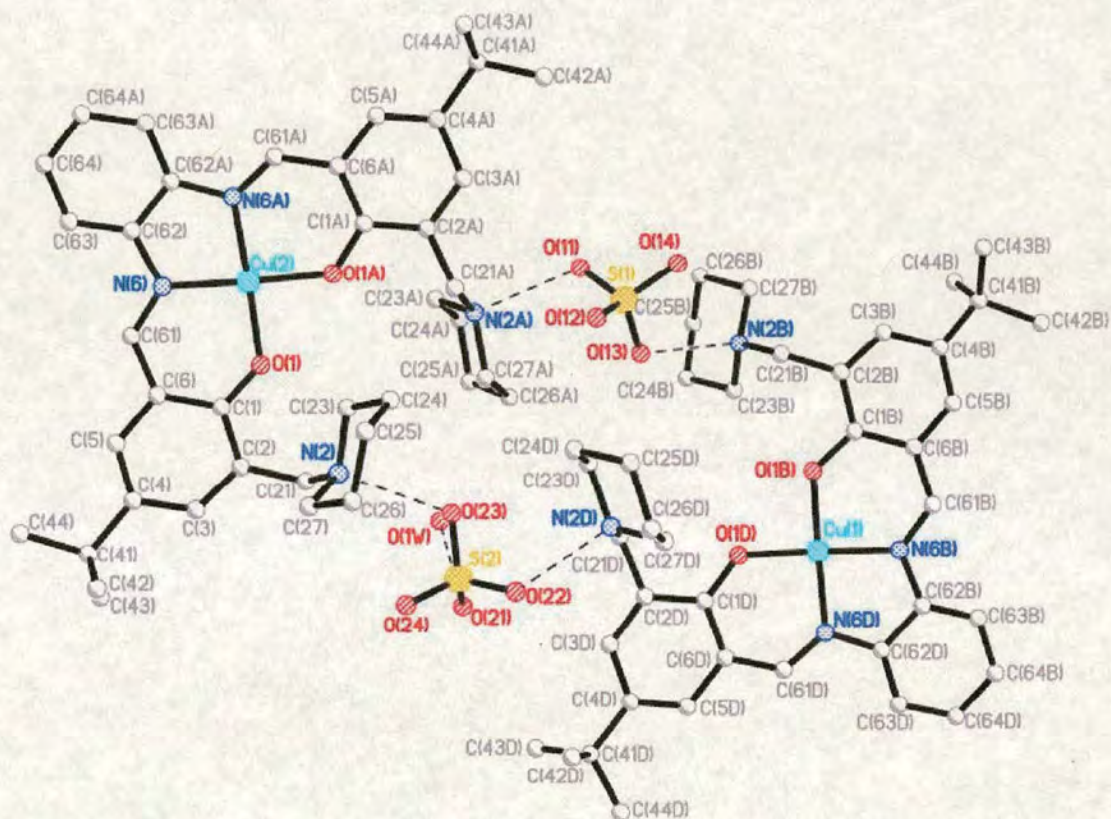
**Table 2.6** Selected Bond lengths [Å] and angles [°] for  $[\text{Cu}(5)\text{SO}_4]_2 \cdot \text{H}_2\text{O} \cdot 8\text{CH}_3\text{OH}.$ <sup>23</sup>

The  $\text{CuN}_2\text{O}_2$  units are approximately planar as the sum of the angles defined by *cis*-donors at the Cu atoms are found to be close to  $360^\circ$  ( $362.9(6)^\circ$  and  $361.4(6)^\circ$ ) and the bond lengths and angles (Table 2.6) in the metal-binding sites are typical of those expected for copper complexes of this type.<sup>24</sup>

The pendant piperidine arms are located above and below the plane of the ligand with two similarly orientated arms coming together to form an inter-molecular dicationic binding cavity for the sulfate anion. The  $\text{N}\cdots\text{S}\cdots\text{N}$  angles (Table 2.6) show that the sulfate is not located directly between the two arms ( $119.59(0.09)^\circ$  and  $145.79(0.10)^\circ$ ) and the potential significance of this is discussed in section 5.6. Another feature of the structure is the large number of methanol and water solvent molecules which form hydrogen-bonds to the sulfate anions. The Hofmeister series (section 1.8) indicates that sulfate is one of the most hydrated anions so it is not

surprising that it is so heavily solvated. The structure therefore reveals some of the challenges associated with promoting sulfate-extraction into non-polar non-coordinating solvents as it prefers to exist in an environment which can supply a number of hydrogen-bond donors. One possible solution to this may be to design receptors which can transport partially hydrated sulfate anions (see section 5.7)

A similar dimeric structure was obtained<sup>23</sup> for the  $\text{CuSO}_4$  complex (14) of ligand 6 (Figure 2.25), which is closely related to the dihexyl-substituted ligand 4.



**Figure 2.25** Assembly of  $[\text{Cu}(6)\text{SO}_4]$  complexes in the solid state structure  $[\text{Cu}(6)\text{SO}_4]_2 \cdot 5\text{CHCl}_3 \cdot \text{H}_2\text{O}$ .<sup>23</sup> For the hydrogen bonds shown  $\text{N}(2) \cdots \text{O}(23)$ , 2.723(11)Å;  $\text{N}(2\text{D}) \cdots \text{O}(22)$ , 2.632(10)Å;  $\text{N}(2\text{A}) \cdots \text{O}(11)$ , 2.646(11)Å;  $\text{N}(2\text{B}) \cdots \text{O}(13)$ , 2.600(11)Å. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.

This structure has a rigidly square planar  $\text{CuN}_2\text{O}_2$  unit (sum of the angles defined by cis-donors at the Cu atom is  $360(1.2)^\circ$ ) and the bond lengths and angles are in the expected range.<sup>24</sup> The copper complexes are again bridged by sulfate anions, bound

between the pendant piperidine groups, with N $\cdots$ S $\cdots$ N angles of 118.02(0.19) $^\circ$  (N(2) $\cdots$ S(2) $\cdots$ N(2D)) and 130.49(0.20) $^\circ$  (N(2A) $\cdots$ S(1) $\cdots$ N(2B)).

The “copper-only” complexes of **1** and **4**, which differ only from **5** and **6** in having pendant di-*n*-hexylamine groups instead of piperidine groups (Table 2.1), displayed similar sulfate-extraction behaviour in the solution studies (section 2.4) so it is possible that sulfate is encapsulated in an almost identical manner in the solid state, in a similar way to the dimeric structures of **5** and **6**. This dimeric arrangement may also be the favoured binding mode for the complexation of sulfate in solution. The crystal packing of both of these structures show that the only hydrogen-bonding interactions with the sulfate anions come from within the discrete 2 : 2 : 2 units.

## 2.7 Conclusions

The work described in this chapter has primarily involved elucidating how sulfate behaves in a two-phase CHCl<sub>3</sub>/H<sub>2</sub>O system and how its extraction into the organic phase can be promoted by constructing well designed binding sites.

Sulfate-loading into the organic phase using the “copper-only” complexes **7** – **10**, “nickel-only” complex **12** and free ligand **4** was found to be pH dependent as the loading of the anion is facilitated by the protonation of the pendant amine arms, in the organic phase, and this becomes unfavourable at high pH. It was also found that at very low pH < 1.5 monocharged HSO<sub>4</sub><sup>-</sup> anions were extracted as the sulfate-loading was greater than 100%.

The sulfate-loading graphs of “metal-only” complexes **10** and **12** both show selectivity for SO<sub>4</sub><sup>2-</sup> over HSO<sub>4</sub><sup>-</sup> as at the pK<sub>a</sub> (1.92) of SO<sub>4</sub><sup>2-</sup> the results suggest that the predominant species is the 1 : 1 : 1 complex M(L)SO<sub>4</sub>.

The “metal-only” complexes **10** and **12** have both been shown to template the formation of an effective anion-binding site for SO<sub>4</sub><sup>2-</sup> as their loading graphs show that extraction takes place at a significantly greater pH than in the untemplated free

ligand **4**. Further evidence for the important influence that metal coordination in these ligands has on  $\text{SO}_4^{2-}$  extraction is provided by the Cu(II) and  $\text{SO}_4^{2-}$  pH dependence graphs of “copper-only” complexes **8** and **9**. In these graphs as the pH is raised the  $\text{SO}_4^{2-}$  loading drops, however it picks up again as the Cu(II) content increases. This shows that metal coordination is required to orientate the binding site into a more effective arrangement for anion-binding.

The ideal profile for a copper sulfate extractant was defined as having a distinct pH region where Cu(II) and  $\text{SO}_4^{2-}$  are loaded > 90% and both Cu(II) and  $\text{SO}_4^{2-}$  can be conveniently recovered by pH adjustment. Ligand **4** did not meet these requirements as the Cu(II) cation can only be removed from the rigid metal coordination site at very low pH and ligand **2** was not effective as it did not contain a region of pH where both Cu(II) and  $\text{SO}_4^{2-}$  loading were > 90%, essentially because it binds Cu(II) too weakly. Ligand **3** was found to meet the requirements but ligand **1** was more successful as the Cu(II) stripping occurs over a shorter pH range allowing Cu(II) to be recovered more efficiently.

The zinc complex **11** was not used in solvent extraction experiments as complete complex formation did not even occur in methanol indicating that the metal-binding was weak.

Studies of the UV-Visible spectra, in butan-1-ol, of the solvent extraction experiments performed on “copper-only” complexes **7** and **9** provide evidence that the cation and anion binding sites in ligands **1** and **3** are well separated. However, there may be a weak interaction between the Cu(II) cation and  $\text{SO}_4^{2-}$  anion when ligand **2** is used as an extractant.

Solid state structures of  $\text{CuSO}_4$  complexes of ligands closely related to **1** and **4** contain 2 : 2 : 2 ligand : Cu(II) :  $\text{SO}_4^{2-}$  assemblies. Consequently it is possible the metal templation effect observed in the solvent extraction experiments may involve the formation of extended structures which can provide favourable binding interactions for sulfate anions.



## 2.8 Experimental

### 2.8.1 Instrumentation

Nuclear magnetic resonance spectra were obtained on Bruker AC 200 and Bruker AC 250 instruments and referenced to  $\text{CHCl}_3$ . FAB mass spectrometry was performed on a Kratos MS 50 machine. FTIR spectra were recorded on a Perkin-Elmer Paragon 1000 spectrometer as oils on NaCl plates or as KBr discs. Electronic absorption spectroscopy was carried out on a Perkin-Elmer  $\lambda$ -900 spectrometer. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis was recorded on a Thermo Jarrell Ash IRIS ICP-AES spectrometer. The measurement of pH was carried out on a Fisher Scientific AR 50 pH meter.

### 2.8.2 Solvent and Reagent Pre-treatment

Unless stated to the contrary, commercial grade chemicals obtained from Aldrich or Acros were used without further purification.

### 2.8.3 Ligand Synthesis

Ligand **5** was made as previously described.<sup>12</sup> 2-Hydroxy-5-*tert*-butyl-benzaldehyde was synthesised by the method described by Levin and co-workers.<sup>14</sup> 2,2'-Diaminobiphenyl was prepared from 2,2'-dinitrobiphenyl by a literature method.<sup>25</sup> Ethoxy-N-dihexylaminomethane and the 2-hydroxy-5-*tert*-butyl-benzaldehyde substituted with a pendant dihexylamine group were made by an adaptation of the method used by Fenton and co-workers<sup>11</sup> as follows.

**Ethoxy-N-dihexylaminomethane.** Dihexylamine (341.85 g, 1.84 mol) was added dropwise to a stirred suspension of paraformaldehyde (68.76 g, 2.29 mol) and potassium carbonate (506.90 g, 3.67 mol) in ethanol (900 ml) at 0°C. This was allowed to warm to room temperature and continually stirred for 72 hours. The

product was then filtered and the potassium carbonate was washed with ethanol (300 ml). The solvent was removed *in vacuo* to yield a red/ brown oil containing a white powder and this oil was filtered to remove any remaining potassium carbonate. The oil was purified by vacuum distillation (1 mm Hg, b.p. 120°C) to yield ethoxy-N-dihexylaminomethane as a *colourless liquid* (260 g, 58%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 4.15 (2H, s,  $\text{OCH}_2\text{N}$ ), 3.43 (2H, q,  $J(\text{OCH}_2\text{CH}_3)$  6.5 Hz), 2.61 (4H, t,  $J(\text{NCH}_2\text{CH}_2)$  7.3 Hz), 1.44 (4H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.28 (12H, m,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 1.18 (3H, t,  $J(\text{OCH}_2\text{CH}_3)$  7 Hz), 0.89 (6H, t,  $J(\text{N}(\text{CH}_2)_5\text{CH}_3)$  6.8 Hz).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 83.7 ( $\text{NCH}_2\text{O}$ ), 63.6 ( $\text{OCH}_2\text{CH}_3$ ), 52.3 ( $\text{NCH}_2\text{CH}_2$ ), 32.1 ( $\text{NCH}_2\text{CH}_2$ ), 28.5 ( $\text{N}(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 27.4 ( $\text{N}(\text{CH}_2)_3\text{CH}_2\text{CH}_2\text{CH}_3$ ), 23.0 ( $\text{N}(\text{CH}_2)_4\text{CH}_2\text{CH}_3$ ), 15.7 ( $\text{OCH}_2\text{CH}_3$ ), 14.4 ( $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $m/z$  198 (M - EtO).

**2-Hydroxy-3-dihexylaminomethyl-5-tert-butyl-benzaldehyde.** A mixture of 2-hydroxy-5-tert-butyl-benzaldehyde (22 g, 0.12 mol) and ethoxy-N-dihexylaminomethane (30.5 g, 0.13 mol) in acetonitrile (200 ml) was heated to reflux under a dinitrogen atmosphere for 90 h. After cooling the solution to room temperature, the solvent was removed *in vacuo* to yield a viscous brown oil. The product was dissolved in dichloromethane (150 ml) and extracted with water (3 × 50 ml). The organic fraction was dried with  $\text{MgSO}_4$ , filtered and then evaporated *in vacuo* to yield a viscous brown oil. The oil was purified by silica column chromatography (hexane: ethyl acetate, 20:1) to yield 2-hydroxy-3-dihexylaminomethyl-5-tert-butyl-benzaldehyde as a *yellow liquid* (24.5 g, 53%). (Found: C, 76.8; H, 11.1; N, 3.8.  $\text{C}_{24}\text{H}_{41}\text{NO}_2$  requires C, 76.8; H, 11.0; N, 3.7%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 10.46 (1H, s, CHO), 7.7 (1H, d,  $J(\text{Ar-H})$  2.5 Hz), 7.3 (1H, d,  $J(\text{Ar-H})$  2.5 Hz), 3.83 (2H, s, Ar- $\text{CH}_2\text{N}$ ), 2.76 (4H, t,  $J(\text{NCH}_2\text{CH}_2)$  7.5 Hz), 1.59 (4H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.33 (21H, m,  $(\text{CH}_3)_3\text{C}$ ,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 0.91 (6H, t,  $J(\text{N}(\text{CH}_2)_5\text{CH}_3)$  6.9 Hz).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 191.5 (Ar CHO), 160.5 (Ar C), 141.7 (Ar C), 132.5 (Ar CH), 124.0 (Ar C), 123.9 (Ar CH), 122.7 (Ar C), 57.8 ( $\text{CCH}_2\text{N}$ ), 53.8 ( $\text{NCH}_2\text{CH}_2$ ), 34.4 ( $\text{C}(\text{CH}_3)_3$ ), 31.9 ( $\text{NCH}_2\text{CH}_2$ ), 31.7 ( $\text{C}(\text{CH}_3)_3$ ), 27.3 ( $\text{N}(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 26.5 ( $\text{N}(\text{CH}_2)_3\text{CH}_2\text{CH}_2\text{CH}_3$ ), 22.9 ( $\text{N}(\text{CH}_2)_4\text{CH}_2\text{CH}_3$ ), 14.3 ( $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  2958s, 1683s, 1233s, 894, 824.  $m/z$  376 ( $\text{M}^+$ )

**4,4'-Di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-**

**(ethylenedinitrilodimethylidyne) diphenol (1).** To a stirred solution of 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzaldehyde (6.43 g, 0.017 mol) in ethanol (50 ml) was added a solution of ethylenediamine (0.51 g, 0.0085 mol) in acetonitrile (25 ml). The yellow solution was stirred overnight and then concentrated *in vacuo* to yield a yellow oil. The product was dissolved in dichloromethane (50 ml) and extracted with water (3 × 25 ml). The organic fraction was dried with MgSO<sub>4</sub>, filtered and then evaporated *in vacuo* to yield **1** as a viscous *yellow oil* (6.55 g, 99%) which was used without further purification. (Found: C, 77.6; H, 11.4; N, 7.0. C<sub>50</sub>H<sub>86</sub>N<sub>4</sub>O<sub>2</sub> requires C, 77.5; H, 11.2; N, 7.2%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.44 (2H, s, N=CH), 7.50 (2H, d, *J*(Ar-*H*) 2.2 Hz), 7.19 (2H, d, *J*(Ar-*H*) 2.4 Hz), 3.92 (4H, s, HC=NCH<sub>2</sub>), 3.64 (4H, s, Ar-CH<sub>2</sub>N), 2.46 (8H, t, *J*(NCH<sub>2</sub>CH<sub>2</sub>) 7.5 Hz), 1.50 (8H, m, NCH<sub>2</sub>CH<sub>2</sub>), 1.30 (42H, m, (CH<sub>3</sub>)<sub>3</sub>C, NCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>), 0.87 (12H, t, *J*(N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>) 6.8 Hz). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 166.4 (N=CH), 157.4 (Ar C), 141.1 (Ar C), 130.5 (Ar CH), 126.9 (Ar C), 126.0 (Ar CH), 118.4 (Ar C), 60.7 (HC=NCH<sub>2</sub>), 54.6 (Ar-CCH<sub>2</sub>N), 53.1 (NCH<sub>2</sub>CH<sub>2</sub>), 34.4 (C(CH<sub>3</sub>)<sub>3</sub>), 32.3 (NCH<sub>2</sub>CH<sub>2</sub>), 31.9 (C(CH<sub>3</sub>)<sub>3</sub>), 27.7 (N(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 27.4 (N(CH<sub>2</sub>)<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 23.1 (N(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 14.5 (N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 2955s, 1634s, 1219, 824. λ<sub>max</sub>/nm (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>) (CHCl<sub>3</sub>) 263 (26600), 330 (11280). *m/z* 776 (M<sup>+</sup>).

**4,4'-Di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(2,2'-**

**biphenylenedinitrilodimethylidyne) diphenol (2).** To a stirred solution of 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzaldehyde (1.84 g, 0.0049 mol) in ethanol (20 ml) was added a solution of 2,2'-diaminobiphenyl (0.45 g, 0.0024 mol) in ethanol (10 ml). The orange solution was stirred overnight and then concentrated *in vacuo* to yield an orange oil. The product was dissolved in chloroform (30 ml) and extracted with water (3 × 15 ml). The organic fraction was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **2** as a viscous *orange oil* (2.1 g, 96 %) which was used without further purification. (Found: C, 80.0; H, 10.2; N, 6.0. C<sub>60</sub>H<sub>90</sub>N<sub>4</sub>O<sub>2</sub> requires C, 80.1; H, 10.1; N, 6.2%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.53 (2H, s, N=CH), 7.13-7.50 (12H, m, Ar-*H*), 3.56 (4H, s, Ar-CH<sub>2</sub>N), 2.42 (8H, t, *J*(NCH<sub>2</sub>CH<sub>2</sub>))

7.1 Hz), 1.48 (8H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.26 (42H, m,  $(\text{CH}_3)_3\text{C}$ ,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 0.87 (12H, t,  $J(\text{N}(\text{CH}_2)_5\text{CH}_3)$  6.8 Hz).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 166.4 (N=CH), 157.2 (Ar C), 148.4 (Ar C), 141.8 (Ar C), 134.9 (Ar C), 132.5 (Ar CH), 131.2 (Ar CH), 130.8 (Ar CH), 129.0 (Ar CH), 127.0 (Ar C), 126.4 (Ar CH), 118.9 (Ar C), 118.7 (Ar CH), 54.6 (Ar-CCH<sub>2</sub>N), 53.9 ( $\text{NCH}_2\text{CH}_2$ ), 34.3 ( $\text{C}(\text{CH}_3)_3$ ), 32.2 ( $\text{NCH}_2\text{CH}_2$ ), 31.8 ( $\text{C}(\text{CH}_3)_3$ ), 27.6 ( $\text{N}(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 27.4 ( $\text{N}(\text{CH}_2)_3\text{CH}_2\text{CH}_2\text{CH}_3$ ), 23.0 ( $\text{N}(\text{CH}_2)_4\text{CH}_2\text{CH}_3$ ), 14.4 ( $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  2956s, 1618s, 1195, 822, 748.  $m/z$  899 ( $\text{M}^+$ ).

**4,4'-Di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-((±)-(trans)-1,2-**

**cyclohexendinitrilodimethylidyne) diphenol (3).** To a stirred solution of 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzaldehyde (1.84 g, 0.0049 mol) in ethanol (20 ml) was added a solution *trans*-1,2-diaminocyclohexane (0.27 g, 0.0024 mol) in acetonitrile (10 ml). The yellow solution was stirred overnight and then concentrated *in vacuo* to yield a yellow oil. The product was dissolved in chloroform (30 ml) and extracted with water (3 × 15 ml). The organic fraction was dried with  $\text{MgSO}_4$ , filtered and evaporated *in vacuo* to yield **3** as a viscous *yellow oil* (1.92 g, 98 %) which was used without further purification. (Found: C, 76.7; H, 11.1; N, 6.9.  $\text{C}_{54}\text{H}_{92}\text{N}_4\text{O}_2 \cdot \text{H}_2\text{O}$  requires C, 76.5; H, 11.2; N, 6.6%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 8.30 (2H, s, N=CH), 7.51 (2H, m, Ar-H), 7.06 (2H, m, Ar-H), 3.60 (4H, m, Ar-CH<sub>2</sub>N), 3.32 (2H, m, CH=NCHCH<sub>2</sub>), 2.44 (8H, t,  $J(\text{NCH}_2\text{CH}_2)$  7.2 Hz), 1.88 (4H, m, CH=NCHCH<sub>2</sub>CH<sub>2</sub>), 1.76 (4H, m, CH=NCHCH<sub>2</sub>CH<sub>2</sub>), 1.48 (8H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.26 (42H, m,  $(\text{CH}_3)_3\text{C}$ ,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 0.85 (12H, m,  $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 165.4 (N=CH), 157.5 (Ar C), 141.1 (Ar C), 130.4 (Ar CH), 127.3 (Ar C), 126.5 (Ar CH), 118.2 (Ar C), 73.3 (CH=NCHCH<sub>2</sub>), 54.9 (Ar-CCH<sub>2</sub>N), 52.7 ( $\text{NCH}_2\text{CH}_2$ ), 34.5 ( $\text{C}(\text{CH}_3)_3$ ), 33.9 (CH=NCHCH<sub>2</sub>CH<sub>2</sub>), 32.5 ( $\text{NCH}_2\text{CH}_2$ ), 32.0 ( $\text{C}(\text{CH}_3)_3$ ), 28.0 ( $\text{N}(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 27.7 ( $\text{N}(\text{CH}_2)_3\text{CH}_2\text{CH}_2\text{CH}_3$ ), 24.8 (CH=NCHCH<sub>2</sub>CH<sub>2</sub>), 23.3 ( $\text{N}(\text{CH}_2)_4\text{CH}_2\text{CH}_3$ ), 14.7 ( $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  2918s, 1632s, 1220s, 824s, 751.  $m/z$  829 ( $\text{M}^+$ ).

**4,4'-Di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(1,2-**

**phenylenedinitrilodimethylidyne) diphenol (4).** To a stirred solution of 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzaldehyde (3 g, 0.0080 mol) in ethanol (30 ml) was added a solution of phenylene-1,2-diamine (0.43 g, 0.0040 mol) in ethanol (25 ml). The orange solution was stirred overnight and then concentrated *in vacuo* to yield an orange oil. The product was dissolved in dichloromethane (50 ml) and extracted with water (3 × 25 ml). The organic fraction was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **4** as a viscous *orange oil* (3.2 g, 98 %). This was used without further purification. (Found: C, 78.3; H, 10.5; N, 6.9. C<sub>54</sub>H<sub>86</sub>N<sub>4</sub>O<sub>2</sub> requires C, 78.8; H, 10.5; N, 6.8%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.83 (2H, s, N=CH), 7.64 (2H, d, Ar-H), 7.46 (2H, m, Ar-H), 7.08 (2H, m, Ar-H), 6.78 (2H, m, Ar-H), 3.73 (4H, s, Ar-CH<sub>2</sub>N), 2.54 (8H, t, J(NCH<sub>2</sub>CH<sub>2</sub>) 6.8 Hz), 1.53 (8H, m, NCH<sub>2</sub>CH<sub>2</sub>), 1.33 (18H, m, (CH<sub>3</sub>)<sub>3</sub>C), 1.29 (24H, m, NCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>), 0.89 (12H, t, J(N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>) 6.6 Hz). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 161.1 (N=CH), 157.8 (Ar C), 141.7 (Ar C), 141.4 (Ar C), 130.3 (Ar CH), 127.1 (Ar CH), 125.4 (Ar CH), 119.8 (Ar CH), 118.4 (Ar C), 115.8 (Ar C), 54.4 (Ar-CCH<sub>2</sub>N), 53.9 (NCH<sub>2</sub>CH<sub>2</sub>), 34.4 (C(CH<sub>3</sub>)<sub>3</sub>), 32.2 (NCH<sub>2</sub>CH<sub>2</sub>), 31.9 (C(CH<sub>3</sub>)<sub>3</sub>), 27.1 (N(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 26.6 (N(CH<sub>2</sub>)<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 22.9 (N(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 14.4 (N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 2954s, 1619s, 1205s, 822, 748s. m/z 823 (M<sup>+</sup>).

## 2.8.4 Synthesis of Metal Complexes

### 2.8.4.1 Neutral “Metal-only” Complexes

[Cu(4-2H)] (**10**). A solution of ligand **4** (1.30 g, 0.0016 mol) in methanol (30 ml) was added to a solution of Cu(CH<sub>3</sub>COO)<sub>2</sub>·H<sub>2</sub>O (0.323 g, 0.00162 mol) in methanol (30 ml) and stirred overnight. The solvent was removed *in vacuo* to yield a black solid which was dissolved in chloroform (30 ml) and washed with a pH 9 ammonia solution (2 × 30 ml). The organic extract was dried with MgSO<sub>4</sub>, filtered and concentrated *in vacuo* to yield **10** as a *black solid* (1.37 g, 98%). The product was then used without further purification; (Cu-content by ICP-OES for a 0.002M solution in butan-1-ol: found 157.2 ppm, C<sub>54</sub>H<sub>84</sub>N<sub>4</sub>O<sub>2</sub>Cu requires 157.9 ppm);

$\nu_{\max}/\text{cm}^{-1}$  2955s, 1618s, 1201, 734;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 318 (23280), 446 (15360), 580 (350).  $m/z$  884 ( $\text{M}^+$ ).

Other “metal-only” complexes were prepared in a similar manner.

[Ni(4-2H)](12). (1.35 g, 96%) (Ni-content by ICP-OES for a 0.002M solution in butan-1-ol: found 144.9 ppm,  $\text{C}_{54}\text{H}_{84}\text{N}_4\text{O}_2\text{Ni}$  requires 145.8 ppm);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 8.26 (2H, s, N=CH), 7.85 (2H, d,  $J(\text{Ar-H})$  2.5 Hz), 7.72 (2H, m, Ar-H), 7.24 (2H, m, Ar-H), 7.17 (2H, m,  $J(\text{Ar-H})$  2.6 Hz), 3.93 (4H, s, Ar- $\text{CH}_2\text{N}$ ), 2.61 (8H, t,  $J(\text{NCH}_2\text{CH}_2)$  7.6 Hz), 1.59 (8H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.31 (42H, m,  $(\text{CH}_3)_3\text{C}$ ,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 0.81 (12H, t,  $J(\text{N}(\text{CH}_2)_5\text{CH}_3)$  6.5 Hz).  $\nu_{\max}/\text{cm}^{-1}$  2954s, 1618s, 1204, 934, 734;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 258 (42000), 299 (22840), 387 (28360), 495 (9160).  $m/z$  879 ( $\text{M}^+$ ).

[Cu(1-2H)] (7). (1.29 g, 96%) (Cu-content by ICP-OES for a 0.002M solution in butan-1-ol: found 157.3 ppm,  $\text{C}_{50}\text{H}_{84}\text{N}_4\text{O}_2\text{Cu}$  requires 157.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  2952s, 1628s, 1203, 830.  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 283 (27400), 382 (11158), 576 (380).  $m/z$  836 ( $\text{M}^+$ )

[Zn(1-2H)] (11). (1.29 g, 96%) (Zn-content by ICP-OES for a 0.002M solution in butan-1-ol: found 134.2 ppm,  $\text{C}_{50}\text{H}_{84}\text{N}_4\text{O}_2\text{Zn}$  requires 162.5 ppm);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 8.30 (2H, br, N=CH), 7.51 (2H, d,  $J(\text{Ar-H})$  2.2 Hz), 7.19 (2H, d,  $J(\text{Ar-H})$  2.2 Hz), 3.93 (4H, s, HC=N $\text{CH}_2$ ), 3.65 (4H, s, Ar- $\text{CH}_2\text{N}$ ), 2.47 (8H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.53 (8H, m,  $\text{NCH}_2\text{CH}_2$ ), 1.30 (42H, m,  $(\text{CH}_3)_3\text{C}$ ,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 0.88 (12H, m,  $\text{N}(\text{CH}_2)_5\text{CH}_3$ ).  $\nu_{\max}/\text{cm}^{-1}$  2965s, 1632s, 1220s, 754s;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 354 (6517).  $m/z$  838 ( $\text{M}^+$ ), 775 ( $\text{L}^+$ ).

[Cu(2-2H)] (8). (1.48 g, 96%) (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 77.9 ppm,  $\text{C}_{60}\text{H}_{88}\text{N}_4\text{O}_2\text{Cu}$  requires 78.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  2952s, 1617s, 1534, 1220, 821;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 286 (34400), 410 (13942), 640 (440).  $m/z$  960 ( $\text{M}^+$ ).

[Cu(3-2H)] (9). (1.39 g, 98%) (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 79.1 ppm,  $C_{54}H_{90}N_4O_2Cu$  requires 78.9 ppm);  $\nu_{max}/cm^{-1}$  2950s, 1615s, 1463, 1261, 834;  $\lambda_{max}/nm$  ( $\epsilon/dm^3 mol^{-1} cm^{-1}$ ) ( $CHCl_3$ ) 281 (18320), 379 (6390), 560 (240).  $m/z$  890 ( $M^+$ ).

#### 2.8.4.2 Metal Sulfate Complexes

The  $CuSO_4$  complex **13** was prepared as described previously.<sup>12</sup> Diffusion of diethyl ether vapours into a solution of the complex **13** in methanol produced crystals suitable for X-ray diffraction. 2-Hydroxy-3-(piperidin-4-ylmethyl)-5-*tert*-butylbenzaldehyde was prepared by a literature method<sup>12</sup> and used as follows.

[Cu(6)SO<sub>4</sub>] (14). To a stirred solution of 2-hydroxy-3-(piperidin-4-ylmethyl)-5-*tert*-butylbenzaldehyde (0.2 g, 0.72 mmol) in methanol (20 ml) was added a solution of phenylene-1,2-diamine (0.039 g, 0.36 mmol) in methanol (10 ml). The resultant orange solution was stirred for 1 h and then intimately mixed with a solution of  $CuSO_4 \cdot 5H_2O$  (0.09 g, 0.36 mmol) in methanol (20 ml) for a further 1 h. The solvent was removed *in vacuo* and the product was recrystallised from ethanol-diethyl ether to yield **14** as a dark brown solid (0.19 g, 67%).  $\nu_{max}/cm^{-1}$  2960s, 1617s, 1120s;  $\lambda_{max}/nm$  ( $\epsilon/dm^3 mol^{-1} cm^{-1}$ ) ( $CHCl_3$ ) 315 (25604), 442 (16342), 574 (330).  $m/z$  782 ( $M^+$ ). Dissolution of the complex in chloroform and layering with hexane produced crystals suitable for X-ray diffraction.

#### 2.8.5 The pH Dependence of Sulfate-loading

The “metal-only” complexes **7** – **10**, and **12** were taken through the following procedure and then analysed for sulfur and metal content.

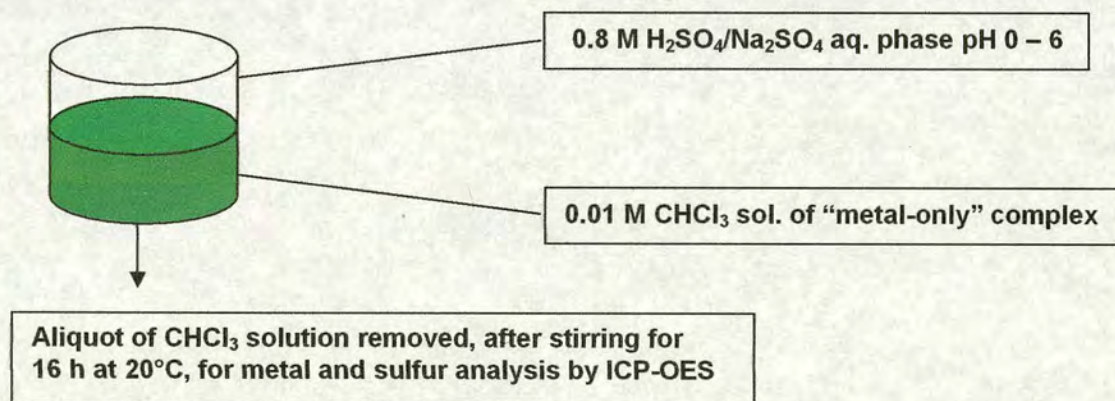
##### 2.8.5.1 Preparation of Acid and “Metal-only” Complex Solutions

Acid solutions of  $H_2SO_4$  were prepared having pH values in the range 0 – 6 (appendix 7.2.1). Calculated amounts of 1M  $Na_2SO_4$  were added in the preparation of these solutions in order to maintain a constant  $SO_4^{2-}$  concentration (0.8 mol  $dm^{-3}$ ).

A 0.01M chloroform stock solution of “metal-only” complex (250 ml) was also prepared.

### 2.8.5.2 Extraction Experiments on “Metal-only” Complexes

An aliquot of each acid solution (10 ml) was intimately mixed with the 0.01M “metal-only” complex (10 ml) for a period of 16 hours at 20°C to allow for equilibration (Figure 2.26). The organic layer was separated and a 2 ml aliquot (only 1 ml was taken for analysis of experiments involving **8** and **9**) was removed from each of the chloroform solutions for metal and sulfur analysis. An aliquot (2 ml for **7**, **10** and **12** and 1 ml for **8** and **9**) of the stock “metal-only” complex was also taken for metal analysis. The removed aliquots were thoroughly dried *in vacuo*, and then redissolved in butan-1-ol (10 ml). Elemental analysis of these solutions was performed by ICP-OES. The maximum sulfate and metal content was defined using the assumption that in the fully loaded complex the ligand to sulfate to metal ratio is 1 : 1 : 1. The pH of each aqueous layer after the extractions was recorded (appendix 7.3.1).



**Figure 2.26** Procedure for solvent extraction experiments on “metal-only” complexes.

### 2.8.5.3 Extraction Experiment on the Free Ligand **4**

Extraction experiments were carried out using the same procedure as before (Figure 2.26) except that a 0.01M chloroform solution of free ligand was used instead of



“metal-only” complex. The maximum loading of sulfate was calculated assuming the ligand binds sulfate in the ratio 1:1 (appendix 7.3.1.4.3).

### 2.8.6 UV-Visible Analysis of the Solvent Extraction Experiments on “Metal-only” Complexes 7 – 9

Aliquots, of 500  $\mu\text{L}$  were removed from each of the butan-1-ol solutions prepared for analysis by ICP-OES and were each subsequently dissolved in butan-1-ol (10 ml). The resulting solutions ( $0.1 \text{ mmol dm}^{-3}$  (7) and  $0.05 \text{ mmol dm}^{-3}$  (8 and 9)) were then analysed by electronic absorption spectroscopy (appendix 7.6.1).

### 2.8.7 X-Ray Structure Determinations of [Cu(5)(SO<sub>4</sub>)] and [Cu(6)(SO<sub>4</sub>)]

Data were collected at 150 K for [Cu(5)(SO<sub>4</sub>)] and 293 K for [Cu(6)(SO<sub>4</sub>)] on a Bruker SMART APEX diffractometer using Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structures were solved by Dr. Paul Plieger using direct methods (SHELXS 97)<sup>26</sup> and refined on  $F^2$  by full-matrix least squares (SHELXL 97).<sup>26</sup> All hydrogen atoms were identified via the difference map then placed in idealised positions using a riding model. However in the structure of [Cu(5)(SO<sub>4</sub>)] the protons were not included in the model for solvent molecules. All non H-atoms were refined anisotropically. The final refinement statistics are presented in Table 2.7.

**Table 2.7** Crystallographic data for [Cu(5)SO<sub>4</sub>] and [Cu(6)SO<sub>4</sub>].

	[Cu(5)SO <sub>4</sub> ]	[Cu(6)SO <sub>4</sub> ]
Emp. Formula	C <sub>80</sub> H <sub>108</sub> Cu <sub>2</sub> N <sub>8</sub> O <sub>21</sub> S <sub>2</sub>	C <sub>85</sub> H <sub>115</sub> Cl <sub>15</sub> Cu <sub>2</sub> N <sub>8</sub> O <sub>13</sub> S <sub>2</sub>
<i>M</i>	1708.94	2179.80
Crystal System	Monoclinic	Triclinic
Space group	P2 <sub>1</sub>	<i>P</i> $\bar{1}$
<i>a</i> /Å	14.1384(15)	16.624(2)
<i>b</i> /Å	16.7070(18)	18.211(2)
<i>c</i> /Å	19.412(2)	19.431(3)
$\alpha$ /°	90	95.711(3)
$\beta$ /°	92.492(2)	115.323(2)
$\gamma$ /°	90	103.497(2)
<i>V</i> /Å <sup>3</sup>	4581.0(9)	5035.8(11)
<i>Z</i>	2	2
$\rho_{\text{calcd}}$ /g cm <sup>-3</sup>	1.239	1.438
$\mu$ /mm <sup>-1</sup>	0.579	0.922
<i>T</i> /K	150(2)	293(2)
Unique data ( <i>R</i> <sub>int</sub> )	16844 (0.0200)	20404 (0.3031)
No. Parameters	1019	1132
<i>R</i> <sub>1</sub> , $\omega$ <i>R</i> <sub>2</sub>	0.0622, 0.1640	0.1138, 0.2147
<i>R</i> <sub>1</sub> , $\omega$ <i>R</i> <sub>2</sub> (all data)	-	0.2903, 0.2901

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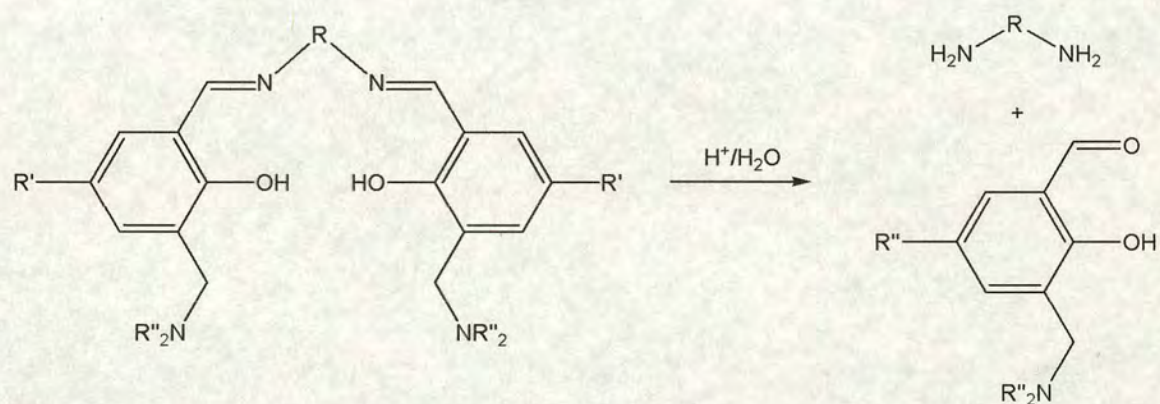
## **Chapter 3 : The Stability of Metal Salt Extractants**

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### 3.1 Introduction

In a commercial solvent extraction process a key requirement for an extractant is that it needs to have stability to both hydrolysis and oxidation to ensure a long lifetime. Hydrolytic stability is particularly important because in the process an organic solution of ligand is usually intimately mixed with an acidic leach solution containing a complex mixture of metal ions, some of which are potential catalysts for hydrolysis. In many circuits the spent electrolyte used for stripping (see section 1.4) is even more acidic.

The ditopic zwitterionic ligands studied in this thesis all contain the imine functionality which is used in metal coordination. The imine bond is intrinsically unstable to hydrolysis in a mildly acidic single phase system (Figure 3.1). The commercial phenolic oxime extractants also contain a carbon to nitrogen double bond (C=N) but although the stability of oximes is poor in an acidic single phase, in a two-phase kerosene-water (acid) system their half-life has been estimated at approximately 2.5 to 4.5 years.<sup>1</sup>



**Figure 3.1** Ligand break-up via hydrolytic attack.

Most degradation of the oxime extractants takes place at the stripping stage of the process as this step requires a high concentration of sulfuric acid in the aqueous phase.<sup>1</sup> However the extent of ligand break-up is minimal, reflecting the low solubility of the extractant in sulfuric acid solutions and the negligible solubility of

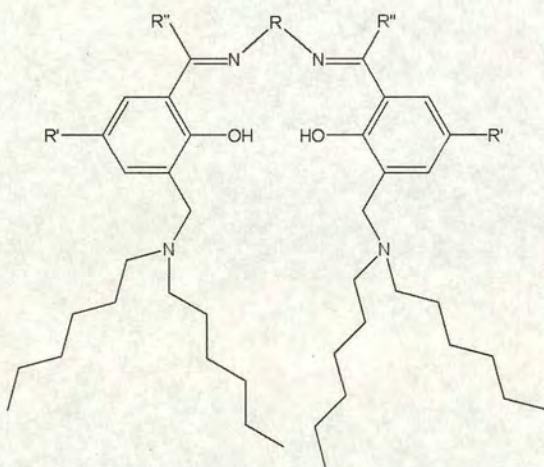
sulfuric acid in the organic phase. Degradation probably only occurs at the solution interface.

The commercial phenolic oxime extractants operate in a kerosene / water two-phase system (often containing a modifier such as tridecanol) but in this thesis nearly all of the extraction experiments have been performed in chloroform / water. The reason for this is that chloroform is a more polar water-immiscible solvent so ligands do not need to be functionalised with bulky alkyl substituents to achieve solubility in the organic phase. This enables them to be more easily synthesised and characterised. Water has a much higher solubility in chloroform than in kerosene making hydrolytic attack more favourable. This is in fact very useful as it allows the relative stability of a variety of ligands to be recorded and compared since degradation will happen at a greater rate than in a kerosene solvent system. The studies detailed in this chapter assess the hydrolytic stability of the ligands detailed in chapter 2 and other new ligands which it was hoped would show an improved resistance to hydrolysis.

## 3.2 Synthesis

### 3.2.1 Ligands and Metal Complexes

The ligands (Figure 3.2) and metal complexes synthesised for this chapter are summarised below (Table 3.1).



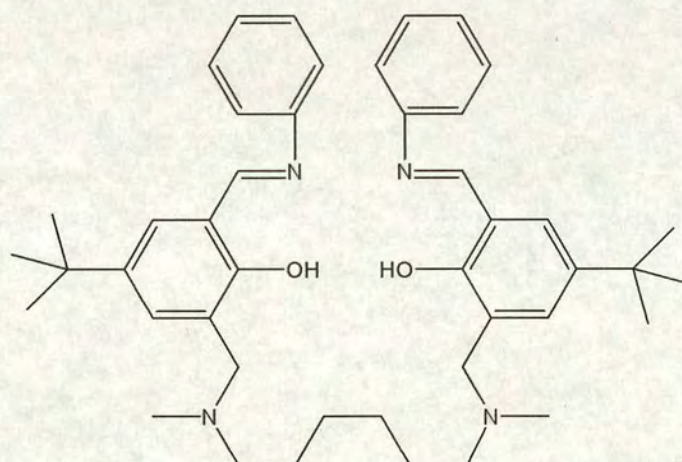
**Figure 3.2** Ditopic ligands for metal sulfate extraction; R = alkyl, aryl; R' = alkyl; R'' = alkyl, aryl.

**Table 3.1** Ligands and metal complexes synthesised and their designated reference numbers.

Ligands	R	R'	R''	Metal Complexes	
1	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	H	6	[Cu(5-2H)]
2	2,2'-biphenyl	Bu <sup>t</sup>	H	7	[Cu(1-2H)]
3	± <i>trans</i> -1,2-cyclohexane	Bu <sup>t</sup>	H		
4	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	Bu <sup>t</sup>	H		
5	-(CH <sub>2</sub> ) <sub>2</sub> -	Bu <sup>t</sup>	-C <sub>6</sub> H <sub>5</sub>		

### 3.2.1.1 Free ligands

1 – 4 were synthesised as previously described in chapter 2. A sample of 8 was provided by Dr. Paul Plieger (Figure 3.3).<sup>2</sup>

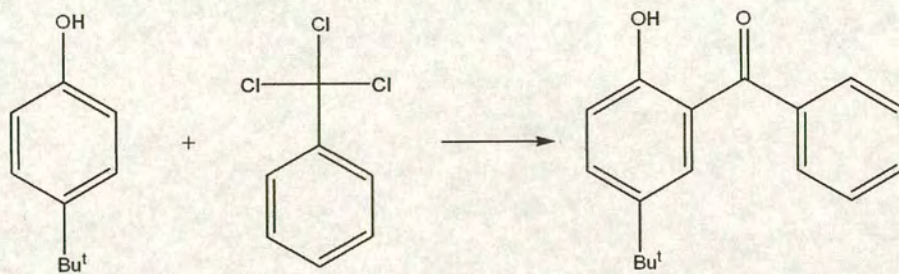


**Figure 3.3** Ligand 8 provided by Dr. Paul Plieger.

5 was made by a similar route to ligands 1 – 4 except for the initial step which involved the synthesis of 2-hydroxy-5-*tert*-butylbenzophenone by a modification of the method used by Kopczynski et al.<sup>3</sup> This required the reaction of benzotrichloride with *tert*-butyl phenol in aqueous sodium hydroxide (Figure 3.4). The product was purified by silica column chromatography (hexane : ethyl acetate, 9 : 1) followed by

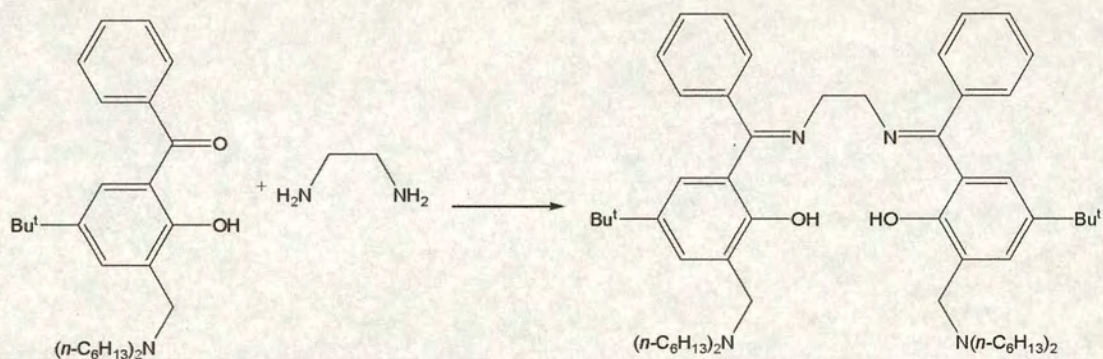


distillation (1mm Hg, b.p. 160°C) to give 2-hydroxy-5-*tert*-butylbenzophenone in a moderate yield (40%).



**Figure 3.4** The synthesis of 2-hydroxy-5-*tert*-butylbenzophenone.

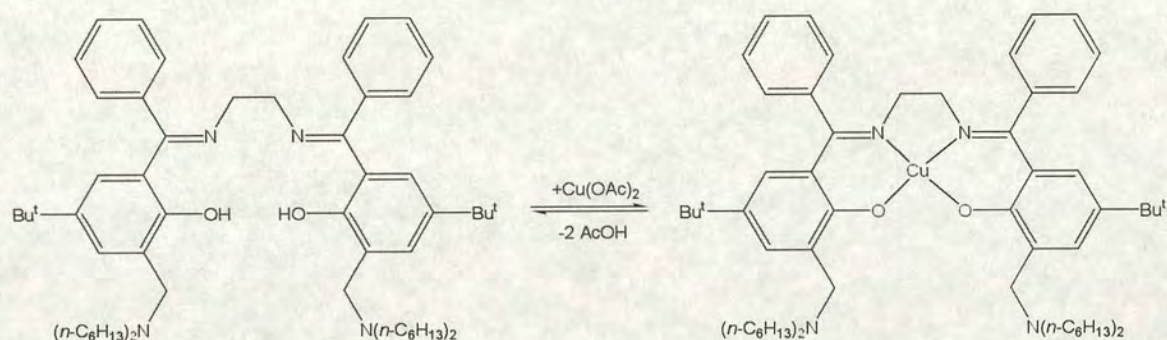
The benzophenone was substituted in the position *ortho* to the hydroxyl group with the Mannich base ethoxy-*N*-dihexylaminomethane and the resulting ketone converted to ligand **5** as in Figure 3.4.



**Figure 3.4** The synthesis of Ligand **5** by a Schiff base condensation.

### 3.2.1.2 Synthesis of “Metal-only” Complexes

The preparation of “copper-only” complex [Cu(1-2H)] is described in chapter 2, and [Cu(5-2H)] was performed similarly, see Figure 3.5.



**Figure 3.5** The synthesis of the “copper-only” complex 6.

## 3.3 Characterisation

### 3.3.1 Free Ligands

The characterisation of 1 – 4 is described in chapter 2. Ligand 5 was characterised by FTIR spectroscopy. A peak was seen for C-H stretches ( $2955 \text{ cm}^{-1}$ ). The presence of the imine ( $\text{C}=\text{N}$ ) band, with a strong absorbance at  $1611 \text{ cm}^{-1}$ , and the absence of a carbonyl stretch ( $\sim 1660 \text{ cm}^{-1}$ ) confirmed the successful completion of the Schiff base condensation reaction. The ketimine peak occurs at a lower frequency than that seen for the closely related aldimine ligand 1 ( $1634 \text{ cm}^{-1}$ ) suggesting that the phenyl group weakens the imine bond. A lowering of the imine frequency is also observed in ligands 2 and 4 which have aromatic substituents attached to the imine nitrogen atoms.

5 was fully characterised by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy. The characteristic imine proton resonance in the  $^1\text{H}$  NMR spectrum of ligands 1 – 4 is not present in ligand 5 but the successful completion of the Schiff base reaction was confirmed using  $^{13}\text{C}$

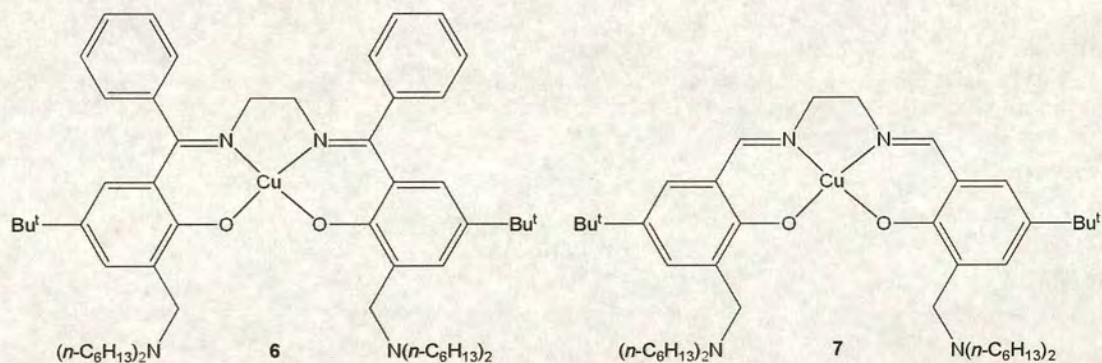
NMR spectroscopy by the presence of the imine carbon signal (176.1 ppm) and the absence of a carbonyl peak (~198 ppm). The FAB mass spectrum adds further evidence as it shows a peak assignable to the formation of the free ligand **5**.

### 3.3.2 “Metal-only” Complexes

The IR spectrum of the “copper-only” complex (**6**) of ligand **5** shows a lowering of the imine frequency (1611 → 1580  $\text{cm}^{-1}$ ) compared to the free ligand, indicating that the imine nitrogen is directly involved in copper-binding.

The FAB mass spectrum and copper analysis by ICP-OES of **6** both confirm a copper to ligand ratio of 1 : 1.

The electronic absorption spectrum of the “copper-only” complex **6** contains a moderately intense peak at 383 nm which is charge-transfer in character and a weak feature at 570 nm which can be assigned to d-d transitions.<sup>4, 5</sup> These wavelengths are close to those in the other 1,2-ethane-bridged “copper-only” complex **7** (Figure 3.6) which suggests that metal coordination in **6** is not significantly affected by the presence of the phenyl groups on the imine carbons.

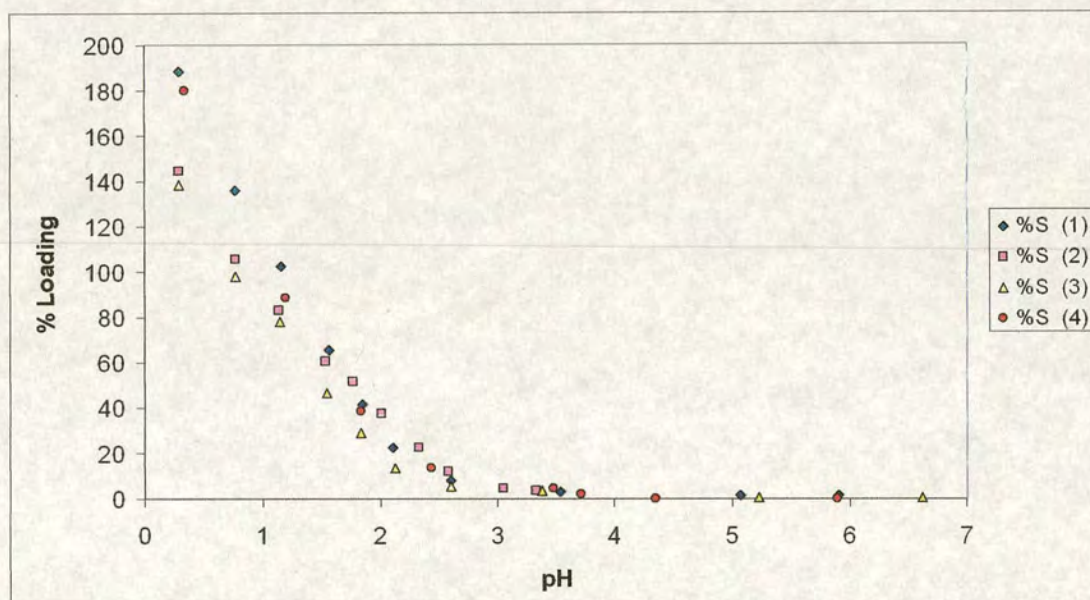


**Figure 3.6** The “copper-only” complexes **6** and **7**. Electronic absorption peaks at 383, 570 nm for **6** and 382, 576 nm for **7**.

### 3.4 The pH Dependence of Sulfate-loading onto Free Ligands 1 - 4

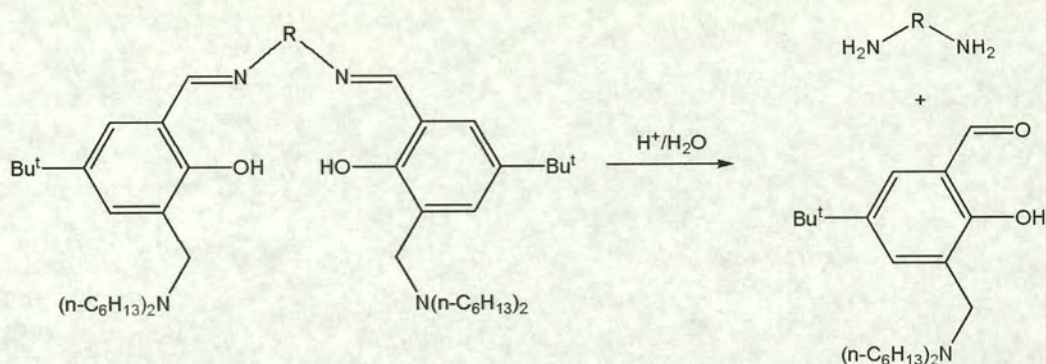
The pH dependence of sulfate-loading onto the free ligand **4** was discussed in chapter 2. It was found that it did not significantly bind sulfate at  $\text{pH} > 2$  whereas the metal complex  $[\text{Cu}(\mathbf{4}\text{-}2\text{H})]$  extracted sulfate at  $\text{pH} < 4.5$ .

The pH dependence of sulfate-loading of the other free ligands **1** – **3** was found to be remarkably similar to that of ligand **4** (Figure 3.7). This is surprising because the “copper-only” complexes of these ligands exhibit varied extraction profiles.



**Figure 3.7** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by free ligands **1** – **4**. All points were measured at least twice.

This raised the issue of whether the pH-dependence profiles all originated from the same compound, the parent aldehyde which would remain in the organic phase following hydrolysis, as shown in Figure 3.8, after loss of most of the parent diamine to the aqueous phase.



**Figure 3.8** The degradation of ligands **L** by hydrolysis where R =  $-(CH_2)-$ , 2,2'-biphenyl, ( $\pm$ )-trans-1,2-cyclohexane,  $o$ - $C_6H_4$  for **1**, **2**, **3**, **4**, respectively.

### 3.5 Hydrolytic Stability Tests

#### 3.5.1 Ligands 1 - 4

The pH-dependence of hydrolysis of the imine bonds in ligands **1** – **4**, in a two-phase  $CHCl_3/H_2O$  system, was monitored by recording the extent of degradation, at different pH, by comparing the integrals of the aldehyde proton and imine proton resonances in the  $^1H$  NMR spectra ( $CDCl_3$ ).

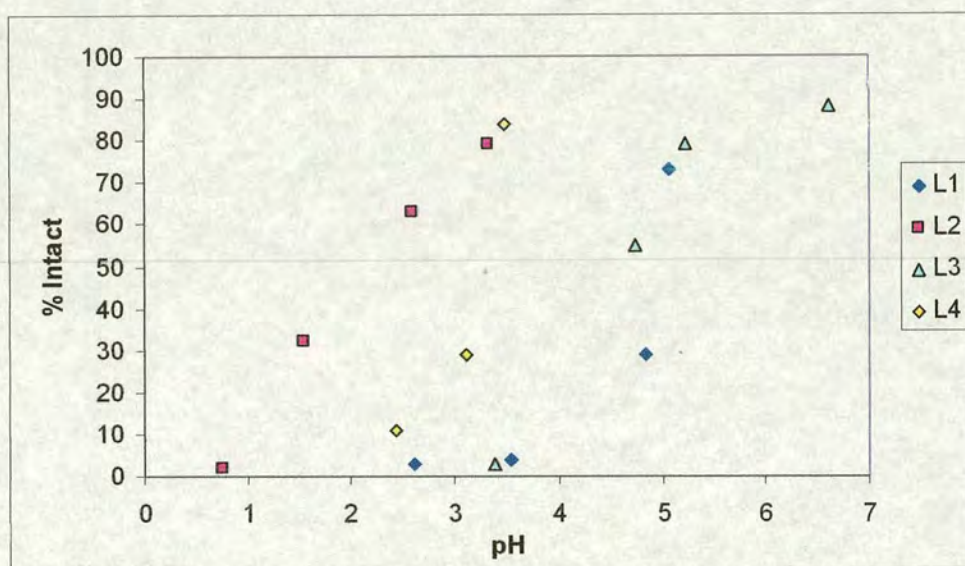
With **4** it was found that after stirring a 0.01M  $CHCl_3$  solution of ligand with an aqueous sulfuric acid solution of  $pH < 2$  for 16 hours the ligand was completely hydrolysed. However, as the pH was increased  $> 3$  this rate of hydrolysis was reduced and above pH 3.5 the majority of ligand remained intact (Table 3.2).

**Table 3.2** The % of **4** remaining after contact with  $H_2SO_4$  solutions of different strengths for 16 hours at  $20^\circ C$ . Equilibrium pH values of the aqueous phase are recorded.

	pH	% Intact
<b>Ligand 4</b>	2.44	11
	3.11	29
	3.48	84

Therefore at  $\text{pH} < 2$  after 16 hours the molecule under study is not the ligand but the parent aldehyde, 2-hydroxy-3-diethylaminomethyl-5-tert-butyl-benzaldehyde. This would explain the poor sulfate-loading by **4**. However at  $\text{pH} \sim 3.5$  the ligand is largely intact and the poor sulfate-loading under these conditions is consistent with the suggestion that the untemplated ligand is a poor sulfate extractant compared to its corresponding “metal-only” complexes (see section 2.4.2).

The results of similar stability tests performed on free ligands **1** – **3** are shown in Figure 3.9.



**Figure 3.9** The % of ligands **1-4** remaining after contact with  $\text{H}_2\text{SO}_4$  solutions of different strengths for 16 hours at  $20^\circ\text{C}$ . Equilibrium  $\text{pH}$  values of the aqueous phase are recorded.

The ligands containing aromatic bridging groups (**2**, 2,2'-biphenyl and **4**, *o*-phenylene) are much more resistant to hydrolysis than those bridged by aliphatic groups (**1**, 1,2-ethane and **3**, ( $\pm$ )-trans-1,2-cyclohexane). This was attributed to the increased stability provided by conjugation of the imine bond into an aromatic ring.

Ligand **2** was found to be the most stable at low  $\text{pH}$  and this may be a result of the increased hydrophobicity, in the area surrounding the imine bond, which is provided by the bulky 2,2'-biphenyl groups. However it is interesting to note that the sulfate-

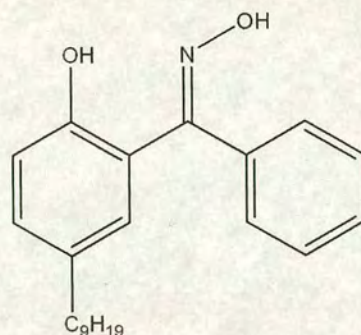
loading graph of **2** was still very similar to those of ligands **1**, **3** and **4**, which mainly involve extraction by the parent aldehyde at low pH (Figure 3.7). This may indicate that **2** and the aldehyde precursor have very similar sulfate-binding strengths. This is not unreasonable when it is considered that without the metal to template the formation of a binding site both the ligand and aldehyde precursor will consist of unorganised ammonium groups.

In chapter 2 **1** was found to fit an ideal profile for a metal sulfate extractant but its stability to hydrolytic attack is poor (Figure 3.9) as significant hydrolysis occurs even at pH 4.5. Conventionally in industry a kerosene/water system is used and this would be expected to reduce the contact the ligand has with acidic solutions due to the low polarity of kerosene. However the fact that **1** has an inferior stability to ligands **2** and **4** gives cause for concern that it would not be able to withstand the rigours of a commercial process.

### 3.5.2 Ligand 5

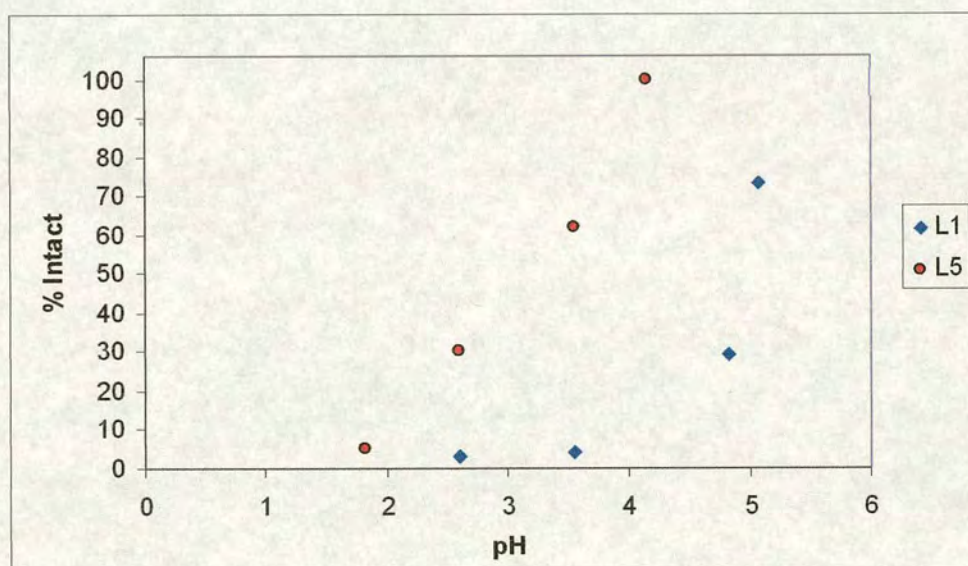
**5** was considered as an extractant with the aim to retain the ideal copper and sulfate loading profiles of **1** but improve the hydrolytic stability of the imine bond, as a consequence of having the imine phenyl substituted.

This approach has been claimed to improve the hydrolytic stability of the phenolic oxime extractants.<sup>1</sup> In LIX 65N (Figure 3.10) a phenyl ring replaces the azomethine hydrogen atom in the aldoxime reagent. This has the effect of improving the stability and it is also found to be more effective than replacing the hydrogen with a methyl group.<sup>1</sup>



**Figure 3.10** The phenolic oxime copper extractant LIX 65N.<sup>1</sup>

As **5** does not contain an imine proton the stability tests were performed by monitoring the integral of the  $-CH_2-$  resonance in the  $^1H$  NMR spectrum ( $CDCl_3$ ), from the 1,2-ethane-bridging unit, after contact with sulfuric acid at various pH. The results for **5** and **1** in Figure 3.11 reveal that the stability has been substantially increased by the incorporation of the phenyl group at the azomethine carbon atom. The ligand **5** is likely to inhibit acid attack, more efficiently than **1**, by increasing the hydrophobicity of the environment surrounding the imine bond and on steric grounds by blocking the approach of hydroxonium ions and water molecules.



**Figure 3.11** The % of ligands **1** and **5** remaining after contact with  $H_2SO_4$  solutions of different strengths for 16 hours at  $20^\circ C$ . Equilibrium pH values of the aqueous phase are recorded.

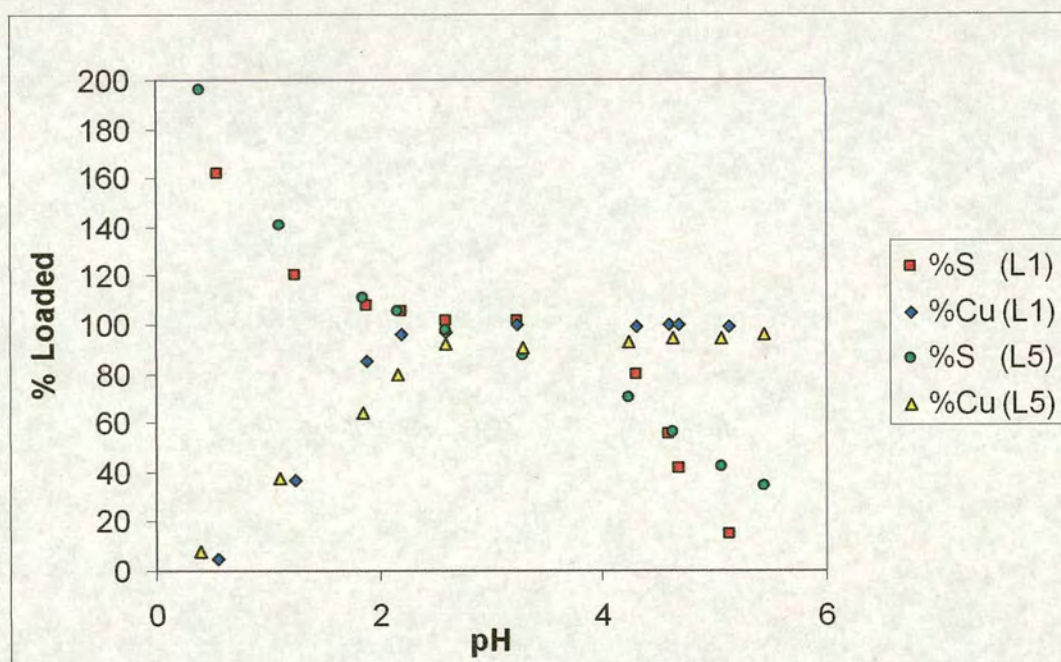


The results also reveal that ligand **2** is more effective at resisting acid attack at low pH than **5**. This could be due to a lack of conjugation of the imine bond into the phenyl ring in ligand **5** as in a closely related solid state structure<sup>6</sup> the phenyl rings are twisted from the plane of the molecule due to steric constraints.

### 3.6 The pH Dependence of Sulfate-loading onto [Cu(5-2H)]

Although **5** has improved hydrolytic stability compared to **1** in order to be a more practicable extractant it must also have the ideal copper and sulfate loading profiles shown by **1**.

The pH dependence of sulfate-loading and “strength” of metal-binding of “copper-only” complex **6** (investigated as described in section 2.4.1) are compared with those of the “copper-only” complex of **1** in Figure 3.12.



**Figure 3.12** The pH dependence of H<sub>2</sub>SO<sub>4</sub> uptake and “strength” of copper-binding by [Cu(5-2H)], **6** and [Cu(1-2H)], **7**.

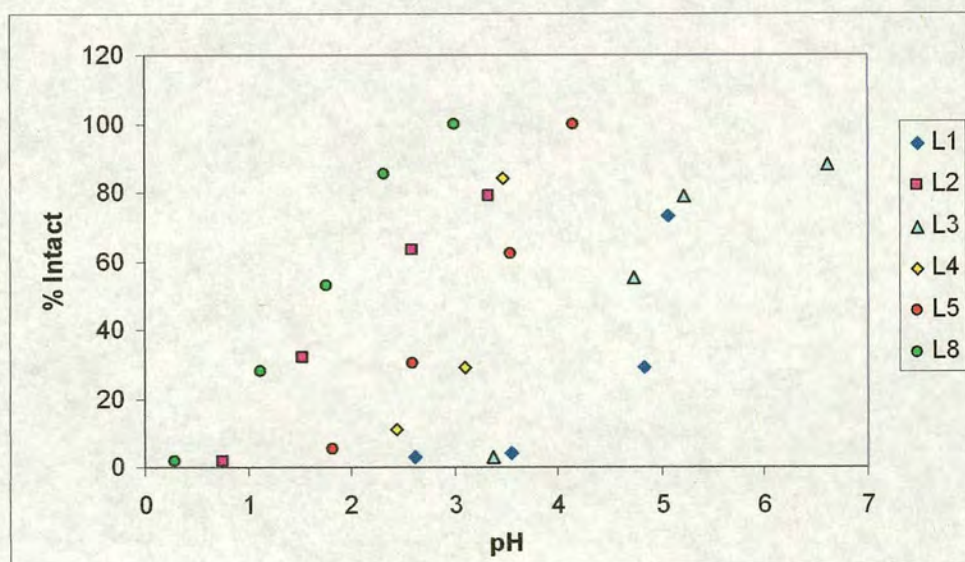
The  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper-binding shown by these reagents were found to be very similar, indicating that the incorporation of the phenyl rings into **6** did not significantly alter the metal-binding geometry.

Extractant **5** is therefore more practicable than **1** as it has the same “ideal” profile for copper sulfate loading but demonstrates improved hydrolytic stability.

### 3.7 The Hydrolytic Stability of Ligand **8**

Conjugation of the imine bond has been shown to be an effective way of improving its hydrolytic stability (section 3.4). The “bottom-up” ligand **8** (Figure 3.3) was studied to monitor this effect further as the phenyl groups should be in the same plane as the imine bond and in the free ligand form it is unlikely that the two phenyl rings would be in close proximity of each other.

The results showed that free ligand **8** has the greatest resistance to hydrolysis of all the ligands studied (Figure 3.13). This can be attributed to the effective conjugation of the imine bond.



**Figure 3.13** The % of ligands **1-5**, & **8** remaining after contact with  $\text{H}_2\text{SO}_4$  solutions of different strengths for 16 hours at  $20^\circ\text{C}$ . Equilibrium pH values of the aqueous phase are recorded.

### 3.8 Conclusions

Although the hydrolytic stability of **1** – **4** in  $\text{CHCl}_3$  when contacted with aqueous solutions of very low pH is poor this problem is likely to be less severe if kerosene is used as the solvent. In order to exploit this effect it will be necessary to develop “greasier” versions of the reagents with high kerosene solubility.

The experiments conducted in  $\text{CHCl}_3$  / water reported in this chapter proved useful as they have allowed the relative stabilities of a variety of closely related ligands to be determined. Changes to the environment of the imine bond significantly affect its stability and systems which have aromatic substituents on the azomethine group show significantly enhanced stability to hydrolysis. This may arise as a consequence of conjugation of the imine bond into an aromatic ring. However, steric factors could also be very important as bulky aryl groups are likely to restrict the approach of hydroxonium ions and water molecules to the azomethine group. This approach may also be inhibited by the general increase in the hydrophobicity of the system caused by increased aromatic substitution. In practice it is possible that it is a combination of these effects which lead to the enhanced hydrolytic stability of the imine bond.

The improvement in stability shown by the ketimine ligand **5**, which has a phenyl group on the azomethine carbon, was not at the expense of its ability to function as an extractant as it was shown to have an ideal  $\text{CuSO}_4$  loading profile similar to ligand **1**.

### 3.9 Experimental

#### 3.9.1 Instrumentation

Details of the instrumentation used have been given in chapter 2 (section 2.8.1).

### 3.9.2 Solvent and Reagent Pre-treatment

Unless stated to the contrary, commercial grade chemicals obtained from Aldrich or Acros were used without further purification.

### 3.9.3 Ligand Synthesis

Ligands 1 – 4 were made as previously described in chapter 2. Ligand 8, *N,N'*-dimethyl-*N,N'*-bis(2-hydroxy-3-[(*E*)-phenyliminomethyl]-5-*tert*-butylbenzyl)hexane-1,6-diamine, was supplied by Dr. Paul Plieger.<sup>2</sup> Ethoxy-*N*-dihexylaminomethane was prepared as detailed previously in chapter 2 and 2-hydroxy-5-*tert*-butylbenzophenone was made by a similar procedure to that described by Kopczynski and co-workers.<sup>3</sup> 2-Hydroxy-5-*tert*-butylbenzophenone substituted with a pendant dihexylamine group was made by an adaptation of the method used by Fenton and co-workers,<sup>7</sup> as in chapter 2.

**2-Hydroxy-5-*tert*-butylbenzophenone.** Benzotrichloride (21.50 g, 0.11 mol) was added slowly, over 3 hours, to a rigorously stirred solution of 4-*tert*-butylphenol (15.0 g, 0.10 mol) in 30% NaOH solution (140 ml) at 75°C. The solution was heated to 100°C, the water was removed by distillation, the residue acidified with 18% hydrochloric acid and extracted with ether (3 × 200 ml). The combined ether layers were washed with water (200 ml), 5% sodium carbonate solution (200 ml) and again with water (200 ml). The ether fraction was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield a yellow oil which was purified by silica column chromatography (hexane: ethyl acetate, 9:1) and by distillation (1 mm Hg, b.p. 160°C) to yield 2-hydroxy-5-*tert*-butylbenzophenone as a crystalline yellow solid (10.1 g, 40%). (Found: C, 80.3; H, 7.2; N, 0.0. Calc. for C<sub>17</sub>H<sub>18</sub>O<sub>2</sub>: C, 80.3; H, 7.1; N, 0.0%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 11.85 (1H, s, ArCOH), 7.69-7.50 (7H, m, Ar-H), 7.03 (1H, m, COCCHCHCH), 1.25 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 202.3 (CO), 161.7 (Ar COH), 142.0 (Ar C), 138.8 (Ar C), 134.6 (Ar CH), 132.6 (Ar CH), 130.5 (Ar CH), 129.9 (Ar CH), 129.0 (Ar CH), 119.1 (Ar C), 118.6 (Ar CH), 34.8 (C(CH<sub>3</sub>)<sub>3</sub>), 31.9 (C(CH<sub>3</sub>)<sub>3</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3180, 2956s, 1639. *m/z* 255 (M<sup>+</sup>).

**2-Hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzophenone.** A mixture of 2-hydroxy-5-*tert*-butyl-benzophenone (10.2 g, 0.04 mol) and ethoxy-N-dihexylaminomethane (9.8 g, 0.04 mol) in acetonitrile (150 ml) was heated to reflux under a dinitrogen atmosphere for 90 h. After cooling the solution to room temperature, the solvent was removed *in vacuo* to yield a viscous brown oil. The oil was purified by silica column chromatography (hexane: ethyl acetate, 25:1) to yield 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzophenone as a *yellow liquid* (7.2g, 40%). (Found: C, 79.5; H, 10.2; N, 3.0. C<sub>30</sub>H<sub>45</sub>NO<sub>2</sub> requires C, 79.8; H, 10.0; N, 3.1%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.90-7.85 (2H, m, Ar-*H*), 7.60-7.35 (5H, m, Ar-*H*), 3.80 (2H, s, ArCCH<sub>2</sub>N), 2.55 (4H, t, *J*(NCH<sub>2</sub>CH<sub>2</sub>) 7.2 Hz), 1.52 (4H, m, NCH<sub>2</sub>CH<sub>2</sub>), 1.31-1.27 (21H, m, (CH<sub>3</sub>)<sub>3</sub>C, NCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>), 0.89 (6H, t, *J*(N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>) 5.9 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 199.0 (CO), 160.8 (Ar COH), 141.7 (Ar C), 139.0 (Ar C), 133.0 (Ar CH), 130.5 (Ar CH), 130.2 (Ar CH), 128.7 (Ar CH), 126.9 (ArCH), 124.9 (Ar C), 124.5 (Ar C), 57.6 (ArCCH<sub>2</sub>N), 54.3 (NCH<sub>2</sub>CH<sub>2</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 32.4 (NCH<sub>2</sub>CH<sub>2</sub>), 32.1 (C(CH<sub>3</sub>)<sub>3</sub>), 27.8 (N(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 27.0 (N(CH<sub>2</sub>)<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 23.2 (N(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 14.7 (N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>).  $\nu_{\text{max}}$ /cm<sup>-1</sup> 2956s, 1660s, 1599s, 1465s, 1271s, 1172, 1004, 698. *m/z* 452 (M<sup>+</sup>).

**4,4'-Di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(ethylenedinitrilo-1,1'-phenyldimethylidyne) diphenol (5).** To a stirred solution of 2-hydroxy-3-dihexylaminomethyl-5-*tert*-butyl-benzophenone (4.1 g, 0.009 mol) in chloroform (50 ml) was added a solution of ethylenediamine (0.27 g, 0.0045 mol) in ethanol (25 ml). The yellow solution was stirred overnight and then concentrated *in vacuo* to yield a yellow oil. The product was dissolved in dichloromethane (75 ml) and extracted with water (3 × 30 ml). The organic fraction was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **5** as a viscous *yellow oil* (4.02 g, 96 %) which was used without further purification. (Found: C, 80.3; H, 10.1; N, 5.9. C<sub>62</sub>H<sub>94</sub>N<sub>4</sub>O<sub>2</sub> requires C, 80.3; H, 10.2; N, 6.0%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.60-7.05 (7H, m, Ar-*H*), 3.77 (4H, s, C=NCH<sub>2</sub>), 3.60 (4H, s, Ar-CH<sub>2</sub>N), 2.45 (8H, t, *J*(NCH<sub>2</sub>CH<sub>2</sub>) 7.0 Hz), 1.45 (8H, m, NCH<sub>2</sub>CH<sub>2</sub>), 1.30-1.20 (34H, m, (CH<sub>3</sub>)<sub>3</sub>C, NCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.08 (8H, m, N(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 0.83 (12H, t, *J*(N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>) 6.7 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 176.4 (N=C), 159.6 (Ar C), 139.6 (Ar C), 135.0 (Ar C), 130.5 (Ar CH), 129.3 (Ar

CH), 128.6 (Ar CH), 127.9 (Ar CH), 126.8 (Ar CH), 124.5 (Ar C), 118.9 (Ar C), 55.1 (ArCCH<sub>2</sub>N), 53.4 (C=NCH<sub>2</sub>), 50.8 (NCH<sub>2</sub>CH<sub>2</sub>), 34.5 (C(CH<sub>3</sub>)<sub>3</sub>), 32.6 (NCH<sub>2</sub>CH<sub>2</sub>), 31.9 (C(CH<sub>3</sub>)<sub>3</sub>), 28.0 (N(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>), 27.8 (N(CH<sub>2</sub>)<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 23.4 (N(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>3</sub>), 14.7 (N(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>).  $\nu_{\max}/\text{cm}^{-1}$  2955s, 1611s, 1467, 1273, 888, 702.  $m/z$  927 ( $M^+$ ).

### 3.9.4 Synthesis of Neutral “Copper-only” Complexes

The “copper-only” complex **7** was prepared as described previously in chapter 2.

[Cu(5-2H)] (**6**). A solution of ligand **5** (1.85 g, 0.002 mol) in chloroform (20 ml) was added to a solution of Cu(CH<sub>3</sub>COO)<sub>2</sub>.H<sub>2</sub>O (0.403 g, 0.00202 mol) in methanol (60 ml) and stirred overnight. The solvent was then removed *in vacuo* to yield a black solid which was dissolved in chloroform (30 ml) and washed with a pH 9 ammonia solution (2 × 30 ml). The chloroform solution was dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo* to yield **6** as a *black solid* (1.90 g, 96%) which was used without further purification; (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 79.6 ppm, C<sub>62</sub>H<sub>92</sub>N<sub>4</sub>O<sub>2</sub>Cu requires 78.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  2954s, 1580s, 1442, 1263, 1086, 736, 705;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 383 (8222), 570 (320).  $m/z$  988 ( $M^+$ ).

### 3.9.5 Ligand Stability Tests

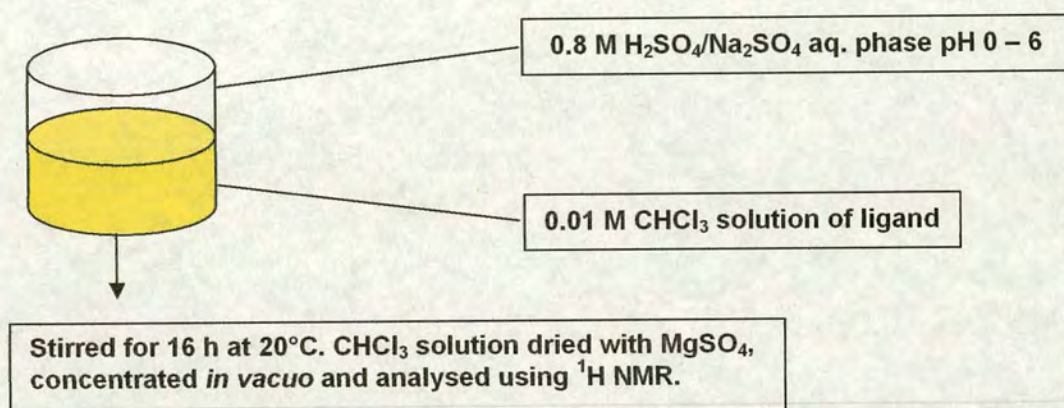
#### 3.9.5.1 Preparation of Sulfuric Acid Solutions

Acid solutions were prepared as described in chapter 2 and appendix 7.2.1.

#### 3.9.5.2 Hydrolytic Stability Tests

An aliquot of each acid solution (10 ml) was intimately mixed with a 0.01M solution of ligand (10 ml) for a period of 16 hours at 20°C (Figure 3.14). The organic layer was separated, dried with MgSO<sub>4</sub> and then concentrated *in vacuo*. The product was

then analysed by  $^1\text{H}$  NMR spectroscopy. The integrals of the imine proton and aldehyde proton were compared to evaluate the extent of hydrolysis of the ligand. In the case of ligand 5 the integral of the  $-\text{CH}_2-$  signal from the 1,2-ethane bridge was compared with the integrals of other  $-\text{CH}_2-$  signals in order to estimate the degree of hydrolysis in the ligand. The pHs of the aqueous layers after the stability experiments were also recorded (appendix 7.7).



**Figure 3.14** Procedure for hydrolytic stability experiments on ligands 1-5 and 8.

### 3.9.6 The pH Dependence of Sulfate-loading

#### 3.9.6.1 Preparation of Acid and “Copper-only” Complex Solutions

Acid solutions were made as described in chapter 2 (appendix 7.2.1). A 0.01M chloroform stock solution of “metal-only” complex (250 ml) was also prepared.

#### 3.9.6.2 Extraction Experiments on “Copper-only” Complexes

The extraction experiments were performed as described in chapter 2 (section 2.8.5). It should be noted that in these extractions a 1 ml aliquot of the  $\text{CHCl}_3$  layer was removed, dried *in vacuo* and re-dissolved in butan-1-ol (10 ml) for analysis of copper and sulfur content by ICP-OES in each case (appendix 7.3.2).

### 3.9.6.3 Extraction Experiments on the Free Ligands 1 – 3

Extraction experiments were carried out using the procedure described in chapter 2, section 2.8.5.3 (appendix 7.3.2).

### 3.10 References

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## **Chapter 4 : Amide-functionalised Metal Salt Extractants**

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## 4.1 Introduction

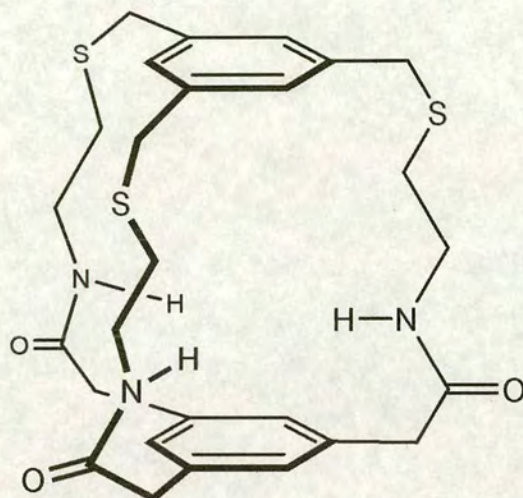
In order to maintain good materials balances in hydrometallurgical processes extractants need to show selectivity. This is complicated in the design of a metal salt extractant because selective binding is needed for both the targeted metal cation and anion. Ways to achieve selectivity in the extraction of metal ions are well defined and a variety of successful methods have been used.<sup>1</sup> However anion coordination chemistry is an emerging field and there are not as yet many examples of selective extraction.<sup>2</sup>

Anion receptors use non-covalent interactions to achieve successful anion encapsulation.<sup>3</sup> Hydrogen-bonds are among the most commonly used as they are directional which allows the design of receptors with specific shapes. This is particularly important as anions have a wide variety of geometries and sizes.

In biology the phosphate binding protein, PBP, uses hydrogen-bonds to bind phosphate anions selectively. The specificity of the phosphate recognition has been developed by the members of a family of bacterial periplasmic proteins which are responsible for the transport of small molecules such as sugars and oligopeptides.<sup>4</sup> Their role is to bind the anion tightly once it has passively diffused across the cell outer membrane.<sup>5, 6</sup> The crystal structure of PBP, with a bound monohydrogen phosphate anion, has been determined.<sup>7</sup> There are found to be 12 hydrogen-bonds involved, 7 from amide NH groups, in the anion's encapsulation. The selectivity of the binding site is achieved by the presence of a negatively charged carboxylate group which can act as a hydrogen-bond acceptor for hydrogenphosphate but repels fully deprotonated anions such as sulfate or tungstate.

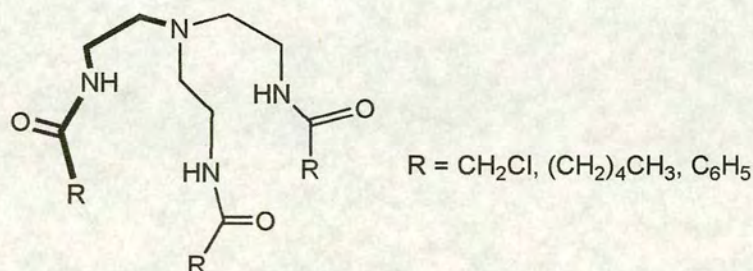
The sulfate binding protein<sup>8</sup> (section 1.7) also functions by hydrogen-bonding interactions with the anion and the significant role of 5 amide NH groups, from the polypeptide backbone, in the sulfate-binding inspired the development of the first purely amide-based receptor by Pascal and co-workers (Figure 4.1).<sup>9</sup> This neutral organic macrocycle was synthesised with the aim of encapsulating anions, using

amide hydrogen-bonds, within a pre-formed cavity. It was found to be successful in binding fluoride anions in deuterated DMSO.



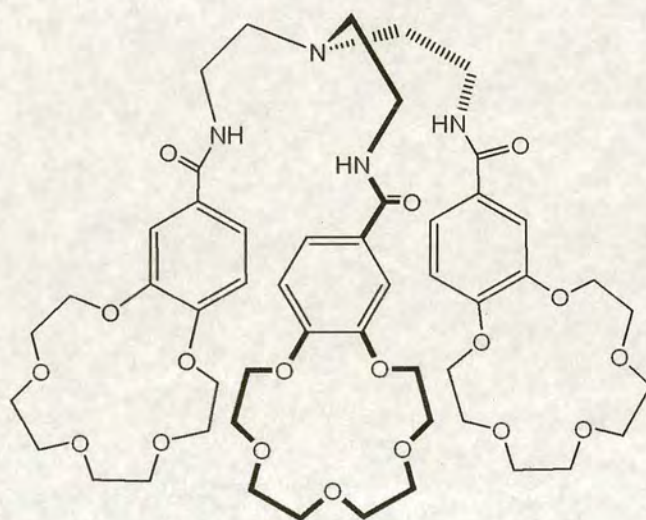
**Figure 4.1** The first purely amide-based anion receptor developed by Pascal and co-workers.<sup>9</sup>

Numerous other amide receptors have now been developed. For example Hamilton and co-workers successfully synthesised synthetic analogues of the amide-based ristocetin binding site which is found to coordinate amino acid carboxylates in biology with considerable strength.<sup>10</sup> Reinhoudt and co-workers created a variety of acyclic tripodal receptors which utilise amide groups for anion-binding (Figure 4.2).<sup>11</sup> These ligands were found to bind the tetrahedral dihydrogenphosphate anion selectively over both chloride and hydrogensulfate. Their selective binding, induced solely by hydrogen-bond formation, makes them excellent mimics of the anion-binding proteins.



**Figure 4.2** Tripodal amide receptors which show selective binding of  $\text{H}_2\text{PO}_4^-$ .<sup>11</sup>

Related tripodal amide ligands, also containing crown ether cation-binding units, were developed by Beer and co-workers (Figure 4.3).<sup>12</sup> They have been shown to function as ion pair extractants for sodium cations and the radioactive pertechnetate anion. These extractants may have useful future applications since the pertechnetate anion is commonly found in nuclear waste solutions and, as a result of discharges from nuclear fuel processing plants, it has been found to have a detrimental effect on the environment.<sup>12</sup> The ligand exhibits cooperative binding as the efficiency of transport of pertechnetate is improved by the complexation of sodium in the cation-binding site.

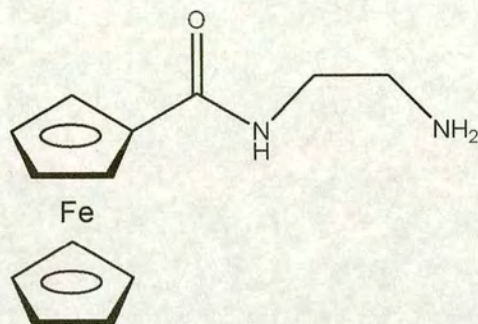


**Figure 4.3** A tripodal tris(amido benzo-15-crown 5) ligand for the extraction of  $\text{NaTcO}_4$ .<sup>12</sup>

In an attempt to enhance sulfate selectivity in the ditopic metal salt extractants described in the previous chapters, amide groups have been incorporated into the ligand framework in addition to the amine binding units because a high density of such hydrogen-bond donors is a feature of the anion-binding proteins and other successful receptors for tetrahedral oxo-anions.<sup>13</sup>

Beer and co-workers<sup>14</sup> have already demonstrated how the combination of amine and amide groups can generate an effective sulfate-binding site with the ferrocene containing receptor shown in Figure 4.4. Protonation of the amine group by the acidic  $\text{HSO}_4^-$  anion generates  $\text{SO}_4^{2-}$  which is strongly bound even in the presence of the  $\text{H}_2\text{PO}_4^-$  anion. It is the aim of this chapter to try and use similar receptor designs

to achieve selectivity for  $\text{SO}_4^{2-}$  over other anions, in solvent extraction experiments, as this is vital to achieving a good materials balance in the hydrometallurgical recovery of metal sulfates.

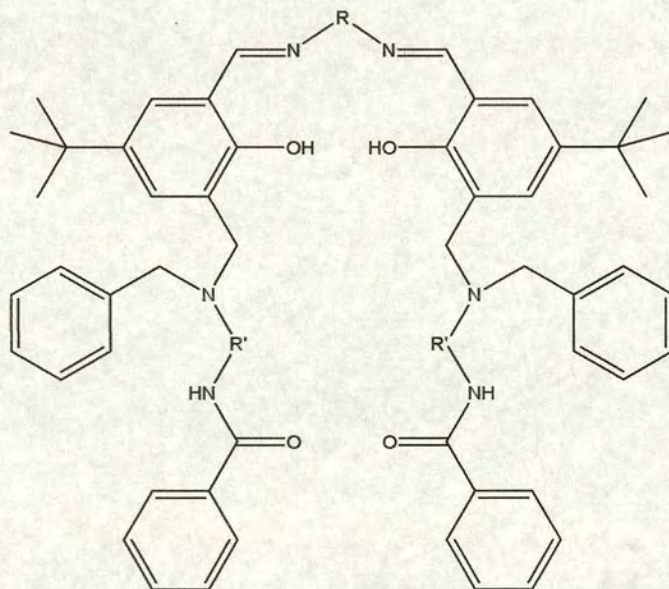


**Figure 4.4** An anion receptor containing amine and amide anion-binding groups.<sup>14</sup>

## 4.2 Synthesis

### 4.2.1 Ligands and Metal Complexes

The ligands (Figure 4.5) and metal complexes synthesised for this chapter are summarised below (Table 4.1).



**Figure 4.5** Amide-functionalised metal salt extractants;  $\text{R}$  = alkyl, aryl;  $\text{R}'$  = alkyl.

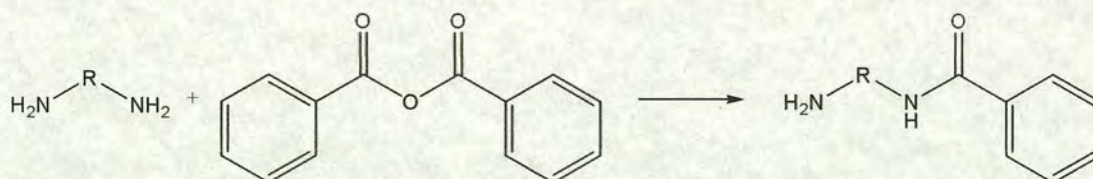
**Table 4.1** Ligands and metal complexes used in Chapter 4 and their designated reference numbers.

Ligands	R	R'	Metal Complexes	
1	-(CH <sub>2</sub> ) <sub>2</sub> -	-(CH <sub>2</sub> ) <sub>3</sub> -	5	[Cu(1-2H)]
2	<i>o</i> -C <sub>6</sub> H <sub>4</sub>	-(CH <sub>2</sub> ) <sub>3</sub> -	6	[Cu(2-2H)]
3	-(CH <sub>2</sub> ) <sub>2</sub> -	-(CH <sub>2</sub> ) <sub>2</sub> -	7	[Cu(3-2H)]
4	-(CH <sub>2</sub> ) <sub>2</sub> -	-(CH <sub>2</sub> ) <sub>6</sub> -	8	[Cu(4-2H)]

#### 4.2.1.1 Synthesis of Free Ligands

The Schiff base ligands **1** – **4** were prepared by a six step convergent synthesis from a diamine, benzoic anhydride, benzaldehyde, sodium borohydride, paraformaldehyde, a substituted salicylaldehyde and finally a diamine of choice.

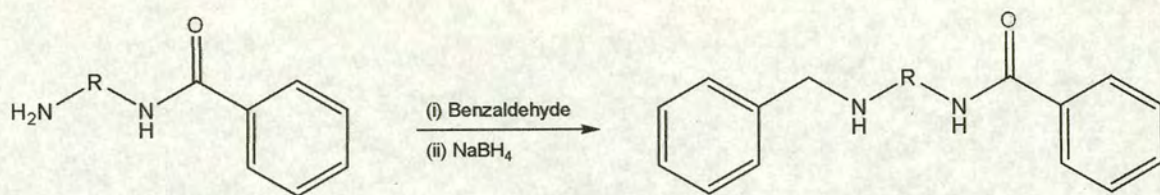
The first step involved the mono-derivatisation of the appropriate diamine with benzoic anhydride (Figure 4.6) by the modification of a literature method.<sup>15</sup> Benzoic anhydride was used because reaction with benzoyl chloride resulted in the formation of the di-substituted product and this was attributed to the high reactivity of acid chlorides. In order to favour the mono-derivatisation of the diamine the reaction was performed at low temperature (-80°C) using high dilution conditions. The products were obtained in high purity and good yield (~ 70%). No evidence of di-substituted material was seen in any of the products.



**Figure 4.6** Synthesis of mono-derivatised diamines. R = -(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>3</sub>-, or -(CH<sub>2</sub>)<sub>6</sub>-.

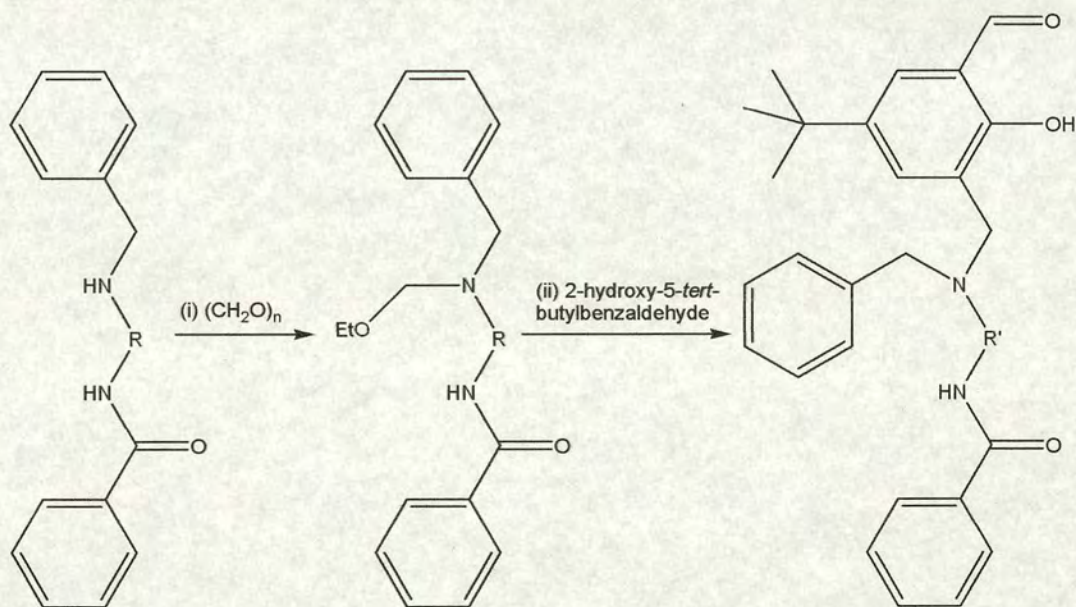
The mono-derivatised diamines were then reacted with benzaldehyde in Schiff base condensations and subsequently reduced with sodium borohydride in ethanol to yield a series of secondary amines (Figure 4.7). The products were obtained in good yields (> 90%) and were used without further purification.





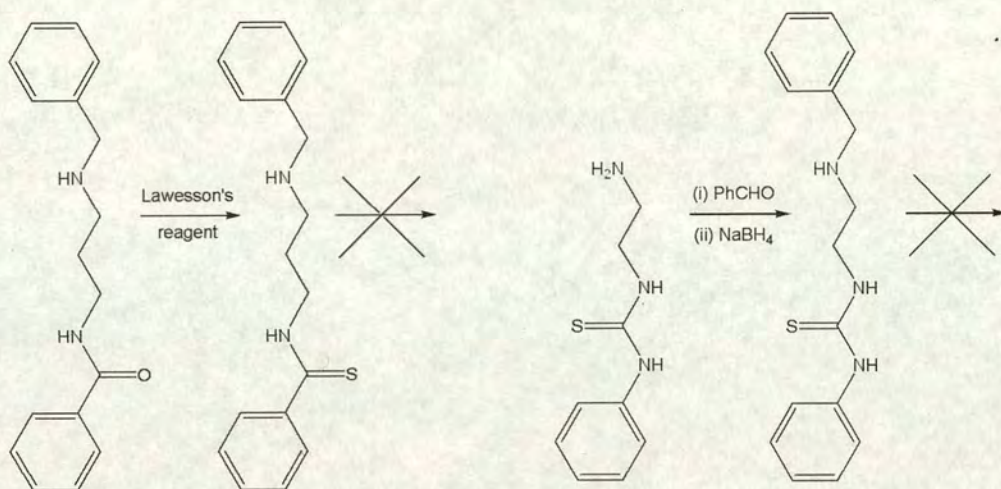
**Figure 4.7** Synthesis of secondary amines. R =  $-(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_3-$ , or  $-(\text{CH}_2)_6-$ .

Substitution of 2-hydroxy-5-*tert*-butylbenzaldehyde (section 2.2.1.1) in the remaining position *ortho* to the hydroxyl group was achieved by two-step Mannich reactions (Figure 4.8). The Mannich bases were synthesised, by an adaptation of the method used by Fenton and co-workers<sup>16</sup>, from the prepared secondary amines and paraformaldehyde in ethanol. These products were used, without purification, in reactions with 2-hydroxy-5-*tert*-butylbenzaldehyde in acetonitrile, under a dinitrogen atmosphere. Purification of the reaction mixtures was achieved by silica column chromatography (ethyl acetate : hexane) to give the products in low yields (30 – 38%).



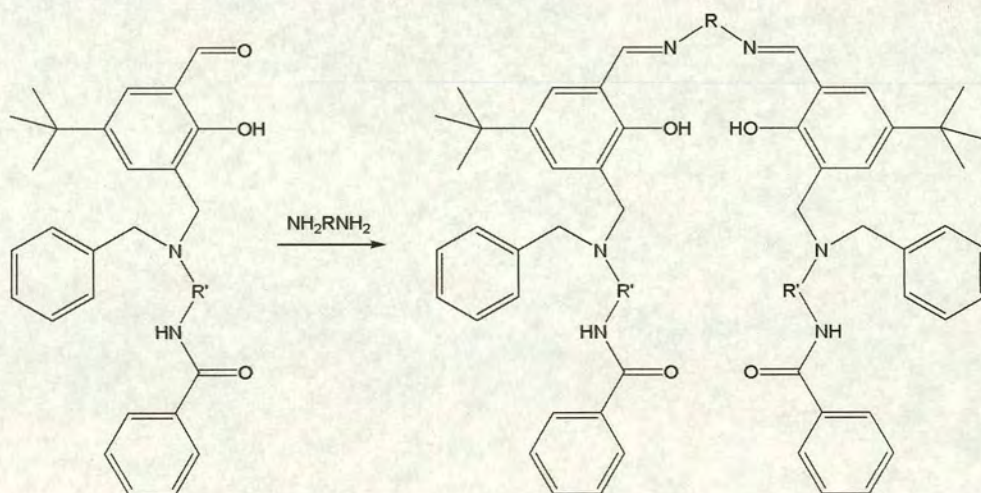
**Figure 4.8** Two-step Mannich reactions on amide-substituted secondary amines. R =  $-(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_3-$ , or  $-(\text{CH}_2)_6-$ .

Similar Mannich reactions were also attempted on thioamide and thiourea substituted secondary amines but all such reactions proved to be unsuccessful (Figure 4.9). This was attributed to side reactions taking place on the thiourea and thioamide groups.



**Figure 4.9** Thioamide and thiourea substituted secondary amines. All attempts to perform the two-step Mannich reaction (Figure 4.8) on these compounds proved unsuccessful.

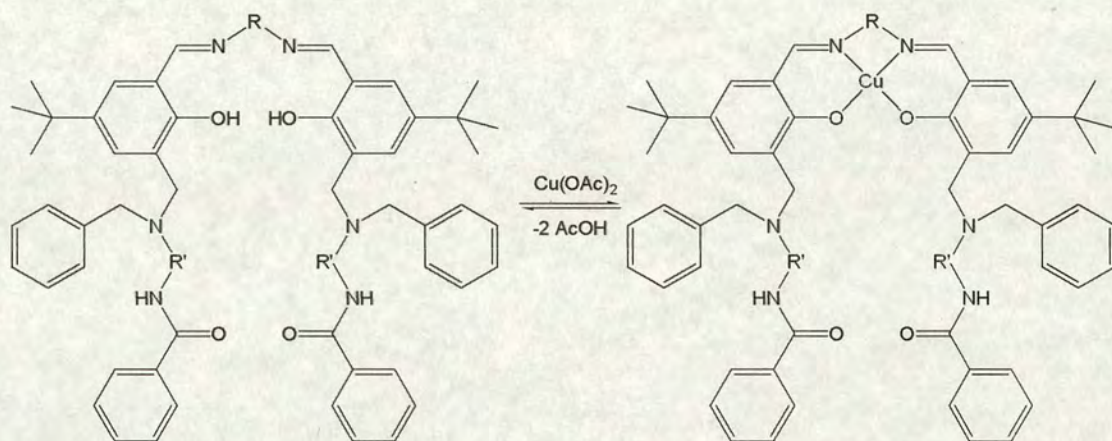
The final reaction (Figure 4.10), to produce ligands **1** – **4**, involved Schiff base condensations of the substituted salicylaldehydes, produced in the Mannich reactions of the amide-functionalised secondary amines (Figure 4.8), with the appropriate diamine. The products were obtained in high yields (95 – 98 %).



**Figure 4.10** Schiff base condensations of substituted salicylaldehydes to give ligands **1** – **4**; R = alkyl, aryl and R' = alkyl.

### 4.2.1.2 Synthesis of Metal Complexes

Neutral “copper-only” complexes of ligands **1** – **4** were prepared by stirring a  $\text{CHCl}_3$  solution of ligand with a methanolic solution of copper(II) acetate (Figure 4.11). The crude complex was washed with pH 9 ammonia solution to remove excess copper(II) acetate and to ensure that the pendant amines groups were not protonated.



**Figure 4.11** The formation of the “Cu-only” complexes **5** – **8**; R = alkyl, aryl; R' = alkyl.

The “copper-only” complexes **5** – **8** were found to have sufficient solubility in  $\text{CHCl}_3$  to make them suitable for use in solvent extraction experiments.

## 4.3 Characterisation

### 4.3.1 IR Spectroscopy

All of the amide functionalised ligands **1** – **4** and their corresponding “copper-only” complexes have been characterised by FTIR spectroscopy. The most notable band is for the imine bond and it is found to be present in the free ligands ( $1617\text{--}1633\text{ cm}^{-1}$ ) and the copper complexes ( $1610\text{--}1628\text{ cm}^{-1}$ ) (Table 4.2).

**Table 4.2** The imine stretching frequencies of ligands **1** – **4** and their Cu complexes. ( $\text{cm}^{-1}$ )

	<b>Ligand</b>	<b>Copper Complex</b>
Ligand <b>1</b>	1633	1624
Ligand <b>2</b>	1617	1610
Ligand <b>3</b>	1633	1628
Ligand <b>4</b>	1630	1626

As in the copper complexes of chapter 2 and 3 the imine stretch is lowered upon coordination of the metal indicating that the imine nitrogen is directly involved in metal-binding. There is a band at  $\sim 1640 \text{ cm}^{-1}$  in ligand **2** and its copper complex **6** and this corresponds to the carbonyl stretching frequency from the amide linkage (-NHCO-). This signal is only seen in the spectrum of ligand **2** and its copper complex **6** because in the other spectra it is obscured by the strong imine stretching band.

### 4.3.2 NMR Spectroscopy

All of the ligands and their precursors have been characterised by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy. Evidence for the complete formation of the ligands was given by the appearance of the characteristic imine proton resonance (8.3 – 8.7 ppm,  $^1\text{H}$  NMR and 163-168 ppm,  $^{13}\text{C}$  NMR) and the absence of the carbonyl signal (9.9 – 10.4 ppm,  $^1\text{H}$  NMR and 192 – 196 ppm,  $^{13}\text{C}$  NMR) in the NMR spectra.

The amide linkage was characterised in the final ligands by a resonance for the NH proton at  $\sim 6.9$  ppm and a peak in the  $^{13}\text{C}$  NMR spectra at  $\sim 167$  ppm for the carbonyl carbon (NHCO).

In ligands **1** – **4** there are two sharp singlets in the 3.5 – 3.8 ppm region which correspond to the two groups of  $\text{CH}_2$  protons directly beside the protonatable amine group. There is an additional singlet in this region for ligands **1**, **3** and **4** which corresponds to the  $\text{CH}_2$  protons on the 1,2-ethane-bridging unit.

### 4.3.3 Mass Spectrometry

The FAB mass spectra of the free ligands **1** – **4** and “copper-only” (1:1) complexes **5** – **8** show, as expected, peaks for the molecular ions. All of the precursors also show the expected peaks apart from the Mannich bases that are generated from the amide-functionalised secondary amines in the first step of the Mannich reaction. There are however peaks assignable, in all of these spectra, to the positively charged iminium ion ( $M - EtO$ ) which must be produced by fragmentation of the parent ion in the mass spectrometer. This is not surprising as the Mannich base is prepared as an intermediate in the Mannich reaction and is expected to be relatively unstable.

### 4.3.4 UV-Visible Spectroscopy

The electronic absorption spectra for ligands **1** – **4** consist of two intense bands at 330 – 337 nm and 261 – 276 nm which involve  $\pi \rightarrow \pi^*$  transitions.<sup>17</sup>

In the electronic absorption spectra of the “copper-only” complexes **5** – **8** there is an intense peak in the 270 – 320 nm region, which is due to ligand-based  $\pi \rightarrow \pi^*$  transitions, a moderately intense band in the 370 – 450 nm region, which is charge transfer in character, and a weak feature 560 – 580 nm which is assigned to d – d transitions.<sup>18, 19</sup>

These absorptions appear in the same regions as did those of the related “copper-only” complexes synthesised in chapter 2 providing evidence that incorporation of amide groups into the ligand framework has had little effect on the metal coordination sphere (Table 4.3).

**Table 4.3** Comparison of the electronic absorption spectra of 1,2-ethane-bridged complexes in Chapters 2 & 4.

“Copper-only” Complex	$\lambda_{\text{max}}$ 1 (nm)	$\lambda_{\text{max}}$ 2 (nm)	$\lambda_{\text{max}}$ 3 (nm)
C <sub>2</sub> H <sub>4</sub> -bridged complex Chpt. 2 (7)	283	382	576
<b>5</b>	278	381	573
<b>7</b>	280	381	572
<b>8</b>	281	382	565

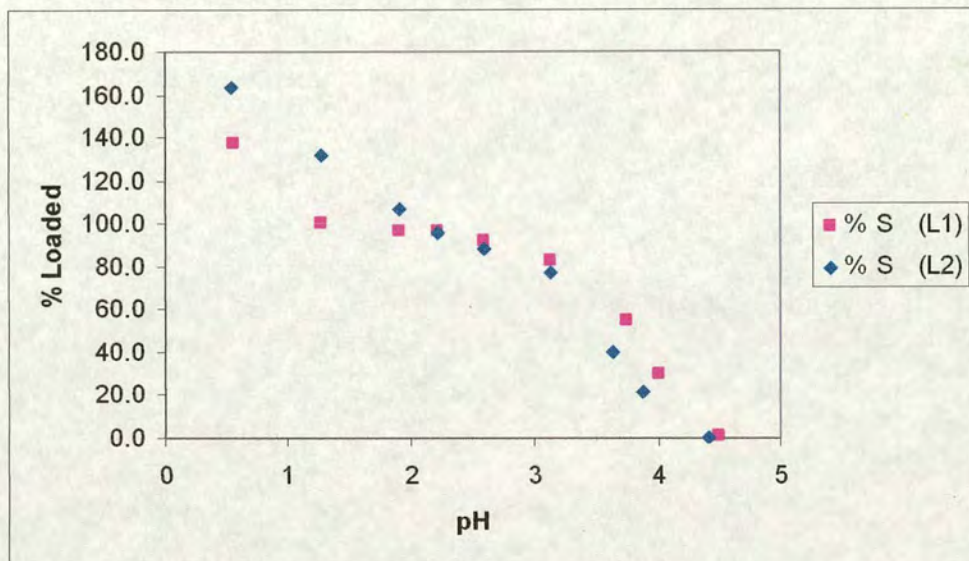
## 4.4 The pH Dependence of Anion-loading

### 4.4.1 The pH Dependence of Sulfate-loading onto Copper Complexes 5 and 6

The development of extractants which show selectivity for sulfate over other anions is very challenging. This is a result of the well established order of hydrophobicity (the Hofmeister series, see section 1.8) which indicates that sulfate is one of the most heavily hydrated anions.<sup>20</sup> Therefore a very strong binding site must be constructed within a hydrophobic ligand before transport into a water immiscible solvent becomes favourable. Extraction was successfully achieved by the ligands developed in chapter 2 but it is unlikely that the selective binding of sulfate over other anions would be achieved by these ligands as the most successful examples in the literature contain multiple hydrogen-bond donors.<sup>13, 21</sup> Consequently the amide-functionalised analogues **1** and **2** were developed (see above). The pH dependence of sulfate-loading and the “strength” of their copper-binding in solvent extraction experiments, were examined using their “copper-only” complexes **5** and **6** as reported below.

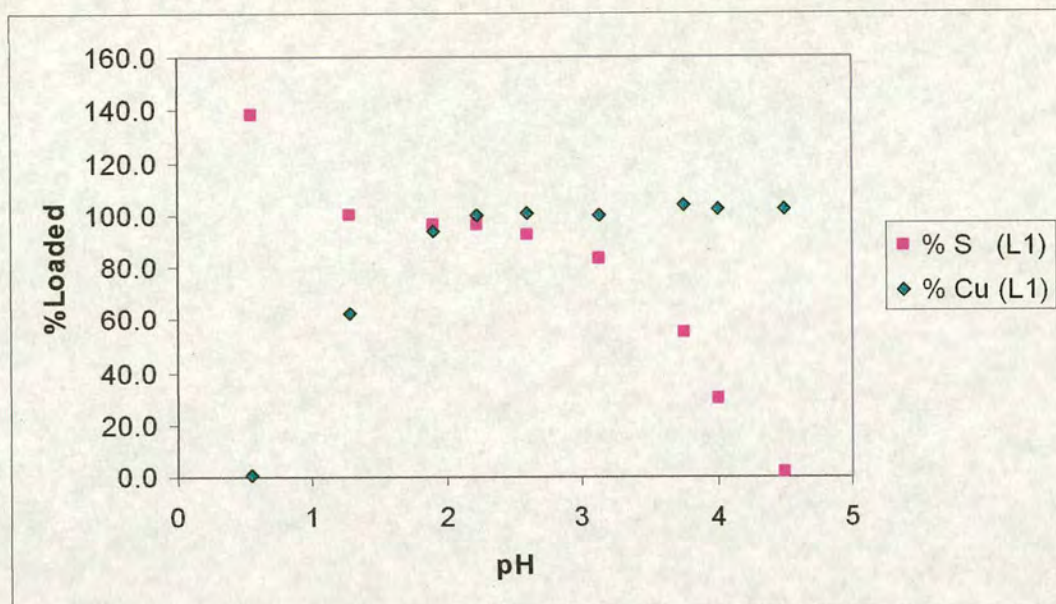
The sulfate-loading by **5** shows good selectivity for  $\text{SO}_4^{2-}$  over  $\text{HSO}_4^-$  as 100% loading (indicating the formation of a 1 : 1 : 1, Cu : L :  $\text{SO}_4$  complex) is achieved (Figure 4.12) at the  $\text{pK}_a$  (1.92) of the  $\text{SO}_4^{2-}$  anion when the  $\text{HSO}_4^-/\text{SO}_4^{2-}$  ratio is 1 : 1. This is also observed in the pH dependence graph of **6** although it shows a lower “strength” of sulfate-binding as the  $\text{pH}_{1/2}$  (pH when sulfate-loading is 50%) is 3.5 compared to 3.8 in **5**. The *o*-phenylene-bridged complex **6** exhibits, as expected, very strong copper-binding as the complex was found to be stable with respect to  $\text{Cu}^{2+}$ -

displacement by protons even at low pH (0 – 1). This makes ligand **2** a poor candidate for a practicable  $\text{CuSO}_4$  extractant (see section 2.4.3) as the copper would not be easily recoverable.



**Figure 4.12** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by “Cu-only” complexes **5** and **6**.

In contrast, the 1,2-ethane-bridged ligand **1** fits an ideal profile for a  $\text{CuSO}_4$  extractant as both the metal and anion can be conveniently recovered by pH adjustment (Figure 4.13). However, although there is a plateau where both copper and sulfate loadings are maximised the pH range is smaller than that observed in the ethylene-bridged extractant discussed in chapter 2 (section 2.4.5). The reason for this is that although the  $\text{pH}_{1/2}$  values for copper-binding in the two “copper-only” complexes are very similar the “strength” of sulfate-binding has decreased; the  $\text{pH}_{1/2}$  is 3.8 compared to 4.6 in the related extractant (**7**, section 2.4.5) in chapter 2. Consequently **1** would have a more limited pH range for efficient  $\text{CuSO}_4$  loading than the related dihexylaminomethyl-substituted ligand. The latter is also a stronger sulfate extractant.

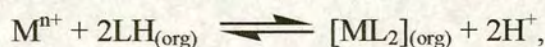


**Figure 4.13** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper-binding in 5.

#### 4.4.2 Anion Selectivity of Ligand 1

Whilst the “strength” of sulfate-extraction has been found to be lower in the amide-functionalised ligand 1 the key aim of developing extractants with additional amide groups was to define whether they would show selectivity for the extraction of sulfate over other anions. The anions most commonly found in the leach solutions produced in hydrometallurgical processes are sulfate and chloride.<sup>22</sup> Therefore achieving sulfate over chloride selectivity (or vice-versa) is an important target.

In hydrometallurgy the  $\text{pH}_{1/2}$  value is commonly used to assess the relative selectivity of metal complexation by an extractant (see section 1.6). The  $\text{pH}_{1/2}$  is defined as the pH associated with 50% loading of the extractant at a stated concentration and for a defined composition of aqueous feed. Conventionally for,

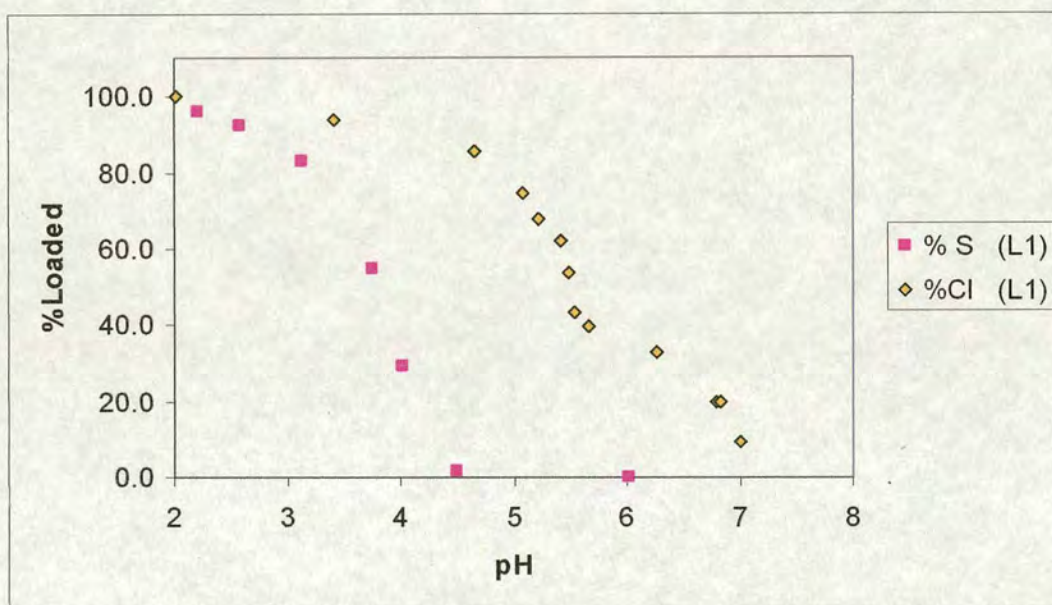


the lower the  $\text{pH}_{1/2}$  the “stronger” the metal complexation.<sup>1</sup>



If the  $\text{pH}_{1/2}$  of anion-complexation in a two-phase solvent extraction experiment can be measured then this same methodology can be used to assess the relative anion selectivity of the ligand. However in this case the higher the  $\text{pH}_{1/2}$  the “stronger” the anion-binding as loading becomes less favourable at high pH.

The pH dependence of hydrochloric acid uptake by “copper-only” complex **5** was studied in order to obtain a value for the  $\text{pH}_{1/2}$  of chloride-extraction as this then allows an assessment of the relative anion selectivity of ligand **1** (Figure 4.14)



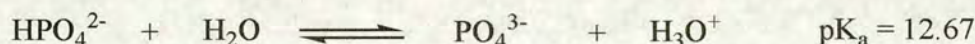
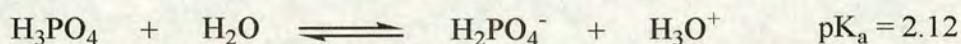
**Figure 4.14** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{HCl}$  uptake by the “Cu-only” complex **5**.

The “copper-only” complex of the ditopic amide-functionalised ligand **1** was clearly found to be selective for chloride over sulfate as the  $\text{pH}_{1/2}$  for chloride-extraction is 5.5 compared to 3.8 for sulfate ( $\Delta\text{pH}_{1/2} = 1.7$ ). Chloride is loaded at pH approaching 7 and this apparent increase in the basicity of the amine arms is consistent with the complex being a more efficient extractant of the chloride anion.

The loading of chloride to 100% corresponds to the formation of a complex with a  $\text{Cu} : \text{L} : \text{Cl}$  ratio of 1 : 1 : 2 instead of the 1 : 1 : 1 ratio in the loading of  $\text{SO}_4^{2-}$  and is a consequence of the chloride anion being mono-charged unlike the di-negative

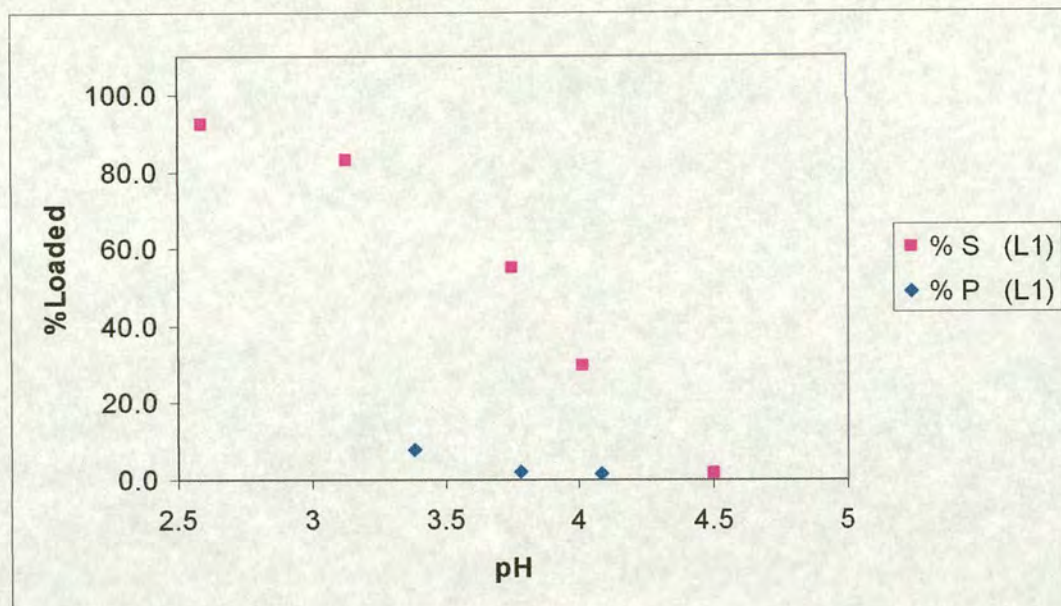
sulfate anion. This affects the pH profile (Figure 4.14). As the pH is lowered to < 7 chloride is loaded, but the loading curve flattens as the pH approaches 6, rising again sharply at pH < 5.5. This is consistent with the chloride anions being loaded separately in two stages into coordination environments of differing stabilities. Such a conclusion is not unreasonable as it is possible that protonation of one of the pendant amine arms makes the protonation of the second arm less favourable.

In an attempt to further probe the anion selectivity of **1** the pH dependence of phosphoric acid uptake by the “copper-only” complex **5** was studied. Phosphoric acid is a triprotic acid which has three pK<sub>a</sub> acidity constants,<sup>23</sup>



and the dominant form between pH 2.12 and 7.21 (the region of interest for comparisons with SO<sub>4</sub><sup>2-</sup> and Cl<sup>-</sup> loading) is the di-protonated H<sub>2</sub>PO<sub>4</sub><sup>-</sup> anion.

The solvent extraction experiments (Figure 4.15) reveal that the “copper-only” complex of **1** is selective for binding SO<sub>4</sub><sup>2-</sup> over H<sub>2</sub>PO<sub>4</sub><sup>-</sup>. At pH 3.38, when there is significant uptake of SO<sub>4</sub><sup>2-</sup>, there is only a very small amount of H<sub>2</sub>PO<sub>4</sub><sup>-</sup> extracted by the “copper-only” complex **5**. At lower pH in the presence of phosphoric acid a precipitate formed so a pH<sub>1/2</sub> value could not be obtained. However it is still clear from the results that the ligand preferentially extracts SO<sub>4</sub><sup>2-</sup>. The low solubility of the H<sub>2</sub>PO<sub>4</sub><sup>-</sup> complex at pH values below 3.3 may be a result of the formation of hydrogen-bonded dimers or polymers of the anion in the CHCl<sub>3</sub> layer. This type of interaction dominates the chemistry of the organophosphorus acid extractants when they are used in commercial solvent extraction processes (see section 1.5).<sup>1</sup>



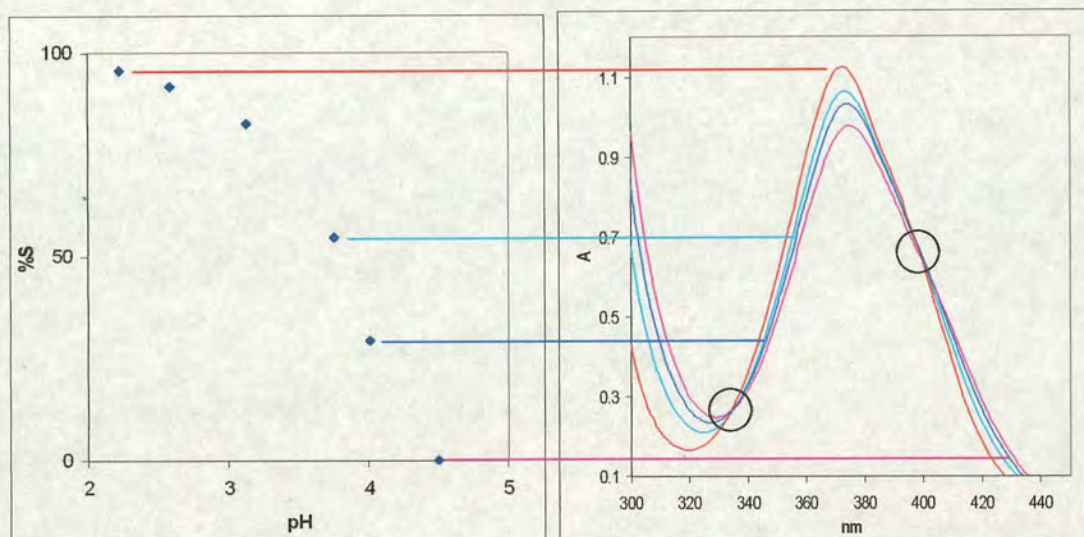
**Figure 4.15** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{H}_3\text{PO}_4$  uptake by “Cu-only” complex **5**.

The Hofmeister series<sup>20, 24</sup> predicts that phosphate, in its protonated forms, is more hydrophobic than sulfate so the “copper-only” complex of ligand **1** displays anti-Hofmeister behaviour by favouring the extraction of sulfate. This is an encouraging result because it shows the complex is selective for sulfate over a closely related oxo-anion. However the main area of interest, developing a practicable  $\text{CuSO}_4$  extractant, requires selectivity for sulfate over chloride and unfortunately **5** shows selectivity in the order  $\text{Cl}^- > \text{SO}_4^{2-} > \text{H}_2\text{PO}_4^-$ .

#### 4.5 UV-Visible Analysis of Solvent Extraction Experiments with Ligand **1**

In order to investigate the modes of anion-binding in the sulfate or chloride loadings by “copper-only” complex **5** electronic spectra of the organic ( $\text{CHCl}_3$ ) phase of the solvent extraction experiments were analysed. Only solutions with 100% copper loading were studied to ensure that differences were only associated with sulfate or chloride loading and not incomplete loading of the metal site.

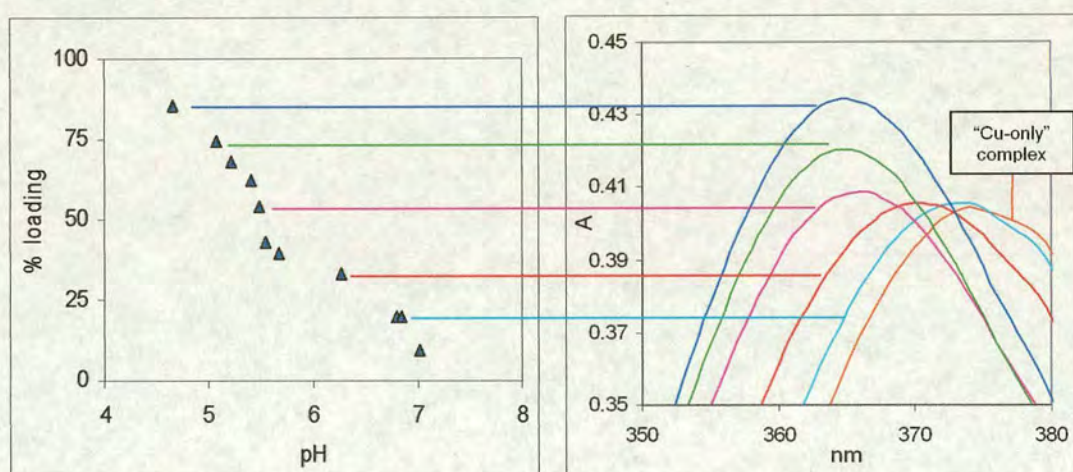
The sulfate-loading curve by the “copper-only” complex **5** and the associated electronic absorption spectra of complexes formed in the organic phase after evaporation to dryness and re-dissolution in butan-1-ol are compared in Figure 4.16. These solutions are prepared from the samples which were analysed by ICP-OES for copper and sulfur content.



**Figure 4.16** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by “Cu-only” complex **5** and the electronic absorption spectra of the products formed in the organic phase after evaporation of  $\text{CHCl}_3$  and re-dissolution in butan-1-ol showing the isosbestic points at ca. 330 and ca. 400 nm.

At  $\text{pH} = 2.22$  there is almost 100% loading of sulfate thus the spectrum corresponds closely to that of a 1 : 1 : 1, Cu : ligand : sulfate complex. In contrast at  $\text{pH} 4.5$  virtually no sulfate is loaded so the spectrum corresponds to that of the “copper-only” complex in butan-1-ol. As the pH is increased and the “copper-only” complex becomes more dominant there is a small bathochromic (red) shift of the charge transfer band at ca. 370 nm and the absorbance drops slightly. These small differences between the spectra suggest that the cation and anion binding sites are well separated in solution. There are also two isosbestic points (ca. 330 and ca. 400 nm) and this indicates that there is conversion from a host (“copper-only” complex **5**) to a host-guest complex (copper sulfate complex) as the pH of the aqueous phase is lowered.<sup>25</sup>

Different behaviour is observed for chloride extraction by **5** (Figure 4.17). In this case there are no isosbestic points. This could be related to the apparent two-step loading observed in the extraction curve as the loading equilibrium then involves more than two species. In the pH range 7 → 6 the charge transfer band at ca. 370 nm undergoes a notable hypsochromic (blue) shift as the chloride anion is extracted. This shift is principally associated with the first step of the extraction curve, pH 6 – 7, and may indicate the presence of a weak metal-chloride interaction. As the pH is lowered (< 5.5) there is no further shift in the band and instead the absorbance increases. This behaviour is seen on the second step of the loading curve and may be related to the extraction of the second chloride anion in a different coordination environment.

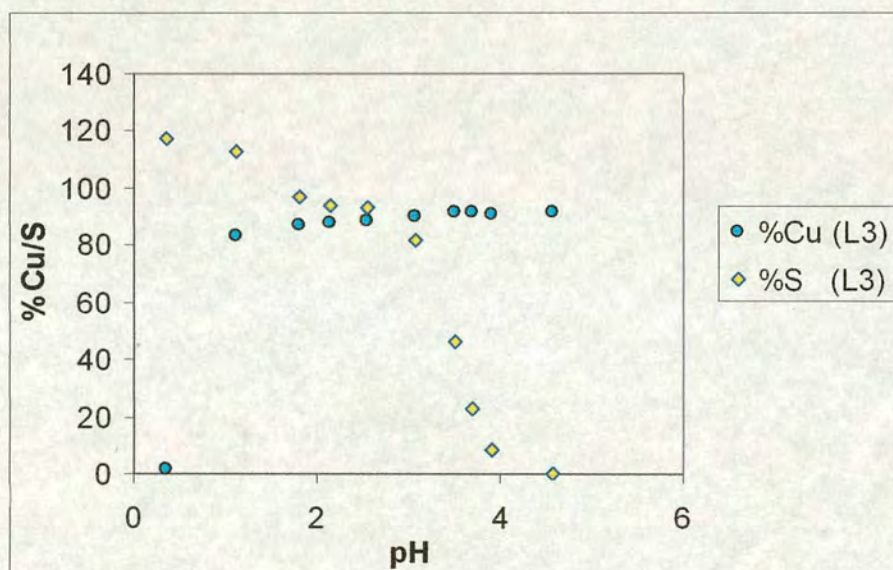


**Figure 4.17** The pH dependence of HCl uptake by “Cu-only” complex **5** and the electronic absorption spectra of the products formed in the organic phase after evaporation of CHCl<sub>3</sub> and redissolution in butan-1-ol. No isosbestic points are seen in the absorption spectra.

However detailed assignments of solution structure using UV-Visible spectroscopy are very difficult and no firm conclusions can be reached from the absorption spectra. Nevertheless it is very interesting to note that the spectra behave very differently in the two parts of the loading curve.

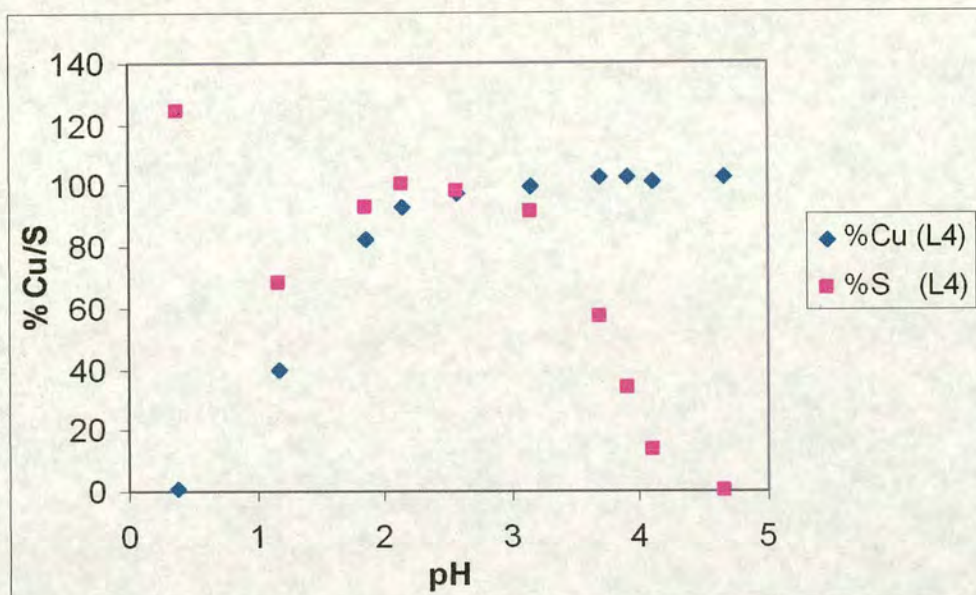
## 4.6 Anion Selectivity Studies of Ligands 3 and 4

Ligands **3** and **4** were developed to try to improve the “strength” and selectivity of sulfate-extraction. They are both closely related to ligand **1** with the difference being the length of alkyl chain between the amine nitrogen and amide group. It was hoped that studying ligands with shorter (**3**) and longer (**4**) chain lengths would provide an insight into the type of binding environment favoured by the sulfate anion. Solvent extraction experiments on the “copper-only” complexes **7** and **8** (Figure 4.18 and Figure 4.19) show that both **3** and **4** have the ideal pH profile for  $\text{CuSO}_4$  extraction but, as with **1** (section 4.4.1), there is only a limited pH region (ca. 2 – 3) where copper and sulfate loading are extracted efficiently (> 80%).



**Figure 4.18** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper-binding in 7.

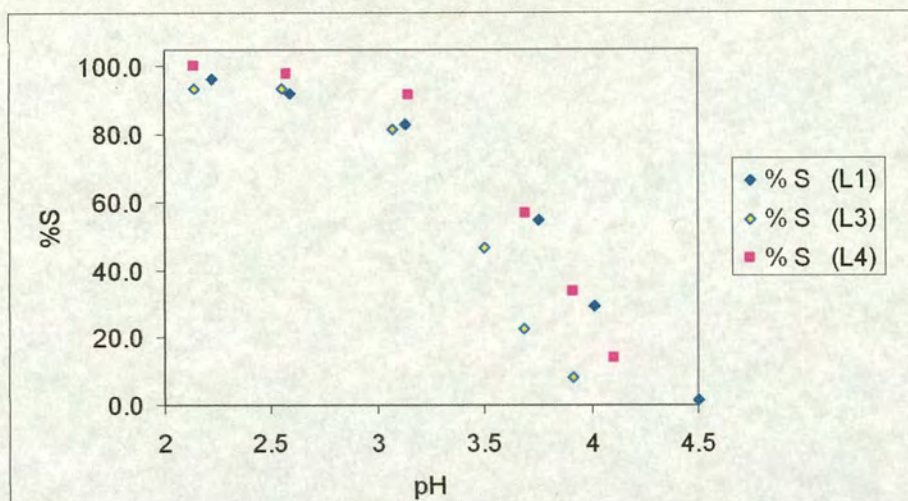
One notable difference is that the copper-binding is found to be weaker in ligand **4** than in ligand **3**. This is particularly evident at  $\text{pH} \sim 1.1$  where ligand **3** is approximately 80% copper-loaded compared to 40% for ligand **4**.



**Figure 4.19** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper-binding in **8**.

The pH-profile for sulfate-loading by the “copper-only” complex of ligand **4** provides further evidence for the metal templation effect, discussed in chapter 2, because the sulfate-loading drops below 100% at  $\text{pH} \sim 1.1$ , when the copper content is low, but increases again when the copper content rises at  $\text{pH} \sim 2$ .

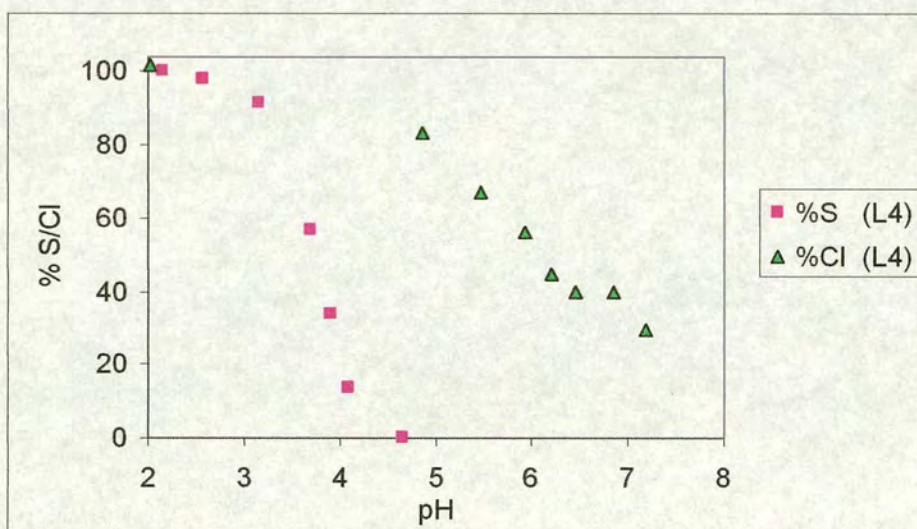
The sulfate loadings of the “copper-only” complexes of amide-functionalised ligands **1**, **3** and **4** are compared in Figure 4.20. It is clear that the “strengths” of binding are very similar, with  $\text{pH}_{1/2}$  values for **5**, **7** and **8** of 3.8, 3.5 and 3.8 respectively. The short 1,2-ethane-bridge in ligand **7** imposed a slight decrease on the “strength” of binding and this could be related to the formation of a more restricted binding cavity than in **5** in which intra-molecular hydrogen-bonding between the pendant amide groups becomes more dominant. It was therefore hoped that the longer 1,6-hexane-bridge in “copper-only” complex **8** would limit such an effect and improve the “strength” of binding by promoting the formation of a larger more flexible cavity which could favourably accommodate the sulfate anion. Unfortunately this was not observed so it appears that changing the length of the alkyl bridge between the amine nitrogen and amide group in these ligands has little effect on their ability to extract sulfate.



**Figure 4.20** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake by “Cu-only” complexes **5**, **7** and **8**.

The selectivity of  $\text{SO}_4^{2-}/\text{Cl}^-$  extraction by “copper-only” complexes of **3** and **4** is summarised in Figures 4.21 and 4.22.

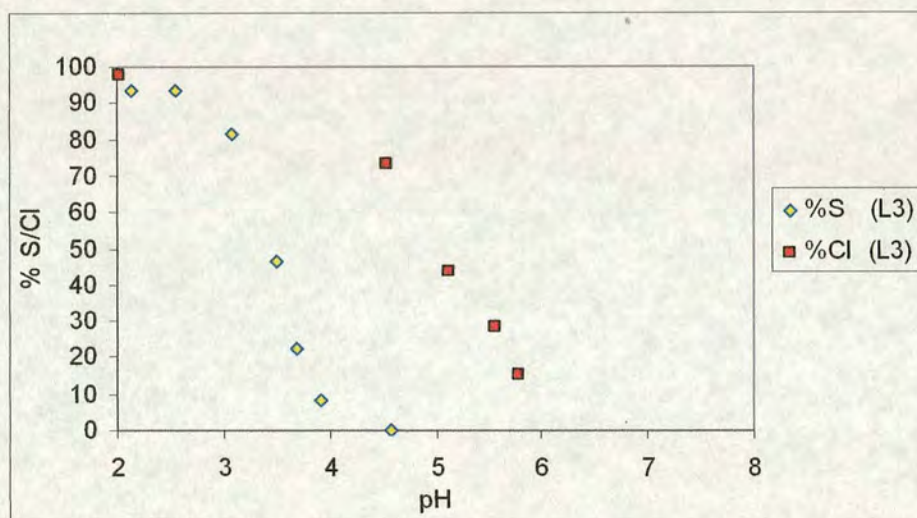
Complex **8** containing the 1,6-hexane-linked amide groups (**4**) is more selective for chloride over sulfate than the 1,3-propane-linked analogue (**1**); the  $2\text{Cl}^-/\text{SO}_4^{2-} \Delta\text{pH}_{1/2} = 2.3$  for **8** which compares with  $\Delta\text{pH}_{1/2} = 1.7$  for **5** (Figure 4.14). A similar two step loading-profile for chloride is observed in Figure 4.21, between pH 6 and pH 7.



**Figure 4.21** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{HCl}$  uptake by “Cu-only” complex **8**. The  $\text{pH}_{1/2}$  values for  $\text{SO}_4^{2-}$  and  $\text{Cl}^-$  loading are 3.8 and 6.1 respectively.



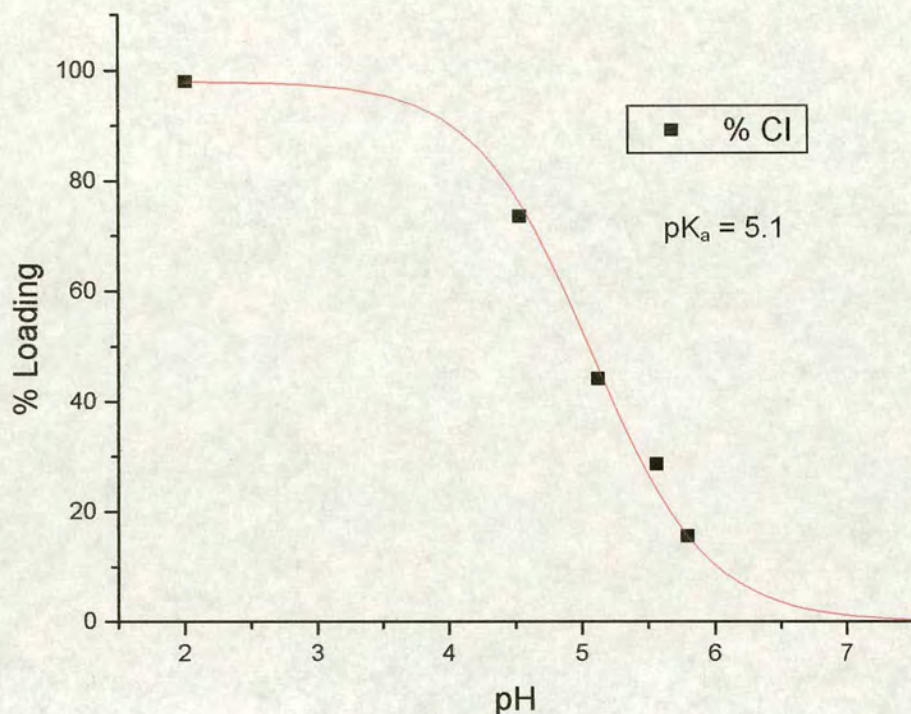
The “copper-only” complex **7** of the 1,2-ethane-linked amide (**3**) begins to load chloride at a lower pH ( $< 6.0$ ) than **5** (Figure 4.22). It still shows selectivity for chloride over sulfate but the  $\text{pH}_{1/2}$  has dropped to 5.1. This gives a  $\Delta\text{pH}_{1/2}$  value of 1.6 as the  $\text{pH}_{1/2}$  for sulfate-loading of 3.5 is also lower than for the other amide-functionalised ligands. Although the  $\Delta\text{pH}_{1/2}$  value is not much lower than that recorded for **5** ( $\Delta\text{pH}_{1/2} = 1.7$ ), the “copper-only” complex **7** has significantly reduced the chloride to sulfate selectivity as no two step loading is observed. This is important as the  $\text{pH}_{1/2}$  value for chloride-loading on complexes **5** and **8** does not take into account the second step of the extraction curve. Hence although  $\Delta\text{pH}_{1/2}$  values for **5** and **7** are similar, in complex **5** chloride is bound until  $\text{pH} \sim 7$  (Figure 4.14) and in **7** this only occurs until  $\text{pH} \sim 6$ .



**Figure 4.22** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{HCl}$  uptake by “Cu-only” complex **7**.

It appears that as the alkyl chain, between the amine nitrogen and amide group, is made more flexible (1,2-ethane **3**  $\rightarrow$  1,3-propane **1**  $\rightarrow$  1,6-hexane **4**) the selectivity of the ligand for chloride over sulfate increases. This may be a result of the longer arms facilitating the formation of more favourable binding environments for chloride possibly by separating the two binding sites to minimise electrostatic repulsion between two bound ions. Conversely, enhancing sulfate over chloride selectivity might be approached by the development of a rigid and pre-organised anion-binding site which would disfavour incorporation of two monoanions.

The  $\text{pH}_{1/2}$  values for sulfate-loading by the amide-functionalised ligands **1** – **4** were calculated using the method described in chapter 2 (section 2.4.3). The  $\text{pH}_{1/2}$  values for chloride-loading were determined in a similar way (eg. Figure 4.23).

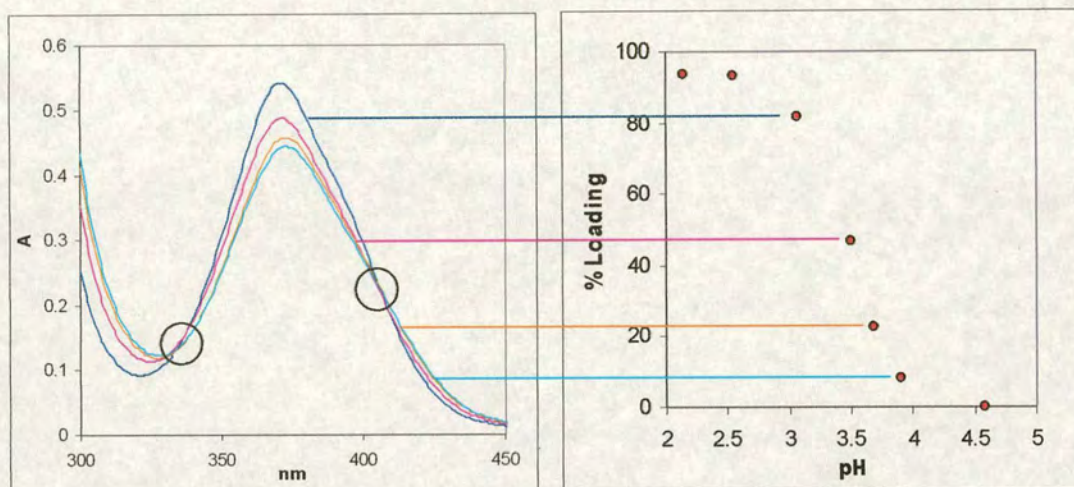


**Figure 4.23** The apparent  $\text{pK}_a$  ( $\equiv \text{pH}_{1/2}$ ) of the “copper-only” complex of ligand **3** in  $\text{CHCl}_3$  when in contact with hydrochloric acid in a two-phase solvent extraction system ( $\text{pK}_a = 5.1 \pm 0.1$ ).

#### 4.7 UV-Visible Analysis of the Solvent Extraction Experiments with Ligands **3** and **4**

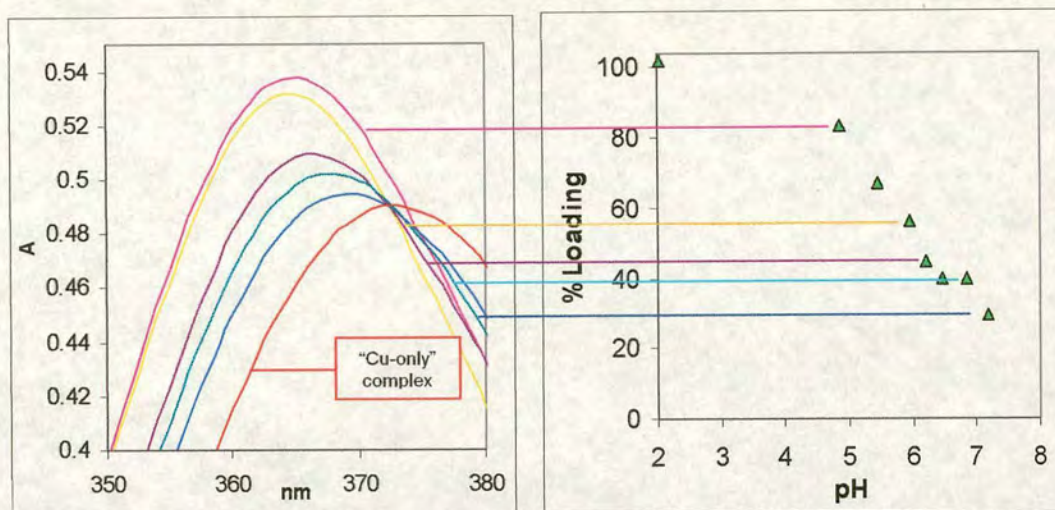
The solvent extraction experiments performed on “copper-only” complexes **7** and **8** were analysed by UV-Visible spectroscopy in the same way as in section 4.5. In these complexes very similar behaviour, to each other and to **5** (Figure 4.16), was observed in the electronic absorption spectra of the sulfate extractions as the charge transfer band at ca. 370 nm experienced a small bathochromic (red) shift and the absorbance of the band changed only slightly with increasing pH (eg. complex **7**,

Figure 4.24). This implied that the cation and anion binding sites were well separated in solution. There are also two isosbestic points (ca. 330 and ca. 410 nm) and this indicates that there is conversion from a host (“copper-only” complex) to a host-guest complex (copper sulfate complex) as the pH of the aqueous phase is lowered.<sup>25</sup>



**Figure 4.24** The pH dependence of H<sub>2</sub>SO<sub>4</sub> uptake by “Cu-only” complex **7** and the electronic absorption spectra of the products formed in the organic phase after evaporation of CHCl<sub>3</sub> and re-dissolution in butan-1-ol showing the isosbestic points at ca. 330 and ca. 410 nm.

The electronic absorption spectra of the chloride extractions again showed no isosbestic points (eg. complex **8**, Figure 4.25) indicating that the loading of chloride involves more than two species in solution. Therefore a variety of different types of copper chloride complexes may be formed depending on the pH of the aqueous phase in the extractions.

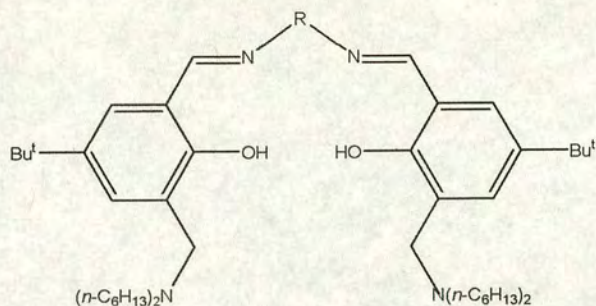


**Figure 4.25** The pH dependence of HCl uptake by “Cu-only” complex **8** and the electronic absorption spectra of the products formed in the organic phase after evaporation of  $\text{CHCl}_3$  and re-dissolution in butan-1-ol. No isosbestic points are seen in the absorption spectra.

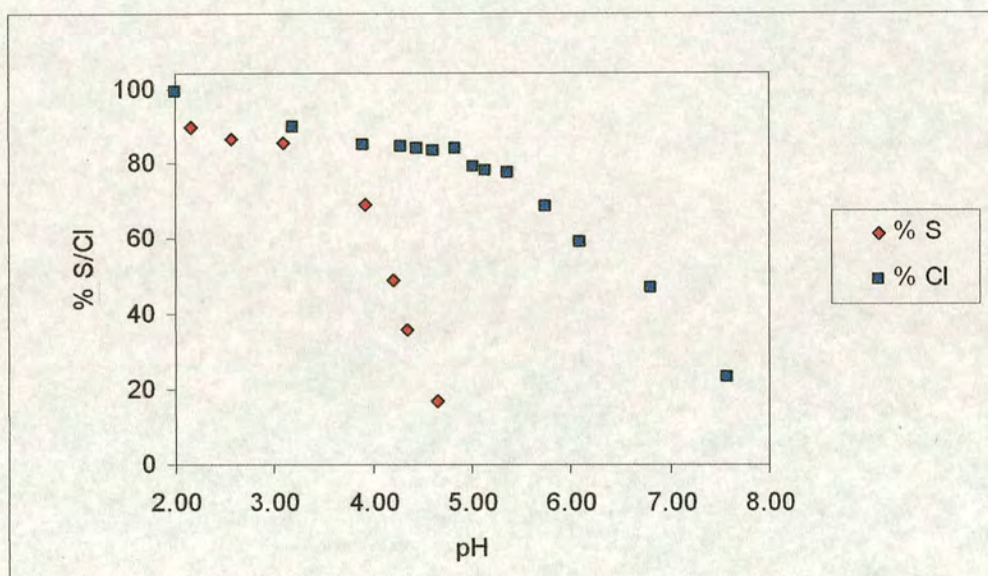
#### 4.8 Anion Selectivity shown by the Copper(II) Complex of an Analogous Ligand with no Pendant Amide Groups

The amide-functionalised ligands described above were studied because the most successful sulfate-selective receptors in the literature contain a number of hydrogen-bond donors.<sup>13, 21, 26</sup> However in practice we found that amide ligands **1** – **4** had a slightly lower “strength” of sulfate-extraction than the dihexylaminomethyl-substituted analogues (Figure 4.26) with no pendant amide groups which are described in chapter 2.

The selectivity of anion-loading by these ligands (**A-D** Figure 4.26) is not described in chapter 2 but is included here for comparison with the amide-functionalised systems. The uptake of hydrochloric acid by the “copper-only” complex of ligand **D**,  $[\text{Cu}(\text{D-2H})]$ , is shown in Figure 4.27 and compared with its sulfate-loading profile.



**Figure 4.26** Dihexylaminomethyl-substituted ditopic ligands discussed in Chapter 2. R =  $-(\text{CH}_2)-$  **A**, 2,2'-biphenyl **B**, ( $\pm$ )-*trans*-1,2-cyclohexane **C**, *o*- $\text{C}_6\text{H}_4$  **D**.



**Figure 4.27** The pH dependence of  $\text{H}_2\text{SO}_4$  and HCl uptake by the “Cu-only” complex of ligand **D** (Figure 4.26),  $[\text{Cu}(\text{D}-2\text{H})]$ , complex **10** in chapter 2 (Table 2.1).

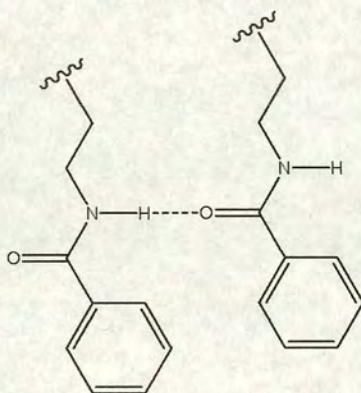
As expected,  $[\text{Cu}(\text{D}-2\text{H})]$ , showed selectivity for chloride over sulfate. The  $\Delta\text{pH}_{1/2}$  was found to be 2.5 ( $\text{pH}_{1/2}$  for  $\text{SO}_4^{2-} = 4.2$  and  $\text{Cl}^- = 6.7$ ). This value is greater than in any of the amide-functionalised ligands (Table 4.4). It appears that incorporation of amide groups into the pendant arms does help to improve the “strength” of sulfate-binding relative to chloride-binding in this series of ditopic ligands but further improvements are required before the preferential extraction of sulfate can be achieved.

**Table 4.4** The  $\text{pH}_{1/2}$  values for  $\text{SO}_4^{2-}$  and  $\text{Cl}^-$  loading and the corresponding  $\Delta\text{pH}_{1/2}$  values for selected “copper-only” complexes.

“Copper-only” Complex	$\text{pH}_{1/2}$ ( $\text{SO}_4^{2-}$ )	$\text{pH}_{1/2}$ ( $\text{Cl}^-$ )	$\Delta\text{pH}_{1/2}$
[Cu(1-2H)]	3.8	5.5	1.7
[Cu(3-2H)]	3.5	5.1	1.6
[Cu(4-2H)]	3.8	6.1	2.3
[Cu(D-2H)]	4.2	6.7	2.5

## 4.9 Conclusions

The amide-functionalised ligands **1** – **4** were synthesised with the aim of improving the “strength” and selectivity of sulfate-extraction by providing extra hydrogen-bond donors. However the “strength” of sulfate-extraction was found to be lower than in the dihexylaminomethyl-substituted analogues (chapter 2) which contained only protonatable amine groups. This may be a result of intra-molecular hydrogen-bonding between pendant amide groups which inhibits the formation of an efficient binding cavity (Figure 4.28). Thiourea and thioamide analogues of **1** – **4** should show a smaller propensity for such intra-molecular hydrogen-bonding between the pendant arms because thioamides and thioureas are much weaker hydrogen-bond acceptors.<sup>27</sup> Unfortunately the Mannich reaction needed to prepare these analogues failed (see section 4.2.1.1) and consequently this approach to increasing the “strength” of sulfate-binding could not be tested.

**Figure 4.28** Possible mode of intra-molecular hydrogen-bonding in the free ligands **1-4** and their “copper-only” complexes [Cu(L-2H)].

The “copper-only” complexes of amide-functionalised ligands **1**, **3** and **4** were all found to be selective for chloride over sulfate. It was hoped that the complexes would show sulfate selectivity but their preference for chloride is not unexpected due to the well established order of hydrophobicity ( $\text{Cl}^- \gg \text{SO}_4^{2-}$ ) first developed by Hofmeister in 1888 (see section 1.8).<sup>20</sup> However it is interesting to note that the “strength” of binding of chloride appears to be dependent on the flexibility of the receptor because as the alkyl chain, between the amine nitrogen and amide group, is reduced (1,6-hexane **4** → 1,3-propane **1** → 1,2-ethane **3**) the selectivity for chloride over sulfate decreases. This opens up the possibility of designing ligands which aim to destabilise the binding of two chloride anions with respect to the encapsulation of a sulfate anion. Such an approach may facilitate the extraction of sulfate over chloride.

In order to further investigate the anion selectivity of the “copper-only” complex (**5**) of ligand **1** the loading of  $\text{H}_2\text{PO}_4^-$  was studied in solvent extraction experiments. The complex showed selectivity for the binding of  $\text{SO}_4^{2-}$  over  $\text{H}_2\text{PO}_4^-$ . This complex also showed selectivity for  $\text{SO}_4^{2-}$  over  $\text{HSO}_4^-$  as at the  $\text{pK}_a$  (1.92), where the  $\text{SO}_4^{2-} : \text{HSO}_4^-$  ratio is 1 : 1 in the aqueous phase, the organic phase was found to contain only the 1 : 1 : 1 complex  $[\text{Cu}(\mathbf{1})\text{SO}_4]$ . These results are encouraging because they show the preference of the anion-binding site in **5** for dianionic oxo-anions over monoanionic oxoanions.

Analysis of the chloride solvent extraction experiments on the “copper-only” complexes of ligands **1**, **3** and **4** with electronic absorption spectroscopy reveals that chloride transport may involve a weak interaction with the copper cation. Such an interaction is likely to enhance chloride-extraction and needs to be avoided if sulfate selectivity is to be achieved. One strategy may be to tailor the copper coordination sphere to instead make it favourable to accept a small bidentate dianion such as sulfate. However, ligands designed to have direct metal-anion interactions do not have the ditopic form which meets the requirements of the loading/stripping protocol outlined in section 1.5.

## 4.10 Experimental

### 4.10.1 Instrumentation

Chloride concentrations were measured with a chloride-selective Thermo Orion Ion Plus electrode. Details of other instrumentation used have been given in chapter 2.

### 4.10.2 Solvent and Reagent Pre-treatment

Unless stated to the contrary, commercial grade chemicals obtained from Aldrich or Acros were used without further purification.

### 4.10.3 Ligand Synthesis

1-(2-Amino-ethyl)-3-phenyl-thiourea was prepared from ethylenediamine and phenyl isothiocyanate by a literature method.<sup>28</sup> *N*-(3-Amino-propyl)-benzamide, *N*-(2-amino-ethyl)-benzamide and *N*-(6-amino-hexyl)-benzamide were made by using a modified version of the method used by Jacobson and co-workers.<sup>15</sup>

***N*-(3-Amino-propyl)-benzamide.** Benzoic anhydride (8.0 g, 0.035 mol) in dichloromethane (200 ml) was added dropwise to a stirred solution of 1,3-diaminopropane (13.1 g, 0.18 mol) in dichloromethane (400 ml) at -80°C and stirred overnight. The solution was concentrated *in vacuo* to 100 ml and extracted with 5% hydrochloric acid (2 × 50 ml). The two aqueous extracts were combined, basified with 10% sodium hydroxide solution and concentrated *in vacuo* to 200 ml. The product was extracted with dichloromethane (3 × 50 ml). The combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield *N*-(3-amino-propyl)-benzamide as a colourless oil (4.92 g, 78%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.85-7.79 (2H, m, Ar-H), 7.46-7.38 (3H, m, Ar-H), 3.58 (2H, q,  $J(\text{NHCH}_2\text{CH}_2)$  6 Hz), 2.90 (2H, t,  $J(\text{NH}_2\text{CH}_2\text{CH}_2)$  6.2 Hz), 1.74 (2H, quintet,  $J(\text{CH}_2\text{CH}_2\text{CH}_2)$  6.2 Hz), 1.45 (2H, s, NH<sub>2</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 168.0 (CO), 135.4 (Ar C), 131.8 (Ar CH), 129.1 (Ar CH), 127.6 (Ar CH), 41.4 (CONHCH<sub>2</sub>), 40.0 (NH<sub>2</sub>CH<sub>2</sub>), 32.0



(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3286s, 2936s, 2869s, 1635s, 1541s, 1490, 1435, 1309, 700;  $m/z$  179 (M<sup>+</sup>).

***N*-(2-Amino-ethyl)-benzamide.** Benzoic anhydride (4.0 g, 0.018 mol) in dichloromethane (150 ml) was added dropwise to a stirred solution of ethylenediamine (4.25 g, 0.071 mol) in dichloromethane (300 ml) at -80°C and stirred overnight. The solution was concentrated *in vacuo* to 100 ml and extracted with 5% hydrochloric acid (2 × 50 ml). The two aqueous extracts were combined, basified with 10% sodium hydroxide solution and concentrated *in vacuo* to 100 ml. The product was extracted with dichloromethane (3 × 50 ml). The combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield *N*-(2-amino-ethyl)-benzamide as a colourless oil (2.0 g, 69%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.98-7.94 (2H, m, Ar-*H*), 7.65-7.55 (3H, m, Ar-*H*), 3.58 (2H, t, *J*(CONHCH<sub>2</sub>) 6.4 Hz), 2.99 (2H, t, *J*(NH<sub>2</sub>CH<sub>2</sub>) 6.4 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 170.0 (CO), 135.8 (Ar C), 132.8 (Ar CH), 129.6 (Ar CH), 128.4 (Ar CH), 43.7 (CONHCH<sub>2</sub>), 42.1 (NH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3275s, 2940s, 2843s, 1642s, 1542s, 1488, 1314, 687;  $m/z$  165 (M<sup>+</sup>).

***N*-(6-Amino-hexyl)-benzamide.** Benzoic anhydride (4.0 g, 0.018 mol) in dichloromethane (150 ml) was added dropwise to a stirred solution of 1,6-diaminohexane (8.25 g, 0.071 mol) in dichloromethane (500 ml) at -80°C and stirred overnight. The solution was concentrated *in vacuo* to 100 ml and extracted with 5% hydrochloric acid (2 × 50 ml). The two aqueous extracts were combined, basified with 10% sodium hydroxide solution and washed with dichloromethane (3 × 50 ml). The organic extracts were washed with water (2 × 50 ml). The combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield *N*-(6-amino-hexyl)-benzamide as a colourless oil (3 g, 77%). (Found: C, 70.9; H, 8.9; N, 12.4. Calc. for C<sub>13</sub>H<sub>20</sub>N<sub>2</sub>O: C, 70.9; H, 9.2; N, 12.7%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.79-7.75 (2H, m, Ar-*H*), 7.51-7.41 (3H, m, Ar-*H*), 6.25 (1H, br, NHCO), 3.48 (2H, q, *J*(CONHCH<sub>2</sub>) 6.7 Hz), 2.70 (2H, t, *J*(NH<sub>2</sub>CH<sub>2</sub>) 6.7 Hz), 1.67 (2H, quintet, *J*(CONHCH<sub>2</sub>CH<sub>2</sub>) 7.0 Hz), 1.45 (6H, m, NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.19 (2H, t, NH<sub>2</sub>CH<sub>2</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 170.0 (CO), 136.0 (Ar C), 132.6 (Ar CH), 129.6

(Ar CH), 128.3 (Ar CH), 42.3 (CONHCH<sub>2</sub>), 40.9 (NH<sub>2</sub>CH<sub>2</sub>), 33.2 (CONHCH<sub>2</sub>CH<sub>2</sub>), 30.5 (NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.9 (CONHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.7 (NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3286s, 2936s, 2869s, 1635s, 1541s, 1490, 1435, 1309, 704;  $m/z$  221 (M<sup>+</sup>).

***N*-(3-Benzylamino-propyl)-benzamide.** *N*-(3-amino-propyl)-benzamide (19.4 g, 0.109 mol) in ethanol (20 ml) was added dropwise to a stirred solution of benzaldehyde (11.6 g, 0.109 mol) in ethanol (200 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (12.38 g, 0.327 mol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (150 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane (2 × 150 ml) was then added to extract the product. The combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield *N*-(3-benzylamino-propyl)-benzamide as a very viscous *colourless oil* (28 g, 95.7%). (Found: C, 76.1; H, 7.7; N, 10.2. C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>O requires C, 76.1; H, 7.5; N, 10.4%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 8.2 (1H, br, NHCO), 7.79-7.70 (2H, m, Ar-*H*), 7.46-7.29 (8H, m, Ar-*H*), 3.8 (2H, s, NHCH<sub>2</sub>Ar), 3.58 (2H, q, *J*(CONHCH<sub>2</sub>) 6 Hz), 2.90 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>) 5.7 Hz), 1.79 (2H, quintet, *J*(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) 5.9 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 167.9 (CO), 139.8 (Ar C), 135.2 (Ar C), 131.8 (Ar CH), 129.2 (Ar CH), 129.1 (Ar CH), 129.0 (Ar CH), 127.9 (Ar CH), 127.6 (Ar CH), 54.7 (ArCH<sub>2</sub>NH), 49.3 (CONHCH<sub>2</sub>), 40.7 (CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>), 28.6 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3296s, 3060, 3028, 2931s, 1640s, 1539s, 1306s, 697s;  $m/z$  269 (M<sup>+</sup>).

***N*-(2-Benzylamino-ethyl)-benzamide.** *N*-(2-amino-ethyl)-benzamide (6.57 g, 0.04 mol) in ethanol (30 ml) was added dropwise to a stirred solution of benzaldehyde (4.24 g, 0.04 mol) in ethanol (150 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (4.54 g, 0.12 mol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (150 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane (2 × 100 ml) was then added to extract the

product. The combined organic extracts were dried over  $\text{MgSO}_4$ , filtered and evaporated *in vacuo* to yield *N*-(2-benzylamino-ethyl)-benzamide as a sticky *white solid* (9.56 g, 94%). (Found: C, 75.3; H, 7.2; N, 10.6.  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}$  requires C, 75.6; H, 7.1; N, 11.0%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 7.80-7.76 (2H, m, Ar-H), 7.50-7.42 (8H, m, Ar-H), 6.95 (1H, br, NHCO), 3.81 (2H, s,  $\text{NHCH}_2\text{Ar}$ ), 3.53 (2H, q,  $J(\text{CONHCH}_2)$  5.6 Hz), 2.87 (2H, t,  $J(\text{CH}_2\text{CH}_2\text{NHCH}_2)$  5.8 Hz), 1.85 (1H, br,  $\text{CH}_2\text{NHCH}_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 168.2 (CO), 140.7 (Ar C), 135.2 (Ar C), 132.0 (Ar CH), 129.4 (Ar CH), 129.1 (Ar CH), 128.7 (Ar CH), 127.7 (Ar CH), 127.6 (Ar CH), 54.1 (ArCH<sub>2</sub>NH), 48.5 (CONHCH<sub>2</sub>), 40.1 ( $\text{CH}_2\text{NHCH}_2\text{CH}_2$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  3256s, 3062, 3027, 2926s, 1638s, 1537s, 1311s, 693s;  $m/z$  255 ( $\text{M}^+$ ).

***N*-(6-Benzylamino-hexyl)-benzamide.** *N*-(6-amino-hexyl)-benzamide (6.39 g, 0.029 mol) in ethanol (50 ml) was added dropwise to a stirred solution of benzaldehyde (3.07 g, 0.029 mol) in ethanol (200 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (3.29 g, 0.87 mol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (150 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane ( $2 \times 100$  ml) was then added to extract the product. The combined organic extracts were dried over  $\text{MgSO}_4$ , filtered and evaporated *in vacuo* to yield *N*-(6-benzylamino-hexyl)-benzamide as a sticky *white solid* (8.78 g, 98%). (Found: C, 77.4; H, 8.4; N, 8.9.  $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}$  requires C, 77.4; H, 8.4; N, 9.0%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 7.78-7.74 (2H, m, Ar-H), 7.49-7.27 (8H, m, Ar-H), 6.27 (1H, br, NHCO), 3.78 (2H, s,  $\text{NHCH}_2\text{Ar}$ ), 3.42 (2H, q,  $J(\text{CONHCH}_2)$  6.7 Hz), 2.62 (2H, t,  $J(\text{CH}_2\text{CH}_2\text{NHCH}_2)$  7.1 Hz), 1.62 (5H, m,  $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.38 (4H, m,  $\text{NHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 168.2 (CO), 141 (Ar C), 135.5 (Ar C), 131.9 (Ar CH), 129.7 (Ar CH), 129.2 (Ar CH), 129.0 (Ar CH), 128.8 (Ar CH), 127.5 (Ar CH), 54.7 (ArCH<sub>2</sub>NH), 49.9 (CONHCH<sub>2</sub>), 40.6 ( $\text{CH}_2\text{NHCH}_2\text{CH}_2$ ), 30.6 (CONHCH<sub>2</sub>CH<sub>2</sub>), 30.3 (NHCH<sub>2</sub>CH<sub>2</sub>), 27.6 (CONHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.5 ( $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{CH}_2$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  3296s, 3060, 3028, 2931s, 1640s, 1539s, 1306s, 697s;  $m/z$  311 ( $\text{M}^+$ ).

***N*-(3-Benzylamino-propyl)-thiobenzamide.** A solution of *N*-(3-benzylamino-propyl)-benzamide (0.55 g, 2.05 mmol) in dry THF (50 ml) was refluxed with Lawesson's reagent (1.24 g, 3.07 mmol), under a dinitrogen atmosphere, for 24 h. The THF was removed *in vacuo* and the resultant yellow oil was purified by silica column chromatography (dichloromethane: methanol, 20: 1) to yield *N*-(3-benzylamino-propyl)-thiobenzamide as a *yellow oil* (0.20 g, 34%). (Found: C, 72.0; H, 7.2; N, 9.7. C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>S requires C, 71.8; H, 7.1; N, 9.9%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 10.58 (1H, br, NHCS), 7.80-7.76 (2H, m, Ar-*H*), 7.31-7.16 (8H, m, Ar-*H*), 3.94 (2H, q, *J*(CSNHCH<sub>2</sub>) 5.3 Hz), 3.78 (2H, s, NHCH<sub>2</sub>Ar), 2.97 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>) 5.5 Hz), 1.93 (2H, quintet, *J*(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) 5.7 Hz), 1.70 (1H, br, CH<sub>2</sub>NHCH<sub>2</sub>).  $\nu_{\text{max}}$ /cm<sup>-1</sup> 3253s, 2943s, 1594s, 1500s, 1259s, 1115, 1025; *m/z* 285 (M<sup>+</sup>).

**1-(2-Benzylamino-ethyl)-3-phenyl-thiourea.** 1-(2-amino-ethyl)-3-phenyl-thiourea (6.05 g, 0.031 mol) in ethanol (50 ml) was added dropwise to a stirred solution of benzaldehyde (3.28 g, 0.031 mol) in ethanol (100 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (3.52 g, 0.092 mol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (100 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane (2 × 100 ml) was then added to extract the product. The combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield 1-(2-benzylamino-ethyl)-3-phenyl-thiourea as a *white solid* (8.02 g, 91%). (Found: C, 67.5; H, 6.4; N, 14.7. C<sub>16</sub>H<sub>19</sub>N<sub>3</sub>S requires C, 67.3; H, 6.7; N, 14.7%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 8.71 (2H, br, NHCSNH), 7.57-7.10 (10H, m, Ar-*H*), 3.78-3.70 (4H, m, NHCH<sub>2</sub>Ar, CSNHCH<sub>2</sub>), 2.82 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>) 5.7 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 180.7 (CS), 140.3 (Ar C), 130.5 (Ar CH), 129.5 (Ar C), 129.0 (Ar CH), 128.6 (Ar CH), 127.7 (Ar CH), 127.3 (Ar CH), 125.4 (Ar CH), 53.8 (ArCH<sub>2</sub>NH), 47.7 (CSNHCH<sub>2</sub>), 45.3 (CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>). *m/z* 286 (M<sup>+</sup>).

***N*-[3-(Benzyl-ethoxymethyl-amino)-propyl]-benzamide.** *N*-(3-benzylamino-propyl)-benzamide (28 g, 0.104 mol) in ethanol (10 ml) was added dropwise to a

stirred suspension of paraformaldehyde (3.13 g, 0.104 mol) and potassium carbonate (28.75 g, 0.208 mol) in ethanol (120 ml) at 0°C. The mixture was allowed to warm to room temperature and continually stirred for 72 hr. The solution was filtered to remove the potassium carbonate and the solvent was then evaporated in vacuo to yield *N*-[3-(benzyl-ethoxymethyl-amino)-propyl]-benzamide as a *colourless oil* which was used without further purification (33.74 g, 99.4%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.76-7.66 (2H, m, Ar-H), 7.53-7.28 (8H, m, Ar-H), 4.13 (2H, s, NCH<sub>2</sub>O), 3.78 (2H, s, NCH<sub>2</sub>Ar), 3.53 (2H, m, CONHCH<sub>2</sub>), 3.43 (2H, m, OCH<sub>2</sub>CH<sub>3</sub>), 2.85 (2H, t,  $J(\text{CH}_2\text{CH}_2\text{N})$  6 Hz), 1.75 (2H, quintet,  $J(\text{CH}_2\text{CH}_2\text{CH}_2)$ , 6.1 Hz), 1.15 (3H, t,  $J(\text{CH}_2\text{CH}_3)$  6.1 Hz).  $\nu_{\text{max}}/\text{cm}^{-1}$  3321s, 3061, 3028, 2929s, 2863s, 1640s, 1541s, 1375, 1064, 699s;  $m/z$  281 (M - EtO).

***N*-[2-(Benzyl-ethoxymethyl-amino)-ethyl]-benzamide.** *N*-(2-benzylamino-ethyl)-benzamide (9.13 g, 0.036 mol) in ethanol (20 ml) was added dropwise to a stirred suspension of paraformaldehyde (1.08 g, 0.036 mol) and potassium carbonate (9.93 g, 0.072 mol) in ethanol (100 ml) at 0°C. The mixture was allowed to warm to room temperature and continually stirred for 48 hr. The solution was filtered to remove the potassium carbonate and the solvent was then evaporated in vacuo to yield *N*-[2-(benzyl-ethoxymethyl-amino)-ethyl]-benzamide as a *colourless oil* which was used without further purification (10.98 g, 98%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.77-7.73 (2H, m, Ar-H), 7.47-7.27 (8H, m, Ar-H), 4.26 (2H, s, NCH<sub>2</sub>O), 3.92 (2H, s, NCH<sub>2</sub>Ar), 3.52 (2H, m, OCH<sub>2</sub>CH<sub>3</sub>), 3.51 (2H, m, CONHCH<sub>2</sub>), 3.05 (2H, t,  $J(\text{CH}_2\text{CH}_2\text{N})$  5.5 Hz), 1.21 (3H, t,  $J(\text{CH}_2\text{CH}_3)$  7 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 167.8 (CO), 139.4 (Ar C), 135.3 (Ar C), 131.6 (Ar CH), 129.1 (Ar CH), 128.9 (Ar CH), 128.8 (Ar CH), 127.7 (Ar CH), 127.4 (Ar CH), 85.9 (NCH<sub>2</sub>O), 63.8 (ArCH<sub>2</sub>N), 55.7 (CH<sub>3</sub>CH<sub>2</sub>O), 51.5 (CONHCH<sub>2</sub>), 37.5 (NCH<sub>2</sub>CH<sub>2</sub>), 15.7 (CH<sub>3</sub>CH<sub>2</sub>).  $\nu_{\text{max}}/\text{cm}^{-1}$  3334s, 3062, 3026, 2934s, 2855s, 1639s, 1537s, 1383, 1062, 704s;  $m/z$  267 (M - EtO).

***N*-[6-(Benzyl-ethoxymethyl-amino)-hexyl]-benzamide.** *N*-(6-benzylamino-hexyl)-benzamide (8.69 g, 0.028 mol) in ethanol (20 ml) was added dropwise to a stirred suspension of paraformaldehyde (0.84 g, 0.028 mol) and potassium carbonate (7.74 g, 0.056 mol) in ethanol (140 ml) at 0°C. The mixture was allowed to warm to room

temperature and continually stirred for 48 hr. The solution was filtered to remove the potassium carbonate and the solvent was then evaporated *in vacuo* to yield *N*-[6-(benzyl-ethoxymethyl-amino)-hexyl]-benzamide as a *colourless oil* which was used without further purification (10 g, 96%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.74-7.70 (2H, m, Ar-H), 7.46-7.24 (8H, m, Ar-H), 4.09 (2H, s, NCH<sub>2</sub>O), 3.76 (2H, s, NCH<sub>2</sub>Ar), 3.39 (2H, m, OCH<sub>2</sub>CH<sub>3</sub>), 3.37 (2H, m, CONHCH<sub>2</sub>), 2.63 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 7.2 Hz), 1.52 (4H, m, CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.32 (4H, m, NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.15 (3H, t, *J*(CH<sub>2</sub>CH<sub>3</sub>) 7.1 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 167.8 (CO), 140.2 (Ar C), 135.3 (Ar C), 131.7 (Ar CH), 129.2 (Ar CH), 129.1 (Ar CH), 129.0 (Ar CH), 128.8 (Ar CH), 127.5 (Ar CH), 85.0 (NCH<sub>2</sub>O), 63.8 (ArCH<sub>2</sub>N), 56.6 (CH<sub>3</sub>CH<sub>2</sub>O), 51.9 (CONHCH<sub>2</sub>), 40.4 (NCH<sub>2</sub>CH<sub>2</sub>), 30.1 (CONHCH<sub>2</sub>CH<sub>2</sub>), 28.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.4 (CONHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.3 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 15.7 (CH<sub>3</sub>CH<sub>2</sub>).  $\nu_{\text{max}}$ /cm<sup>-1</sup> 3321s, 3061, 3028, 2929s, 2863s, 1640s, 1541s, 1375, 1064, 699s; *m/z* 323 (M - EtO).

***N*-{3-[Benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}-**

**benzamide.** A solution of *N*-[3-(benzyl-ethoxymethyl-amino)-propyl]-benzamide (33.7 g, 0.103 mol) and 5-*tert*-butyl-2-hydroxybenzaldehyde (18.4 g, 0.103 mol) (prepared as outlined in section 2.8.3) in acetonitrile (400 ml) was refluxed under a dinitrogen atmosphere for 72 h. The reaction was cooled to room temperature and the solvent evaporated *in vacuo* to yield a dark brown oil which was purified by silica column chromatography (ethyl acetate: hexane, 1:2) to yield *N*-{3-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}-benzamide as a *yellow oil* (18.2 g, 38%). (Found: C, 76.0; H, 7.3; N, 6.1. C<sub>29</sub>H<sub>34</sub>N<sub>2</sub>O<sub>3</sub> requires C, 76.0; H, 7.5; N, 6.1%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 10.15 (1H, s, CHO), 7.58-7.25 (12H, m, Ar-H), 6.42 (1H, br, NHCO), 3.78 (2H, s, NCH<sub>2</sub>CCOH), 3.66 (2H, s, NCH<sub>2</sub>Ar), 3.49 (2H, q, *J*(CONHCH<sub>2</sub>) 6.2 Hz), 2.64 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 6.5 Hz), 1.91 (2H, quintet, *J*(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) 6.3 Hz), 1.27 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 194.3 (CHO), 168.2 (NHCO), 159.2 (Ar C), 142.8 (Ar C), 138.3 (Ar C), 135.2 (Ar C), 134.8 (Ar CH), 131.9 (Ar CH), 130.0 (Ar CH), 129.2 (Ar CH), 129.0 (Ar CH), 128.2 (Ar CH), 127.5 (Ar CH), 127.0 (Ar CH), 125.5 (Ar C), 121.8 (Ar C), 59.1 (NCH<sub>2</sub>CCOH), 55.2 (NCH<sub>2</sub>Ar), 51.6 (CONHCH<sub>2</sub>), 38.7 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 31.9

(C(CH<sub>3</sub>)<sub>3</sub>), 26.9 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3326, 3062, 3027, 2961s, 1651s, 1538s, 1479s, 1216, 753;  $m/z$  459 (M<sup>+</sup>).

***N*-{2-[Benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-ethyl}-**

**benzamide.** A solution of *N*-[2-(benzyl-ethoxymethyl-amino)-ethyl]-benzamide (10.53 g, 0.034 mol) and 5-*tert*-butyl-2-hydroxybenzaldehyde (6.01 g, 0.034 mol) in acetonitrile (100 ml) was refluxed under a dinitrogen atmosphere for 72 h. The reaction was cooled to room temperature and the solvent evaporated *in vacuo* to yield a viscous brown oil which was purified by silica column chromatography (ethyl acetate:hexane, 2:5) to yield *N*-{2-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-ethyl}-benzamide as a *yellow oil* (4.52 g, 30%). (Found: C, 72.0; H, 7.1; N, 5.3. C<sub>28</sub>H<sub>32</sub>N<sub>2</sub>O<sub>3</sub>.C<sub>4</sub>H<sub>8</sub>O<sub>2</sub> requires C, 72.2; H, 7.6; N, 5.3%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 9.99 (1H, s, CHO), 7.74-7.22 (12H, m, Ar-H), 6.90 (1H, br, NHCO), 3.74 (2H, s, NCH<sub>2</sub>CCOH), 3.62 (2H, s, NCH<sub>2</sub>Ar), 3.58 (2H, q, J(CONHCH<sub>2</sub>) 5.6 Hz), 2.75 (2H, t, J(CH<sub>2</sub>CH<sub>2</sub>N) 5.8 Hz), 1.27 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 196.3 (CHO), 168.0 (NHCO), 159.0 (Ar C), 143.0 (Ar C), 138.9 (Ar C), 135.8 (Ar CH), 135.3 (Ar C), 132.0 (Ar CH), 129.7 (Ar CH), 129.1 (Ar CH), 129.0 (Ar CH), 128.4 (Ar CH), 128.1 (Ar CH), 127.5 (Ar CH), 126.3 (Ar C), 121.4 (Ar C), 59.1 (NCH<sub>2</sub>CCOH), 54.4 (NCH<sub>2</sub>Ar), 53.0 (CONHCH<sub>2</sub>), 37.7 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 31.9 (C(CH<sub>3</sub>)<sub>3</sub>).  $\nu_{\max}/\text{cm}^{-1}$  3339, 3062, 3027, 2963s, 1649s, 1535s, 1480s, 1217, 754;  $m/z$  445 (M<sup>+</sup>).

***N*-{6-[Benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-hexyl}-**

**benzamide.** A solution of *N*-[6-(benzyl-ethoxymethyl-amino)-hexyl]-benzamide (8.84 g, 0.024 mol) and 5-*tert*-butyl-2-hydroxybenzaldehyde (4.28 g, 0.024 mol) in acetonitrile (80 ml) was refluxed under a dinitrogen atmosphere for 72 h. The reaction was cooled to room temperature and the solvent evaporated *in vacuo* to yield a viscous brown oil which was purified by silica column chromatography (ethyl acetate : hexane, 1:3) to yield *N*-{6-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-hexyl}-benzamide as a *light yellow oil* (4.38 g, 36%). (Found: C, 77.2; H, 8.2; N, 5.8. C<sub>32</sub>H<sub>40</sub>N<sub>2</sub>O<sub>3</sub> requires C, 76.8; H, 8.0; N, 5.6%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 10.35 (1H, s, CHO), 7.78-7.28 (12H, m, Ar-H), 6.28 (1H, br, NHCO), 3.77

(2H, s, NCH<sub>2</sub>CCOH), 3.65 (2H, s, NCH<sub>2</sub>Ar), 3.40 (2H, q, *J*(CONHCH<sub>2</sub>) 6.7 Hz), 2.52 (2H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 7.2 Hz), 1.58 (4H, m, CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.34 (4H, m, NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.30 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 192.6 (CHO), 168.1 (NHCO), 159.9 (Ar C), 142.5 (Ar C), 137.7 (Ar C), 135.4 (Ar C), 133.5 (Ar CH), 132.0 (Ar CH), 130.0 (Ar CH), 129.2 (Ar CH), 129.0 (Ar CH), 128.2 (Ar CH), 127.5 (Ar CH), 125.1 (Ar CH), 124.7 (Ar C), 122.7 (Ar C), 58.9 (NCH<sub>2</sub>CCOH), 56.6 (NCH<sub>2</sub>Ar), 53.9 (CONHCH<sub>2</sub>), 40.6 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.7 (C(CH<sub>3</sub>)<sub>3</sub>), 32.0 (C(CH<sub>3</sub>)<sub>3</sub>), 30.2 (CONHCH<sub>2</sub>CH<sub>2</sub>), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.3 (CONHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.0 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3335, 3062, 3029, 2930s, 1735, 1653s, 1539s, 1472s, 1242, 894; *m/z* 501 (M<sup>+</sup>).

**4,4'-Di-*tert*-butyl-6,6'-bis([3-benzoylamidopropyl]benzylaminomethyl)-2,2'-(ethylenedinitrilodimethyldyne) diphenol (1).**

Ethylenediamine (0.13 g, 0.0021 mol) in methanol (50 ml) was added to a stirred solution of *N*-{3-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}-benzamide (1.93 g, 0.0042 mol) in chloroform (50 ml). After stirring for 10 hours the solvent was removed *in vacuo* to give a yellow oil which was dissolved in chloroform (100 ml) and washed with water (2 × 50 ml). The chloroform solution was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **1** as a *yellow oil* (1.93 g, 98%). (Found: C, 73.6; H, 8.0; N, 8.2. C<sub>60</sub>H<sub>72</sub>N<sub>6</sub>O<sub>4</sub>·2H<sub>2</sub>O requires C, 73.7; H, 7.8; N, 8.6%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.30 (2H, s, N=CH), 7.57-7.52 (4H, m, Ar-H), 7.42-7.20 (20H, m, Ar-H), 7.07 (2H, br, NHCO), 3.72 (4H, s, NCH<sub>2</sub>CCOH), 3.70 (4H, s, CH=NCH<sub>2</sub>), 3.64 (4H, s, NCH<sub>2</sub>Ar), 3.50 (4H, q, *J*(CONHCH<sub>2</sub>) 6.5 Hz), 2.60 (4H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 6 Hz), 1.81 (4H, quintet, *J*(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) 5.8 Hz), 1.26 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 167.8 (CONH), 167.3 (N=CH), 158.0 (Ar C), 141.5 (Ar C), 139.7 (Ar C), 135.4 (Ar C), 131.8 (Ar CH), 131.5 (Ar CH), 129.9 (Ar CH), 129.8 (Ar CH), 128.9 (Ar CH), 128.8 (Ar CH), 128.7 (Ar CH), 127.7 (Ar CH), 126.4 (Ar C), 118.4 (Ar C), 60.2 (NCH<sub>2</sub>CCOH), 59.5 (CH=NCH<sub>2</sub>), 53.2 (NCH<sub>2</sub>Ar), 52.5 (CONHCH<sub>2</sub>), 39.8 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 32.0 (C(CH<sub>3</sub>)<sub>3</sub>), 26.6 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3325, 3060, 2952s, 1633s, 1538, 1273, 1026, 697; λ<sub>max</sub>/nm (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>) (CHCl<sub>3</sub>) 261 (23342), 331 (8616). *m/z* 941 (M<sup>+</sup>).



**4,4'-Di-*tert*-butyl-6,6'-bis([3-benzoylamidopropyl]benzylaminomethyl)-2,2'-(1,2-phenylenedinitrilodimethylidyne) diphenol (2).** Phenylene-1,2-diamine (0.24 g, 0.0022 mol) in ethanol (50 ml) was added to a stirred solution of *N*-{3-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}-benzamide (2 g, 0.0044 mol) in chloroform (50 ml). After stirring for 10 hours the solvent was removed *in vacuo* to yield an orange-yellow oil which was dissolved in chloroform (100 ml) and washed with water (2 × 50 ml). The chloroform solution was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **2** as an *orange-yellow oil* (1.93 g, 98%). (Found: C, 77.3; H, 7.6; N, 8.4. C<sub>64</sub>H<sub>72</sub>N<sub>6</sub>O<sub>4</sub> requires C, 77.7; H, 7.3; N, 8.5%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.63 (2H, s, N=CH), 7.58-7.16 (28H, m, Ar-H), 6.90 (2H, br, NHCO), 3.78 (4H, s, NCH<sub>2</sub>CCOH), 3.68 (4H, s, NCH<sub>2</sub>Ar), 3.48 (4H, m, CONHCH<sub>2</sub>), 2.58 (4H, m, CH<sub>2</sub>CH<sub>2</sub>N), 1.82 (4H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.30 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 168.0 (NHCO), 163.9 (N=CH), 158.3 (Ar C), 143.4 (Ar C), 141.8 (Ar C), 139.8 (Ar C), 135.4 (Ar C), 131.7 (Ar CH), 131.5 (Ar CH), 130.3 (Ar CH), 129.9 (Ar CH), 129.8 (Ar CH), 129.0 (Ar CH), 128.8 (Ar CH), 128.1 (Ar CH), 127.7 (Ar C), 127.6 (Ar CH), 126.5 (Ar C), 120.3 (Ar CH), 59.5 (NCH<sub>2</sub>CCOH), 53.0 (NCH<sub>2</sub>Ar), 52.1 (CONHCH<sub>2</sub>), 39.4 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 32.1 (C(CH<sub>3</sub>)<sub>3</sub>), 26.7 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3335, 2953s, 1640s, 1617s, 1486, 1291, 697; λ<sub>max</sub>/nm (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>) (CHCl<sub>3</sub>) 276 (24128), 337 (16638). *m/z* 989 (M<sup>+</sup>).

**4,4'-Di-*tert*-butyl-6,6'-bis([2-benzoylamidoethyl]benzylaminomethyl)-2,2'-(ethylenedinitrilodimethylidyne) diphenol (3).** Ethylenediamine (0.26 g, 0.0043 mol) in methanol (20 ml) was added to a stirred solution of *N*-{2-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-ethyl}-benzamide (3.82 g, 0.0086 mol) in ethanol (80 ml). The reaction was refluxed for one hour and the solvent was removed *in vacuo* to give a yellow oil which was dissolved in chloroform (150 ml) and washed with water (2 × 75 ml). The chloroform solution was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **3** as a *yellow oil* (3.75 g, 95%). (Found: C, 74.2; H, 7.6; N, 9.0. C<sub>58</sub>H<sub>68</sub>N<sub>6</sub>O<sub>4</sub>·<sup>3</sup>/<sub>2</sub>H<sub>2</sub>O requires C, 74.1; H, 7.6; N, 8.9%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.25 (2H, s, N=CH), 7.76-7.72 (4H, m, Ar-H), 7.41-7.10 (20H, m, Ar-H), 3.80 (4H, s, NCH<sub>2</sub>CCOH), 3.76 (4H, s, CH=NCH<sub>2</sub>), 3.58 (4H, s,

NCH<sub>2</sub>Ar), 3.57 (4H, m, CONHCH<sub>2</sub>), 2.69 (4H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 5.7 Hz), 1.22 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 167.7 (CONH), 167.6 (N=CH), 158.2 (Ar C), 141.5 (Ar C), 140.1 (Ar C), 135.7 (Ar C), 132.1 (Ar CH), 131.5 (Ar CH), 129.5 (Ar CH), 128.9 (Ar CH), 128.8 (Ar CH), 127.8 (Ar CH), 127.7 (Ar CH), 127.6 (Ar CH), 126.3 (Ar C), 118.4 (Ar C), 60.2 (NCH<sub>2</sub>CCOH), 58.9 (CH=NCH<sub>2</sub>), 53.1 (NCH<sub>2</sub>Ar), 52.4 (CONHCH<sub>2</sub>), 37.5 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.5 (C(CH<sub>3</sub>)<sub>3</sub>), 32.0 (C(CH<sub>3</sub>)<sub>3</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3358, 3062, 2962s, 1633s, 1479, 1277, 754; λ<sub>max</sub>/nm (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>) (CHCl<sub>3</sub>) 263 (22800), 332 (8540). *m/z* 913 (M<sup>+</sup>).

**4,4'-Di-*tert*-butyl-6,6'-bis([6-benzoylamidohexyl]benzylaminomethyl)-2,2'-**

**(ethylenedinitrilodimethylidyne) diphenol (4).** Ethylenediamine (0.25 g, 0.0042 mol) in ethanol (20 ml) was added to a stirred solution of *N*-{6-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-hexyl}-benzamide (4.21 g, 0.0084 mol) in chloroform (80 ml). The reaction was refluxed for one hour and the solvent was removed *in vacuo* to give a light yellow oil which was dissolved in chloroform (150 ml) and washed with water (2 × 75 ml). The chloroform solution was dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **4** as a *light yellow oil* (4.10 g, 95%). (Found: C, 76.2; H, 8.4; N, 8.2. C<sub>66</sub>H<sub>84</sub>N<sub>6</sub>O<sub>4</sub>·H<sub>2</sub>O requires C, 76.0; H, 8.3; N, 8.1%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.36 (2H, s, N=CH), 7.75-7.12 (24H, m, Ar-H), 6.30 (2H, br, NHCO), 3.88 (4H, s, NCH<sub>2</sub>CCOH), 3.65 (4H, s, CH=NCH<sub>2</sub>), 3.58 (4H, s, NCH<sub>2</sub>Ar), 3.35 (4H, q, *J*(CONHCH<sub>2</sub>) 6.7 Hz), 2.44 (4H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>N) 7 Hz), 1.53 (8H, m, CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.29 (8H, m, NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.27 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 168.1 (CONH), 167.1 (N=CH), 157.5 (Ar C), 141.4 (Ar C), 140.7 (Ar C), 135.5 (Ar C), 131.9 (Ar CH), 130.7 (Ar CH), 129.3 (Ar CH), 129.1 (Ar CH), 128.7 (Ar CH), 127.5 (Ar CH), 127.3 (Ar CH), 127.1 (Ar C), 126.7 (Ar CH), 118.3 (Ar C), 60.6 (NCH<sub>2</sub>CCOH), 59.2 (CH=NCH<sub>2</sub>), 54.3 (NCH<sub>2</sub>Ar), 52.3 (CONHCH<sub>2</sub>), 40.6 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 32.1 (C(CH<sub>3</sub>)<sub>3</sub>), 30.2 (CONHCH<sub>2</sub>CH<sub>2</sub>), 27.7 (NCH<sub>2</sub>CH<sub>2</sub>), 27.6 (CONHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3330, 3062, 2935s, 1630s, 1540, 1216, 745; λ<sub>max</sub>/nm (ε/dm<sup>3</sup> mol<sup>-1</sup> cm<sup>-1</sup>) (CHCl<sub>3</sub>) 264 (24300), 330 (9018). *m/z* 1025 (M<sup>+</sup>).

#### 4.10.4 Neutral “Copper-only” Complex Synthesis

[Cu(1-2H)] (5): A solution of ligand **1** (1.3 g, 0.0014 mol) in chloroform (30 ml) was added to Cu(CH<sub>3</sub>COO)<sub>2</sub>·H<sub>2</sub>O (0.28 g, 0.0014 mol) in methanol (50 ml) and stirred overnight. The solvent was then removed *in vacuo* to yield a black oil which was dissolved in chloroform (60 ml) and washed with a pH 9 ammonia solution (2 × 30 ml). The chloroform solution was dried with MgSO<sub>4</sub>, filtered and then concentrated *in vacuo* to yield **5** as a *black solid* (1.37 g, 98%) which was used without further purification. (Cu-content by ICP-OES for a 0.002M solution in butan-1-ol: found 157.0 ppm, C<sub>60</sub>H<sub>70</sub>N<sub>6</sub>O<sub>4</sub>Cu requires 157.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  3310, 2958s, 1624s, 1536, 1442, 1261, 697;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 278 (24460), 381 (11672), 573 (400).  $m/z$  1003 (M<sup>+</sup>).

Other metal-only complexes were prepared in a similar manner.

[Cu(2-2H)] (6): (1.43 g, 97%). (Cu-content by ICP-OES for a 0.002M solution in butan-1-ol: found 158.2 ppm, C<sub>64</sub>H<sub>70</sub>N<sub>6</sub>O<sub>4</sub>Cu requires 157.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  3323, 2958s, 1645, 1610s, 1531s, 1261, 698;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 317 (21130), 443 (14170), 580 (380).  $m/z$  1051 (M<sup>+</sup>).

[Cu(3-2H)] (7): (1.33 g, 97%). (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 77.8 ppm, C<sub>58</sub>H<sub>66</sub>N<sub>6</sub>O<sub>4</sub>Cu requires 78.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  3337, 2962s, 1628s, 1539, 1444, 1216, 753;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 280 (23600), 381 (9862), 572 (430).  $m/z$  974 (M<sup>+</sup>).

[Cu(4-2H)] (8): (1.45 g, 95%). (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 79.7 ppm, C<sub>66</sub>H<sub>82</sub>N<sub>6</sub>O<sub>4</sub>Cu requires 78.9 ppm);  $\nu_{\max}/\text{cm}^{-1}$  3313, 2933s, 1626s, 1538, 1443, 754;  $\lambda_{\max}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 281 (25800), 382 (10514), 565 (450).  $m/z$  1086 (M<sup>+</sup>).

#### 4.10.5 The pH Dependence of Anion-loading

##### 4.10.5.1 The pH Dependence of Sulfate-loading

The “copper-only” complexes **5** – **8** were taken through the following procedure and then analysed for copper and sulfur content.

###### 4.10.5.1.1 Preparation of Acid and “Copper-only” Complex Solutions

Acid solutions of H<sub>2</sub>SO<sub>4</sub> were prepared as described in chapter 2 (appendix 7.2.1). A 0.01 M chloroform stock solution of “copper-only” complex (250 ml) was also prepared.

###### 4.10.5.1.2 Extraction Experiments on “Copper-only” Complexes

The extraction experiments were performed as described in chapter 2 (section 2.8.5). It should be noted that a 1 ml aliquot of the CHCl<sub>3</sub> layer was removed, dried *in vacuo* and re-dissolved in butan-1-ol (10 ml) for copper and sulfur analysis by ICP-OES for the extraction experiments involving **5** and **6** and a 2 ml aliquot was taken for experiments involving **7** and **8** (appendix 7.3.3.1).

##### 4.10.5.2 The pH Dependence of Phosphoric Acid Uptake by Complex **5**

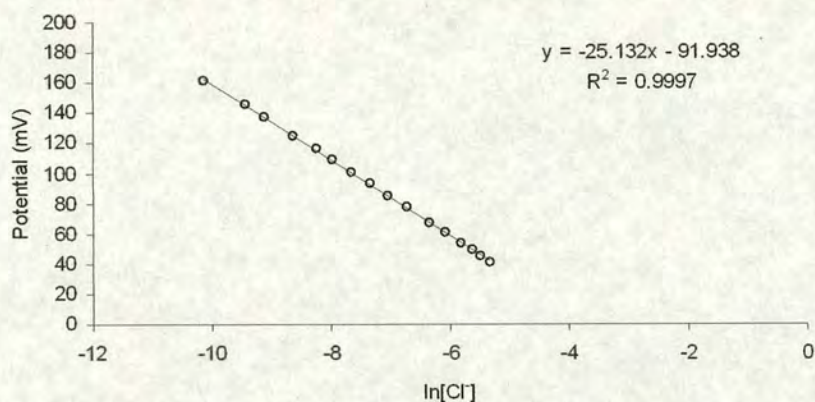
Extraction experiments were carried out using the same procedure used for determining the pH dependence of sulfate-loading (section 2.8.5) except that phosphoric acid solutions containing a total phosphate concentration of 0.8 M, with pHs in the range 2 – 5 (appendix 7.2.3), were used instead of the sulfuric acid solutions and the aliquots of CHCl<sub>3</sub> (1 ml) were removed, dried *in vacuo* and re-dissolved in butan-1-ol for copper and phosphorus analysis by ICP-OES. The maximum loadings of Cu and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> were calculated assuming that in the fully loaded complex the ligand to H<sub>2</sub>PO<sub>4</sub><sup>-</sup> to Cu ratio is 1 : 2 : 1 (appendix 7.3.3.3).

#### 4.10.5.3 The pH Dependence of Chloride-loading

The procedure outlined in section 2.8.5 for sulfate-loading was followed except that hydrochloric acid solutions, with pHs in the range 0 – 8, containing a total chloride concentration of 0.8 M were used instead of the sulfuric acid solutions (appendix 7.2.2).

The contacted solutions had a 2 ml aliquot of the  $\text{CHCl}_3$  solution removed for chloride analysis (1 ml was also taken for analysis by UV-Visible spectroscopy, Section 4.10.6). The analysis was performed by contacting the aliquots with 10 ml of a 0.1 M  $\text{HNO}_3$  solution for 3 hours to transfer all chloride anions to the aqueous phase. 5 ml portions of the resulting aqueous solutions were transferred to 10 ml volumetric flasks, diluted with 0.1 M NaOH solution to ensure a pH in the range (2 – 12) suitable for use of the chloride-selective electrode and then made up to volume. The chloride concentration was determined by a chloride-selective electrode (appendix 7.3.3.2).

Assuming the chloride to ligand to copper ratio is 2 : 1 : 1 in a fully loaded complex then 100% chloride-loading in the extraction experiments will generate an aqueous solution, after back stripping as above, with a chloride concentration of 0.002 M. The chloride-selective electrode was therefore calibrated in the concentration range of 0.005 M to 0.0001 M. This was performed before each analysis by titration of 10 ml of 0.01 M NaCl solution into 10 ml of 0.1 M  $\text{NaNO}_3$  while monitoring the change in potential (mV) (Figure 4.29). The 0.01 M NaCl solution used was prepared using 0.09 M  $\text{NaNO}_3$  solution in order to maintain a constant ionic strength of 0.1 M.



**Figure 4.29** Calibration of the chloride electrode.

#### 4.10.6 UV-Visible Analysis of the Solvent Extraction Experiments on “Copper-only” Complexes 5, 7 and 8.

500  $\mu\text{L}$  aliquots from each of the butan-1-ol solutions, prepared for analysis by ICP-OES (see section 4.10.5.1), were made up to 10.0 ml in butan-1-ol. The resulting solutions ( $0.05 \text{ mmol dm}^{-3}$  for experiments on 7 and 8 and  $0.1 \text{ mmol dm}^{-3}$  for 5) were then analysed by electronic absorption spectroscopy (appendix 7.6.2).

In the analysis of the chloride extractions the 1 ml samples, taken from the  $\text{CHCl}_3$  layer (Section 4.10.5.3), were evaporated *in vacuo* and each dissolved in butan-1-ol (10 ml). Aliquots, of 500  $\mu\text{L}$ , were removed from each of these solutions and again dissolved in butan-1-ol (10 ml). The resulting solutions ( $0.05 \text{ mmol dm}^{-3}$ ) were then analysed by electronic absorption spectroscopy (appendix 7.6.2).

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## **Chapter 5 : Macrocyclic Metal Salt Extractants**



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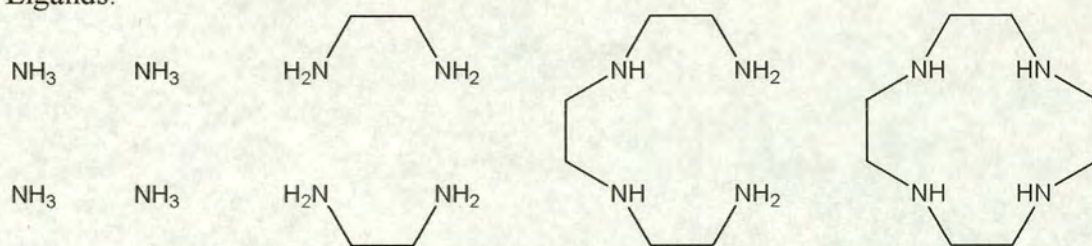
## 5.1 Introduction

It has already been stressed in this thesis that a key requirement of a commercial metal extractant is that it needs to show selectivity. This is an especially difficult target for a metal *salt* extractant as selective binding is needed for both the targeted metal cation and its attendant anion(s).

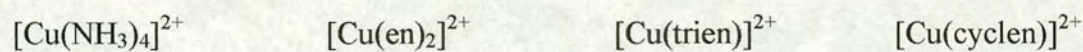
Anions have a wide range of geometries (see section 1.7)<sup>1</sup> so a successful binding site requires very careful positioning of anion binding units, such as hydrogen-bonding groups, in order to complement the shape of the targeted anion. This can be efficiently done if the binding groups are well placed within a rigid and pre-organised ligand framework such as a macrocycle.

The use of more rigid and pre-organised structures to improve the stability of complexation is well known in metal coordination chemistry through the chelate and macrocyclic effects.<sup>2</sup> These effects can be used to predict which ligands will form the most stable metal complexes. The chelate effect states that ligands with more than one donor will form more stable complexes than analogous monodentate ligands (generally chelates of higher denticity will give more stable complexes than chelates of lower denticity) and the macrocyclic effect indicates that macrocyclic ligands, of appropriate size, form more stable complexes than their straight chain counterparts. This is well demonstrated by comparison of the overall stability constants of the ammine and amine copper complexes<sup>3, 4</sup> shown in Figure 5.1 as the pre-organised macrocyclic ligand cyclen forms the most stable complexes. In this example the formation of the complexes involves the replacement of four coordinated water molecules hence in  $[\text{Cu}(\text{NH}_3)_4]^{2+}$  there are four stepwise equilibria ( $K_1K_2K_3K_4 = \beta_4$ ) and in  $[\text{Cu}(\text{cyclen})]^{2+}$  there is only one ( $K_1 = \beta_1$ ). The chelating ligands en and trien are also found to be more stable than the copper ammine complex which illustrates the chelate effect.

Ligands:



Metal Complexes:



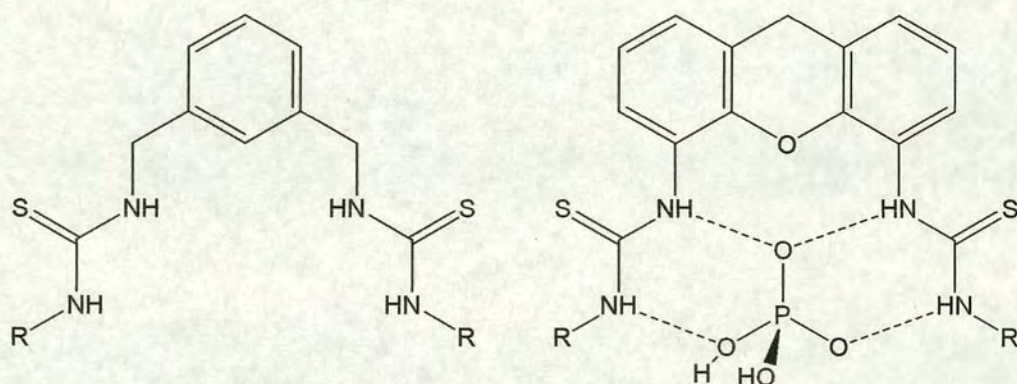
Overall Stability Constants:



**Figure 5.1** The overall stability constants for the formation of copper ammine and amine complexes.<sup>3,4</sup>

The macrocyclic effect can also be used to explain the high stability of the *pseudo*-macrocyclic copper complex which is formed by the phenolic oxime extractant P50 (see section 1.4).

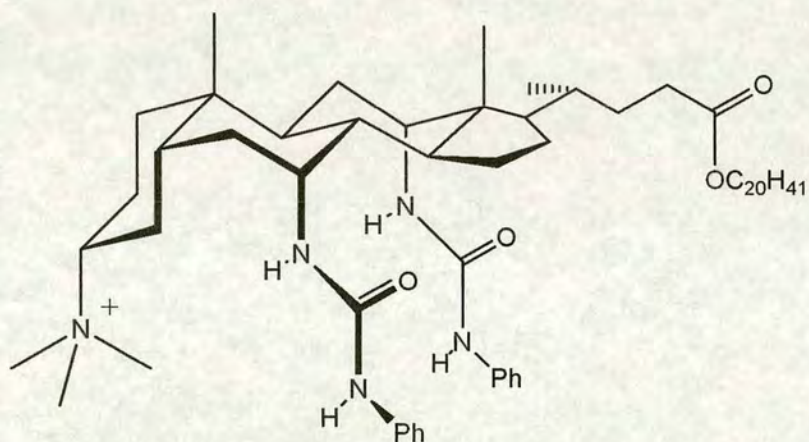
Rigidity and pre-organisation have also been found to be extremely important to achieving high stability and selectivity in anion receptors. Umezawa and co-workers<sup>5</sup> developed bis-thiourea receptors, based on a xanthene spacer, which were highly pre-organised and were found to form much stronger complexes with anions than more flexible, related bis-thiourea receptors (Figure 5.2).



**Figure 5.2** Bis-thiourea receptors which show selectivity for H<sub>2</sub>PO<sub>4</sub><sup>-</sup>. R = Bu<sup>†</sup>, Ph.<sup>5</sup>

The ligands were found to be selective for  $\text{H}_2\text{PO}_4^-$  over  $\text{CH}_3\text{COO}^-$  and  $\text{Cl}^-$  and this was attributed to the well-placed thiourea hydrogen-bond donors (Figure 5.2). The strength of binding was greater in the receptors containing the xanthene spacer as the hydrogen-bond donors were firmly fixed in a suitable binding arrangement.

Another example of successful receptor pre-organisation is the steroid-based anion receptor developed by Davis and co-workers which contains urea and quaternary ammonium groups (Figure 5.3).<sup>6</sup> This ligand has been found to show anti-Hofmeister<sup>7</sup> extraction behaviour as it shows selectivity for iodide over the more hydrophobic perchlorate anion. The receptor also demonstrates an affinity for other halide anions ( $\text{Br}^-$ ,  $\text{Cl}^-$ ) so it is likely that these spherical anions have the ideal shape for the pre-formed cavity.



**Figure 5.3** A steroid-based anion receptor which has a high affinity for halide anions.<sup>6</sup>

Numerous pre-organised macrocyclic ligands have also been developed for anion encapsulation and some of these even show selectivity for the hydrophilic sulfate anion (section 1.7).<sup>8,9</sup>

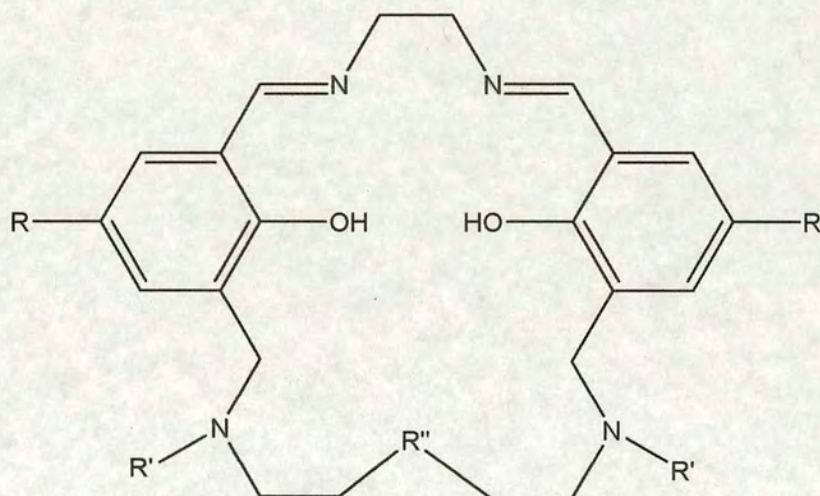
Achieving a high “strength” and selectivity of  $\text{CuSO}_4$  extraction in a hydrometallurgical process may be possible by using a well designed, pre-organised macrocyclic ligand. In this chapter zwitterionic macrocyclic metal *salt* extractants are

synthesised and their “strength” and selectivity are analysed in solvent extraction experiments.

## 5.2 Synthesis

### 5.2.1 Ligands and Metal Complexes

The ligands (Figure 5.4) and metal complexes synthesised for this chapter are summarised below (Table 5.1).



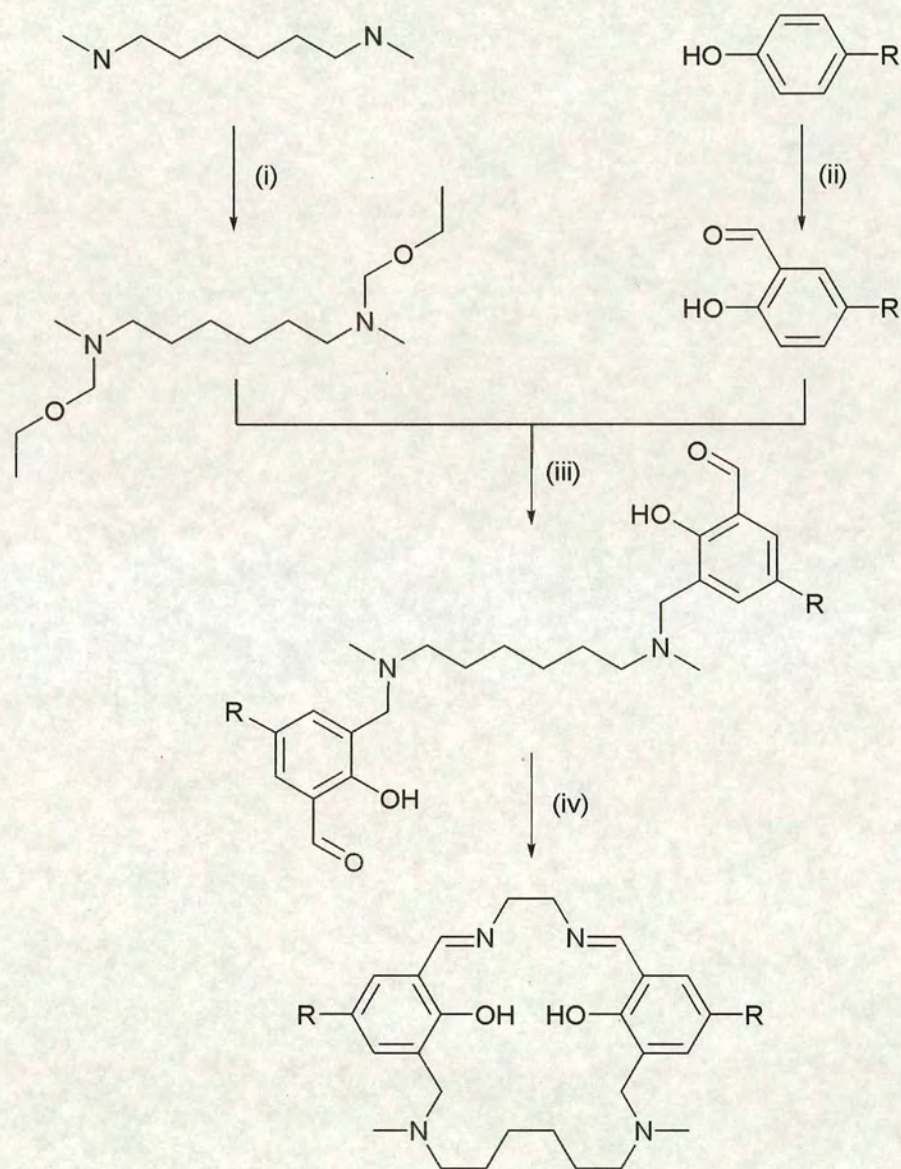
**Figure 5.4** Zwitterionic macrocyclic metal salt extractants; R = alkyl, R' = alkyl, aryl, R'' = alkyl, alkyl amide chain.

**Table 5.1** Ligands and metal complexes used and their designated reference numbers.

Ligands	R	R'	R''	Metal Complexes	
1	Bu <sup>t</sup>	Me	-(CH <sub>2</sub> ) <sub>2</sub> -	4	[Cu(1)SO <sub>4</sub> ]
2	C <sub>9</sub> H <sub>19</sub>	Me	-(CH <sub>2</sub> ) <sub>2</sub> -	5	[Cu(2-2H)]
3	Bu <sup>t</sup>	-CH <sub>2</sub> Ph	-CH <sub>2</sub> NHCO(CH <sub>2</sub> ) <sub>3</sub> CONHCH <sub>2</sub> -	6	[Cu(3-2H)]

## 5.2.1.1 Synthesis of Free Ligands

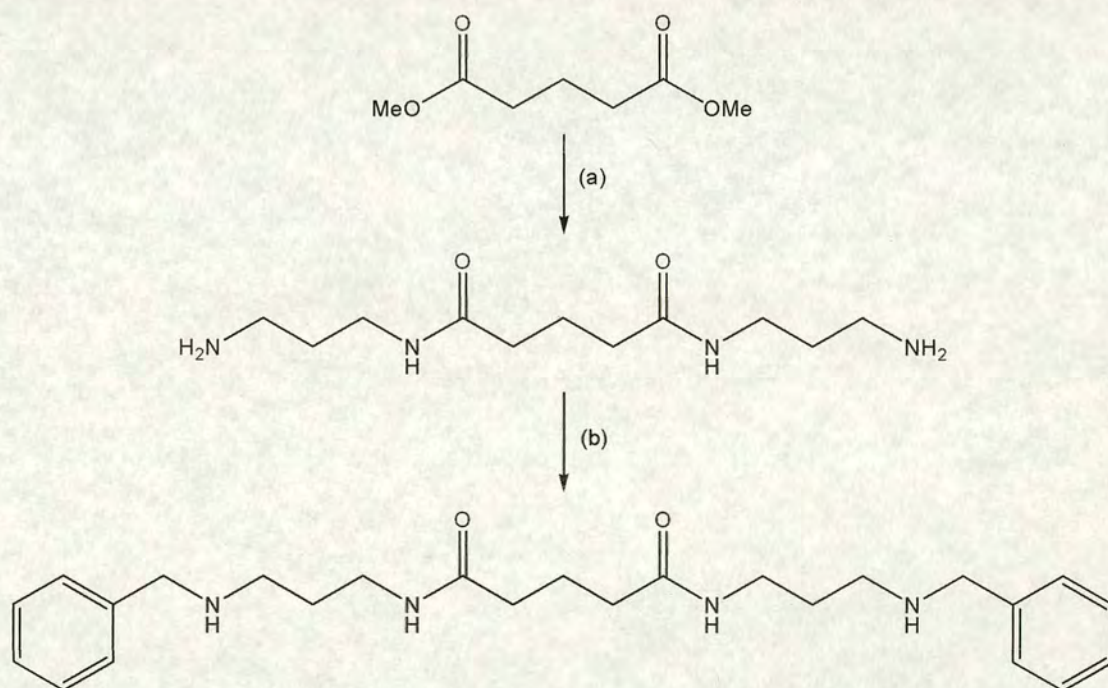
The 22-membered macrocycles **1** and **2** were prepared from 2-hydroxy-5-alkylbenzaldehyde (alkyl = Bu<sup>t</sup> (**1**) and C<sub>9</sub>H<sub>19</sub> mixed isomer (**2**))<sup>10</sup>, paraformaldehyde, *N,N*-dimethyl-1,6-hexanediamine and ethylenediamine as outlined in Figure 5.5.



**Figure 5.5** Synthesis of ligands, R = Bu<sup>t</sup> (**1**) or C<sub>9</sub>H<sub>19</sub> (**2**). Reagents and conditions: (i) paraformaldehyde, ethanol, distillation; (ii) MgOMe, MeOH-toluene, reflux 3 h; (iii) MeCN, N<sub>2</sub>, reflux 66h; (iv) 1,2-ethanediamine, Et<sub>2</sub>O-EtOH (10:1) (**1**) and MeOH-CHCl<sub>3</sub> (1:2) (**2**), r.t. 24h.

The dialdehydes were both synthesised by two-step Mannich reactions.<sup>11</sup> The Bu<sup>t</sup>-substituted dialdehyde was purified by first sonicating the oil in pentane and then recrystallising the resultant pale yellow solid from hexane (81% yield). The related dialdehyde, containing C<sub>9</sub>H<sub>19</sub> mixed isomer chains, was purified by collecting the light brown oil, which separated from the CH<sub>3</sub>CN reaction mixture on cooling, and washing it with CH<sub>3</sub>CN several times to yield the pure product in moderate yield (57%). The ligands **1** and **2** were then synthesised from the dialdehydes by Schiff base condensation reactions with ethylenediamine.

Ligand **3** was prepared in a slightly different way as in this case the secondary diamine, used in the first step of the Mannich reaction (step (i), Figure 5.5), needed to be synthesised in two steps. The first step (Figure 5.6 (a)) in the procedure involved heating dimethyl glutarate in an excess of 1,3-diaminopropane at 100°C for 5 days to give a *N,N'*-di-3-aminopropyl diamide.

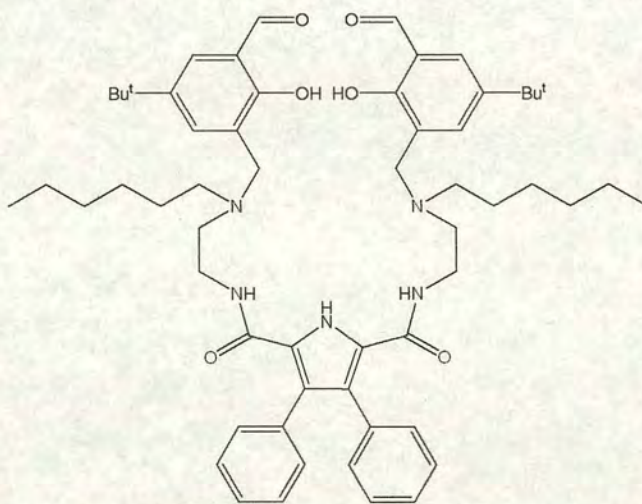


**Figure 5.6** Preparation of diamide-functionalised secondary diamine precursor for ligand **3** synthesis. Reagents and conditions: (a) Xs  $\text{NH}_2(\text{CH}_2)_3\text{NH}_2$ , 100°C, 5 days; (b) Benzaldehyde, reflux 1 h,  $\text{NaBH}_4$ , reflux 1 h.

The dibenzyl derivative was then prepared in high yield (94%) by reductive amination of benzaldehyde (Figure 5.6, (b)).

A two-step Mannich reaction (similar to Figure 5.5, steps (i) and (iii)) produced the desired dialdehyde. The product was purified by silica column chromatography (DCM:MeOH, 30:1) but it was only obtained in a very low yield of 8%. The low yield was attributed to side reactions taking place on the amide protons. Ligand **3** was subsequently prepared by a Schiff base condensation with ethylenediamine.

Pyrrole NH groups have emerged as one of the most useful anion-binding motifs (see section 1.7) so it was hoped that incorporating these hydrogen-bond donor groups into a macrocyclic ligand, also containing amide and ammonium groups, would improve the “strength” and selectivity of sulfate-extraction. Unfortunately the Mannich reaction on 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-[(2-hexylamino-ethyl)-amide] failed to yield the desired dialdehyde (Figure 5.7). Electrospray mass spectroscopy provided evidence for the existence of the product in the reaction mixture but the yield must have been extremely small as it could not be isolated. This problem was attributed to interference by the amide and pyrrole groups during the reaction.

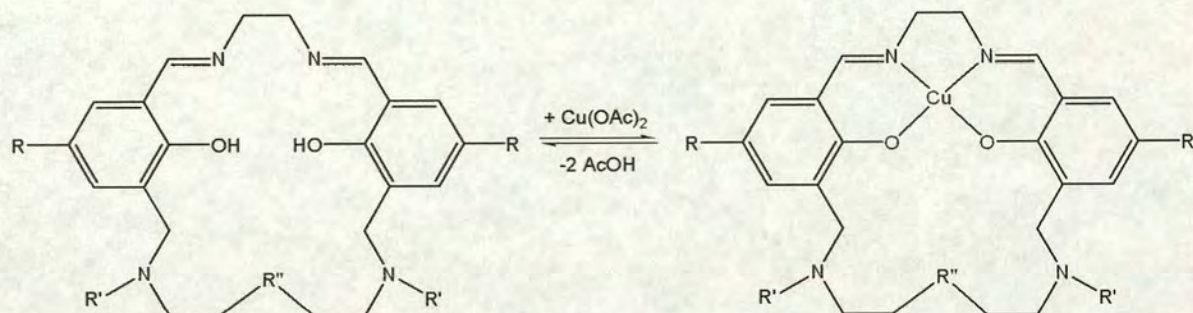


**Figure 5.7** Mannich product 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-({2-[(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-hexyl-amino]-ethyl}-amide) which could not be isolated.



### 5.2.1.2 Synthesis of Metal Complexes

Neutral “copper-only” complexes were synthesised from ligands **2** and **3** using similar conditions to those reported in chapter 2 (Figure 5.8).



**Figure 5.8** The synthesis of “Cu-only” complexes **5** and **6**. For **5**,  $\text{R} = \text{C}_9\text{H}_{19}$ ,  $\text{R}' = \text{Me}$ ,  $\text{R}'' = -(\text{CH}_2)_2-$ ; **6**,  $\text{R} = \text{Bu}^t$ ,  $\text{R}' = -\text{CH}_2\text{Ph}$ ,  $\text{R}'' = -\text{CH}_2\text{NHCO}(\text{CH}_2)_3\text{CONHCH}_2-$ .

The “copper-only” complex **6** was found to have sufficient solubility in  $\text{CHCl}_3$  to make it suitable for use in solvent extraction experiments. Despite **5** having  $\text{C}_9$ -alkyl substituents sufficient solubility was only achieved when  $\text{CHCl}_3$  with 5% added butan-1-ol was used as the solvent.

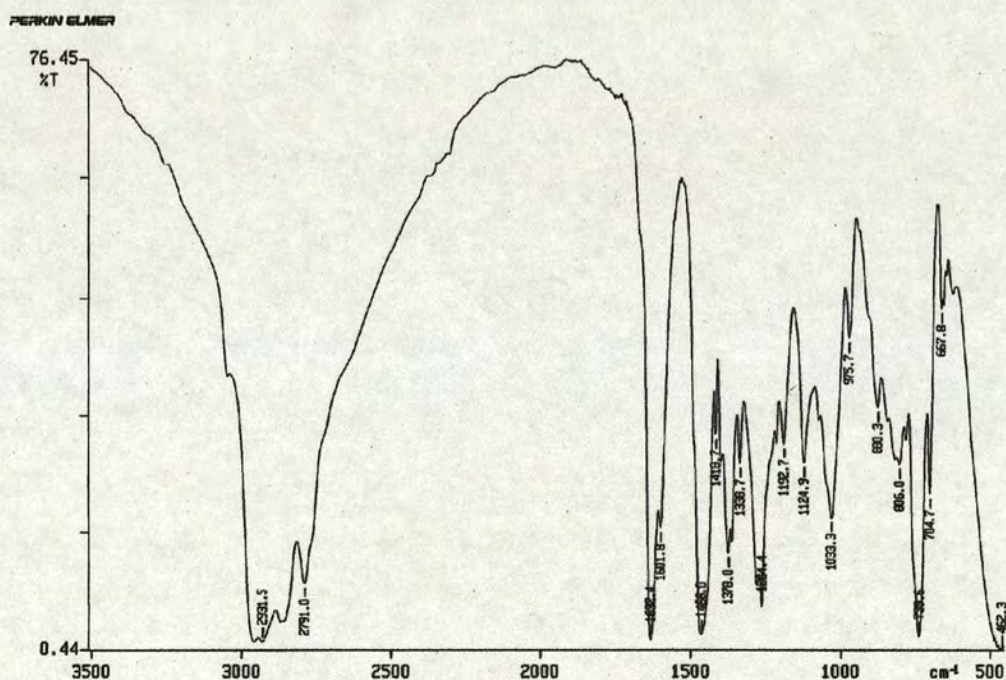
The copper sulfate complex **4** was prepared by Dr. Paul Plieger by adding a methanolic solution of copper sulfate to **1** in methanol and on recrystallisation gave crystals suitable for X-Ray diffraction.<sup>12</sup>

## 5.3 Characterisation

### 5.3.1 IR Spectroscopy

All of the macrocyclic ligands and their corresponding copper complexes have been characterised by FTIR spectroscopy. The imine peak is present in the spectra of all of the ligands ( $1635 - 1632 \text{ cm}^{-1}$ ) and copper complexes ( $1633 - 1625 \text{ cm}^{-1}$ ). The

presence of this signal and the absence of a carbonyl stretch ( $\sim 1680\text{ cm}^{-1}$ ), from the aldehyde precursor, in the spectra of ligand **1** and **2** (Figure 5.9) confirms that the Schiff base condensation reactions have gone to completion. In the case of ligand **3** it is difficult to assign the absence or presence of the carbonyl stretch, from the aldehyde precursor, because the carbonyl stretch from the amide groups in the ligand have a peak in the same region. Nevertheless the presence of the imine band indicates a successful reaction. It is notable that the energy of the imine peak lowers upon metal complexation, for all of the ligands, and this suggests that the imine nitrogen is directly involved in copper coordination as has been seen in similar complexes.<sup>13</sup>

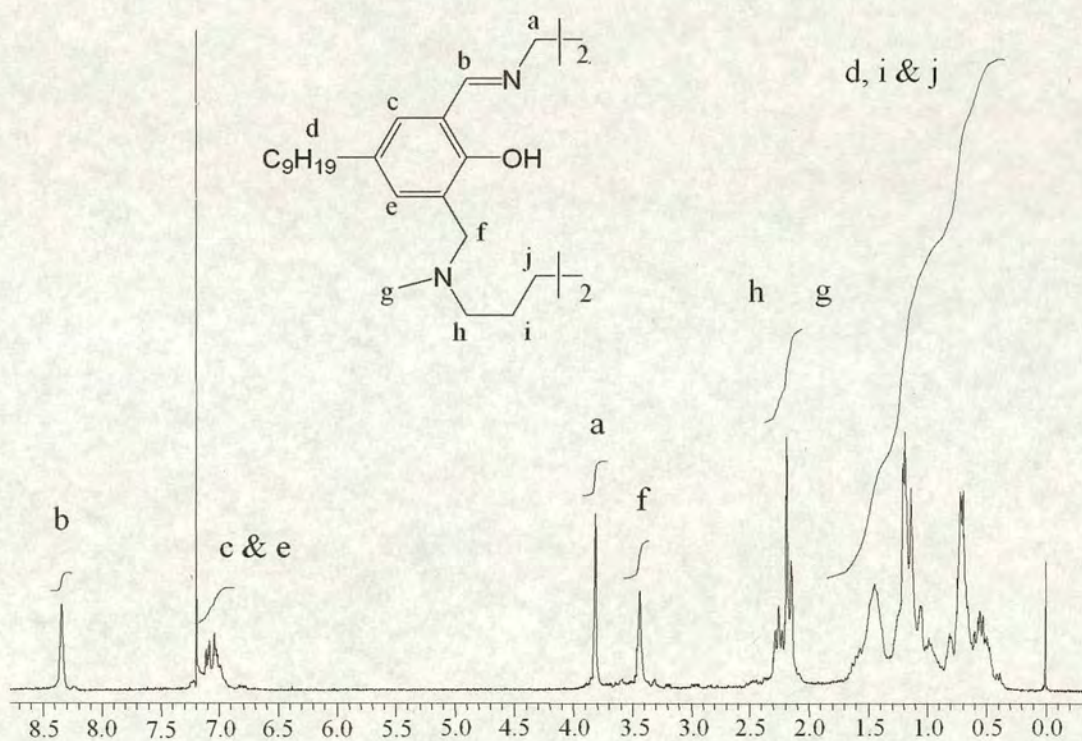


**Figure 5.9** The IR spectrum of ligand **2** containing a strong band for the imine bond at  $1632\text{ cm}^{-1}$ .

In the IR spectra of ligand **3** and the “copper-only” complex **6** there are peaks at  $\sim 3400$  and  $3300\text{ cm}^{-1}$  and these are likely to be due to N-H stretches from the amide groups.

## 5.3.2 NMR Spectroscopy

The free ligands **1** – **3** were all characterised by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy in  $\text{CDCl}_3$  (eg. Figure 5.10). The successful completion of the Schiff base condensation reactions was confirmed by the presence of an imine signal ( $\sim 8.4$  ppm,  $^1\text{H}$  NMR ( $\text{CH}=\text{N}$ ) and  $\sim 167$  ppm,  $^{13}\text{C}$  NMR ( $\text{CH}=\text{N}$ )) and the absence of an aldehyde resonance ( $\sim 10.3$  ppm,  $^1\text{H}$  NMR ( $\text{CH}=\text{O}$ ) and  $\sim 192$  ppm,  $^{13}\text{C}$  NMR ( $\text{CH}=\text{O}$ )) in each case. Further evidence was provided by the presence of a  $-\text{CH}_2-$  signal, from the 1,2-ethane-bridging unit, in all of the  $^1\text{H}$  NMR (3.6 – 3.9 ppm) and  $^{13}\text{C}$  NMR ( $\sim 60$  ppm) spectra.

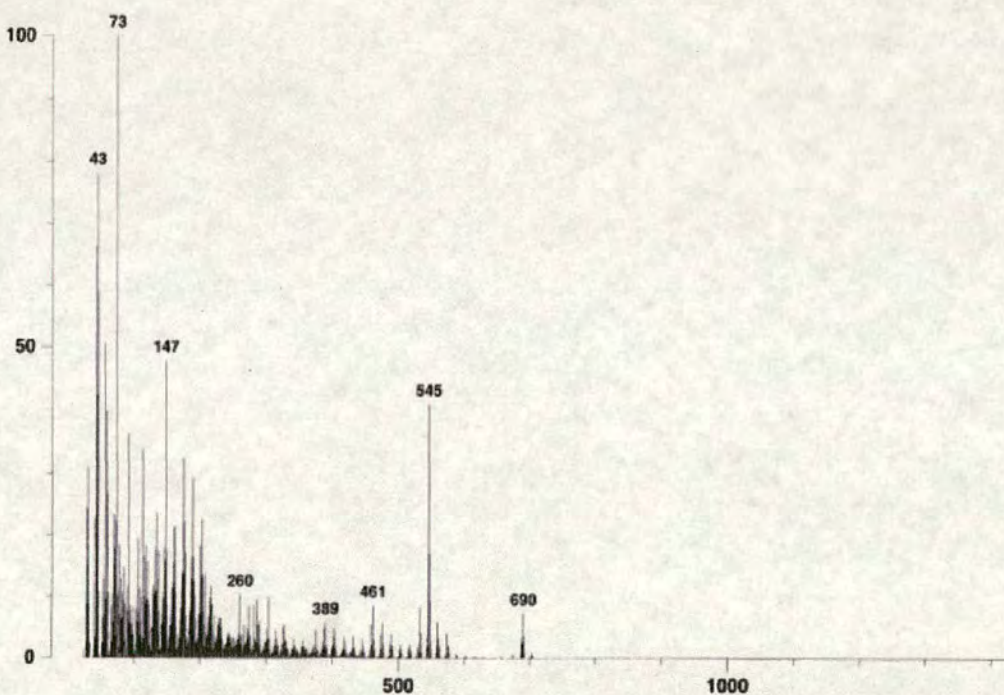


**Figure 5.10** The  $^1\text{H}$  NMR spectrum of ligand **2** ( $\text{CDCl}_3$ ).

The spectra of the free ligand **3** show peaks for the amide groups as in the  $^1\text{H}$  NMR spectrum there is a resonance for the NH protons at 6.25 ppm and in the  $^{13}\text{C}$  NMR spectrum there is a signal for the carbon atoms on the amide linkages ( $\text{NHCO}$ ) at 172.9 ppm.

### 5.3.3 Mass Spectrometry

All of the ligands **1** – **3** were characterised by FAB mass spectrometry (eg. Figure 5.11) and all of the precursors show the expected peaks. The synthesis of 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-({2-[(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-hexyl-amino]-ethyl}-amide) (Figure 5.7) was attempted and electrospray mass spectrometry indicated the presence of the product in the crude mixture but no evidence was seen in the FAB mass spectrum. The dialdehyde could not be isolated due to the large number of impurities so it is likely that the product was obtained in a very small yield. It should also be noted that the Mannich base prepared in the synthesis of ligand **3** only shows a peak for the iminium ion, as seen in previous chapters.



**Figure 5.11** The FAB mass spectrum of **2** ( $\text{CDCl}_3$ ) with a peak at  $m/z = 690$  for the ligand.

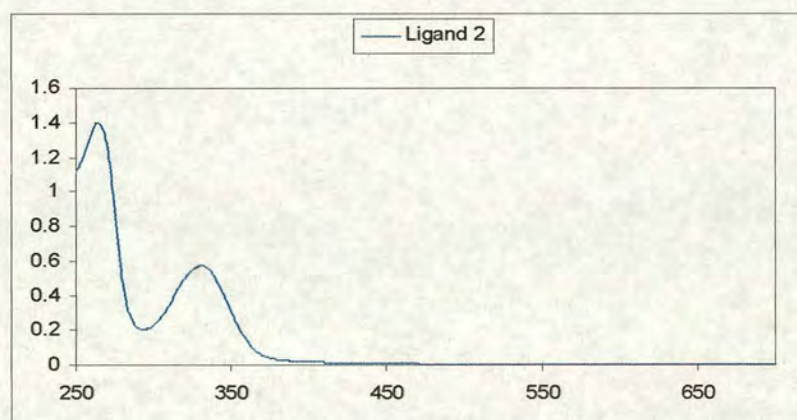
The FAB mass spectrum of ligands **1** and **3** indicated that some of the related 44-membered and 58-membered macrocycles, resulting from 2 + 2 condensations of the corresponding dialdehyde and ethylenediamine, had been formed. There were only

very weak peaks with  $m/z$  greater than the molecular ion in the mass spectra of ligand **2** but it is probable, as in **1** and **3**, that a small quantity of large ring 2 + 2 condensation product was present.

The FAB mass spectra of **4** – **6** all showed peaks that indicated a ligand to copper ratio of 1:1. No peaks were observed for complexes containing more than one metal ion. It should be noted however that, in the spectrum of **6**, although no peak was seen for the free ligand **3** there was evidence for the 58-membered 2 + 2 ligand. This suggests the complexation may have gone to completion in the 1 + 1 ligand but not in the 2 + 2 condensation product. This would help explain why the copper content of complex **6** was found to be a little lower than expected (found 71.0 ppm, expected 78.9).

### 5.3.4 UV-Visible Spectroscopy

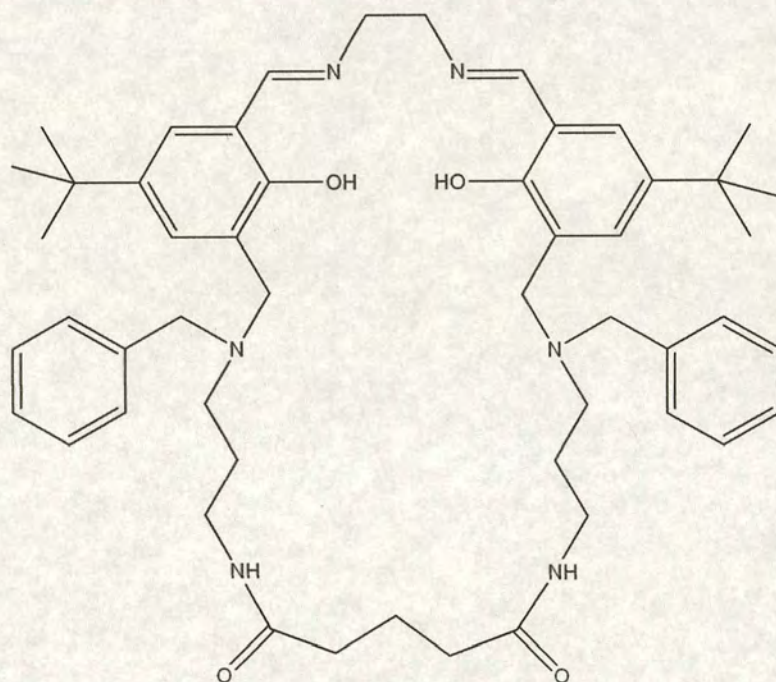
The electronic absorption spectra of the copper complexes **4** – **6** show very similar spectra to those of the 1,2-ethane-bridged complexes synthesised in chapters 2, 3 and 4. This implies that, like the acyclic complexes, the copper is bound in a square planar geometry. The main points of note in the spectra are a peak at ~ 380 nm which has charge transfer character and a weak feature at around 570 nm which is assigned to d-d transitions.<sup>14, 15</sup> The electronic absorption spectra of free ligand **2** (Figure 5.12) contains two bands at 264 nm and 331 nm due to  $\pi \rightarrow \pi^*$  ligand based transitions.



**Figure 5.12** The electronic absorption spectrum of **2**, bands at 264 and 331 nm (0.05 mM,  $\text{CHCl}_3$ ).

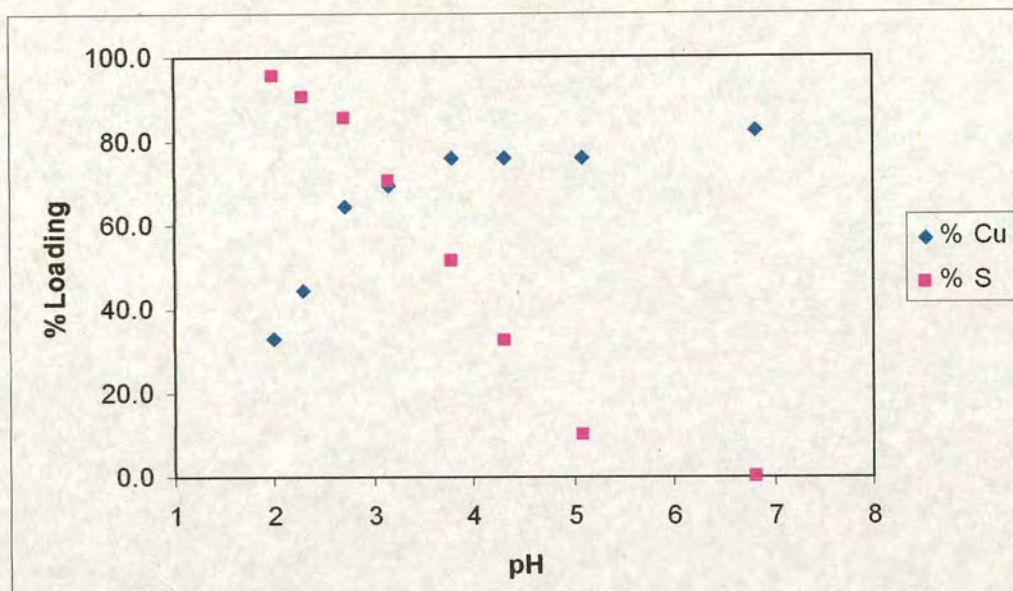
### 5.4 The pH Dependence of Anion-loading by Ligand 3

The amide-functionalised ligands developed in chapter 4 were found to have a low “strength” of sulfate-extraction when compared to the dihexyl-substituted extractants developed in chapters 2 and 3. This result was attributed to intramolecular hydrogen-bonding between the pendant amide arms. Amide groups were incorporated into a macrocyclic ligand framework in **3** in an attempt to reduce this effect (Figure 5.13). It was hoped that the pre-organised binding environment would also contribute to increasing the “strength” of sulfate-extraction.



**Figure 5.13** The diamide-functionalised macrocyclic ditopic ligand **3**.

The pH-dependence of sulfate-loading and the “strength” of copper-binding in ligand **3** were analysed by studying the uptake of  $\text{H}_2\text{SO}_4$  by the “copper-only” complex **6**, in  $\text{CHCl}_3$ , over a range of pH (Figure 5.14).



**Figure 5.14** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper binding for **6** in a  $\text{CHCl}_3/\text{H}_2\text{O}$  system.

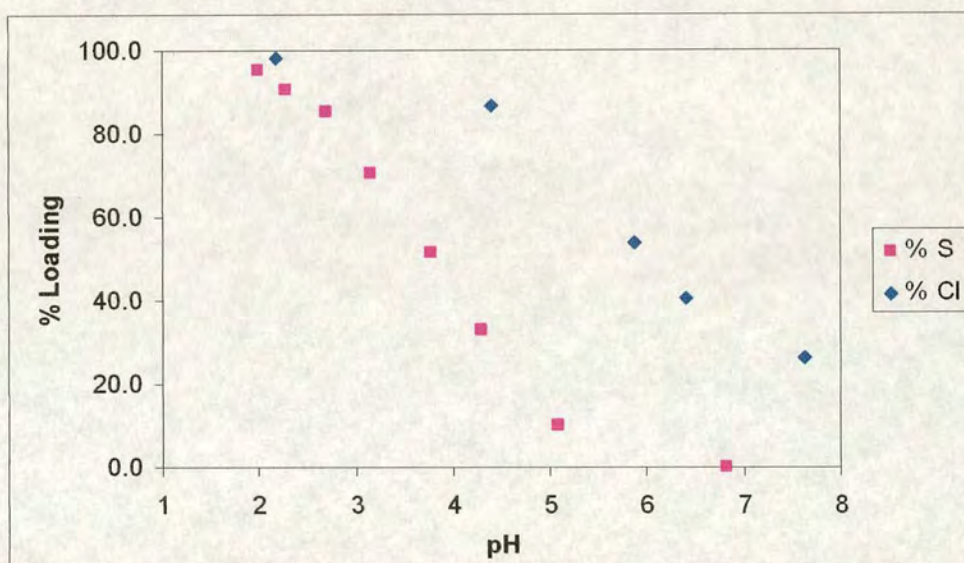
The pH-dependence studies revealed that ligand **3** does not operate as an efficient extractant for  $\text{CuSO}_4$ . Both the copper and sulfate binding are “weak” so there is no pH region where both copper and sulfate loadings are maximised.

The sulfate-loading drops below 100% at  $\text{pH} > 2$  and this is likely to be a result of the low copper concentration in the ligand. As the copper content increases the sulfate-loading continues to decrease until no sulfate is bound at approximately pH 5.5. The  $\text{pH}_{1/2}$  for sulfate binding is found to be 3.8 and this is comparable to values for the previous acyclic amide ligands. However in the macrocycle it is notable that sulfate is bound at  $\text{pH} < 5.5$  and in the acyclic amide ligands it is only bound until pH 4.5. Therefore there has been a small improvement in the “strength” of sulfate-binding, relative to the amide ligands developed in chapter 4.

The “strength” of copper-binding by ligand **3** is very low and is markedly different from the other 1,2-ethane-bridged ligands (chapter 2, 3 and 4). This could be a result of the long amide-functionalised strap, between the amine groups, imposing a distortion from the square planar binding environment which is preferred by  $\text{Cu}(\text{II})$ .

However it could also be a feature of the reagent containing a significant quantity of the larger, 58-membered ring, 2 + 2 condensation product as it is quite probable that this will not as readily form the desired copper complexes. This could be an explanation for the low copper content found in the “copper-only” complex **6** (found 71.0 ppm, expected 78.9 ppm).

The hydrochloric acid uptake by “copper-only” complex **6** was also studied and compared with the sulfate-loading to evaluate the sulfate / chloride selectivity (Figure 5.15).



**Figure 5.15** The pH dependence of H<sub>2</sub>SO<sub>4</sub> and HCl uptake by “Cu-only” complex **6** in a CHCl<sub>3</sub>/H<sub>2</sub>O system.

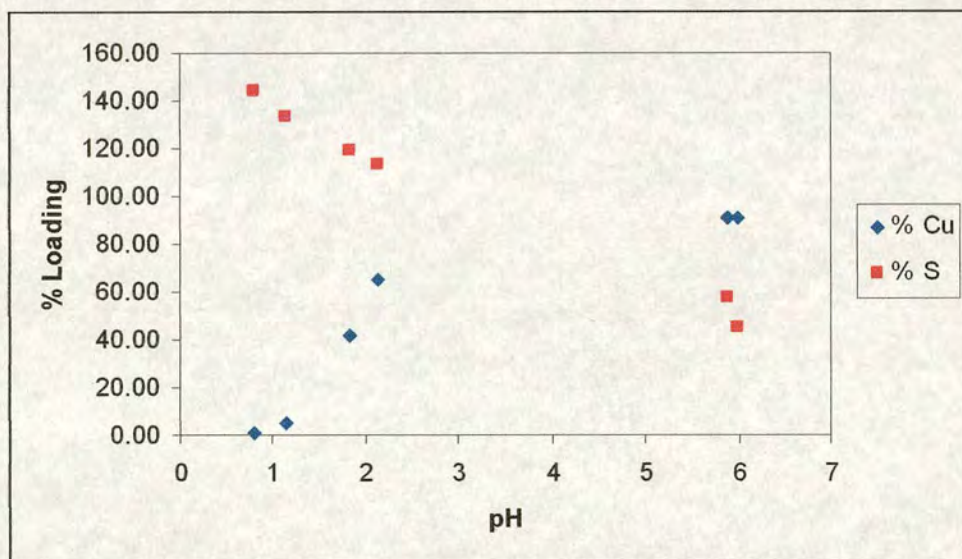
The  $\text{pH}_{1/2}$  for chloride-binding (6.0) was found to be higher than that of sulfate-binding (3.8) indicating that the macrocycle was selective for chloride over sulfate. The value for  $\Delta\text{pH}_{1/2}$ , 2.2, indicates that the selectivity is similar to that of the acyclic amide ligands ( $\Delta\text{pH}_{1/2} = 1.6 - 2.3$ ).

The diamide-functionalised macrocycle **3** is thus a poor CuSO<sub>4</sub> extractant in terms of both “strength” and selectivity over chloride.



## 5.5 The pH Dependence of Anion-loading by Ligand 2

The copper sulfate complex of ligand **1** was found to have insufficient solubility in chloroform for solvent extraction experiments. Consequently ligand **2** with C<sub>9</sub>H<sub>19</sub> mixed isomer chains was prepared. When the “copper-only” complex of this ligand was contacted with H<sub>2</sub>SO<sub>4</sub> solutions in the pH range 2.5 – 5.5 a small amount of solid formed which was assumed to be the copper sulfate complex [Cu(2)SO<sub>4</sub>]. Consequently copper and sulfate loadings could only be recorded at low and high pH (Figure 5.16). These limited data were useful however as they allowed the pH<sub>1/2</sub> values for sulfate and copper binding to be roughly estimated. The pH at which 50% loading of sulfate is observed is ca. 5.9 and this is the highest value recorded for any of the ditopic ligands described in this thesis. It therefore appears that the pre-organised macrocycle **2** is effective in creating a favourable binding environment for the sulfate anion. Nevertheless it should be noted that the small number of data points mean that there are large errors associated with this value.

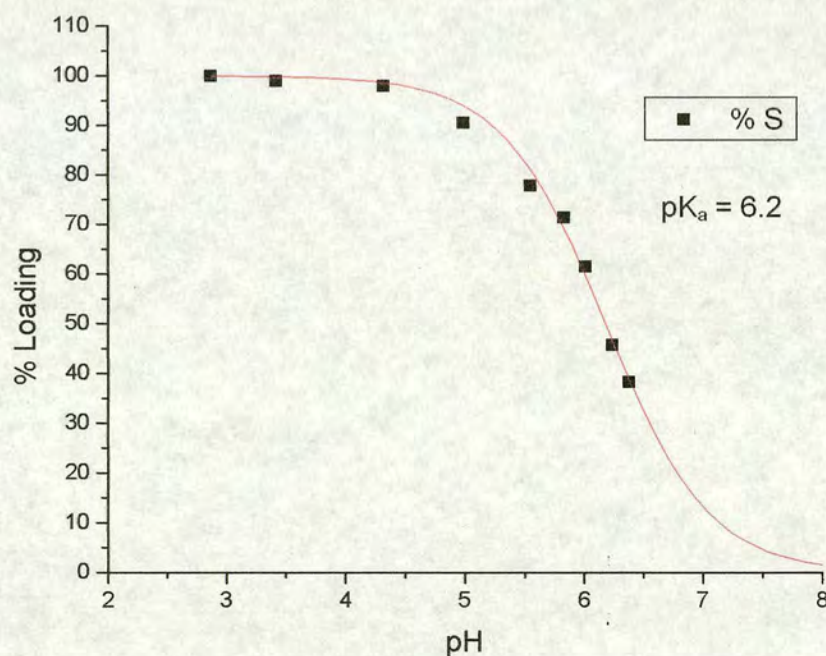


**Figure 5.16** The pH dependence of H<sub>2</sub>SO<sub>4</sub> uptake and “strength” of copper-binding by **5**. Data were not recorded in the pH range 2.5 – 5.5 because a third (solid) phase was present.

The pH<sub>1/2</sub> for copper-binding was found to be approximately 1.9 and this is closer to the values of other 1,2-ethane-bridged ligands (chapters 2, 3 and 4) than ligand **3**

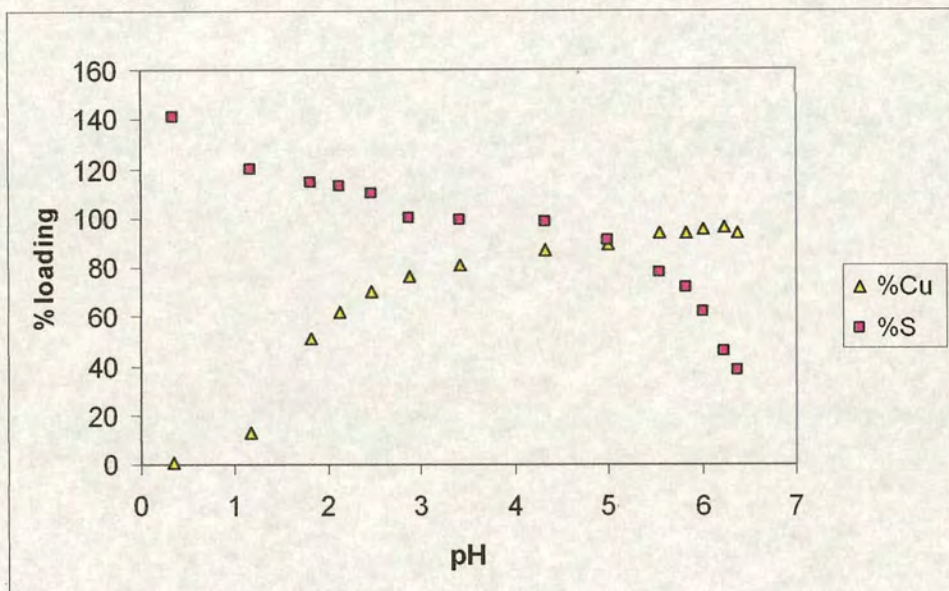
which had a very “weak” copper-binding. However the value is lower than in the 1,2-ethane-bridged dihexyl extractant (chapter 2, ligand 1,  $\text{pH}_{1/2}(\text{Cu}) = 1.4$ ) indicating that the hexamethylene strap imposes some distortion from the preferred arrangement of the  $\text{N}_2\text{O}_2^-$  donor set.

The main problem with analysing this system in neat  $\text{CHCl}_3$  is that the  $\text{pH}_{1/2}$  value for sulfate-loading cannot be accurately calculated due to solubility problems at intermediate pH and the subsequent lack of data points. In order to obtain a more accurate value for the  $\text{pH}_{1/2}$  solvent extraction experiments were attempted in chloroform containing 5% butan-1-ol as a phase modifier. Under these conditions there were no solubility problems and the  $\text{pH}_{1/2}$  was measured for the “copper-only” complex of ligand 2 by using the same method employed in section 2.4.3. The procedure yielded a value for the apparent  $\text{pK}_a$  of 5 in  $\text{CHCl}_3$  when in contact with sulfuric acid in a two phase solvent extraction system of 6.2 (Figure 5.17). This value can be directly related to the  $\text{pH}_{1/2}$  of sulfate-loading.



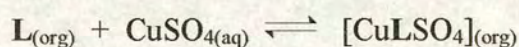
**Figure 5.17** The apparent  $\text{pK}_a$  ( $\equiv \text{pH}_{1/2}$ ) of the “copper-only” complex of ligand 2 in  $\text{CHCl}_3$  when in contact with sulfuric acid in a two-phase solvent extraction system ( $\text{pK}_a = 6.2 \pm 0.1$ ).

A full loading profile for copper and sulfate was also able to be recorded in this solvent system (Figure 5.18). Similar  $\text{pH}_{1/2}$  values were calculated to those estimated in  $\text{CHCl}_3 / \text{H}_2\text{O}$ . The graph obtained fitted an idealised profile for a  $\text{CuSO}_4$  extractant as the plateau pH region 3.5 – 5.5 is consistent with more than 80% of the ligand having the form  $[\text{Cu}(2)\text{SO}_4]$  in the organic phase.

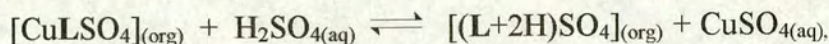


**Figure 5.18** The pH dependence of  $\text{H}_2\text{SO}_4$  uptake and “strength” of copper-binding by **5** in  $\text{CHCl}_3$  (+ 5% BuOH)/ $\text{H}_2\text{O}$ .

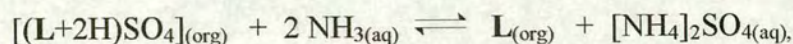
The advantage of this extractant is that the plateau region occurs in a higher pH region than for previous ligands (section 2.4.5, ligand **1**, plateau pH 2 – 4) so this macrocyclic ligand could efficiently recover copper from sulfate feeds of a higher pH (3.5 – 5.5). For example at  $\text{pH} \sim 4.5$ , > 85% loading of  $\text{CuSO}_4$  is possible without pH adjustment,



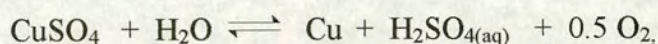
and an efficient materials balance for a circuit will result if the copper is stripped with sulfuric acid at  $\text{pH} < 1.0$ ,



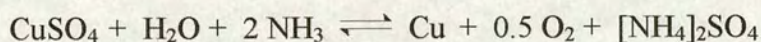
followed by reagent regeneration with base to  $\text{pH} \approx 7.0$ ,



and electrolytic recovery of the metal,

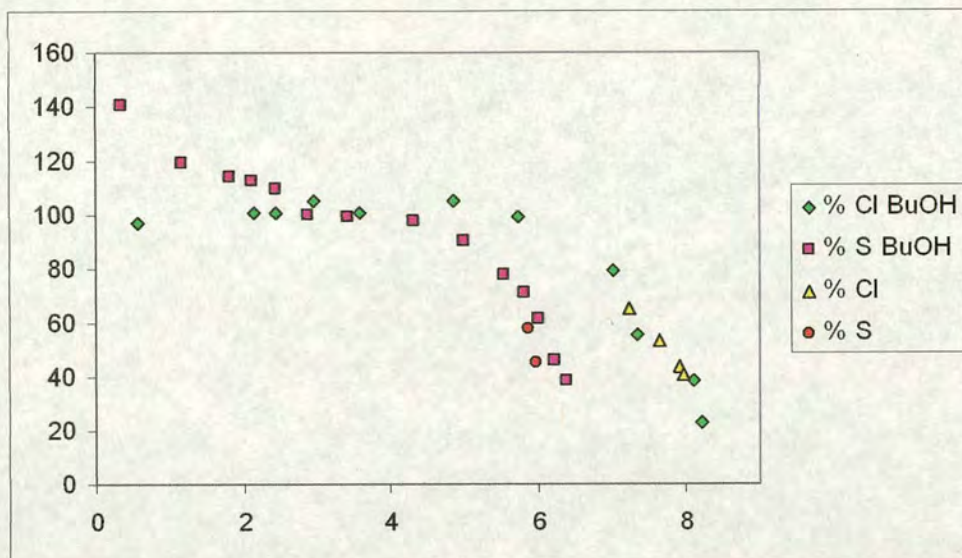


which will regenerate the acid for stripping and gives overall:



The slow rise of copper-loading with increase of pH and the failure to load fully until the pH is  $> 5.5$  may be a feature of the reagent containing a significant quantity of the larger ring 2 + 2 condensation product. It is quite probable that this will not so readily form the desired  $\text{CuSO}_4$  complex, and 100% metal-loading can only be achieved in the “metal only” form by deprotonation of the ligand at  $\text{pH} > 5.5$ .

In order to assess the anion selectivity of ligand **2** the uptake of hydrochloric acid by the “copper-only” complex **5** was studied over a range of pH. The solvent extraction experiments were done in  $\text{CHCl}_3$  and in  $\text{CHCl}_3$  containing 5% butan-1-ol and these results, together with the sulfate-loadings by **5**, are displayed in Figure 5.19.

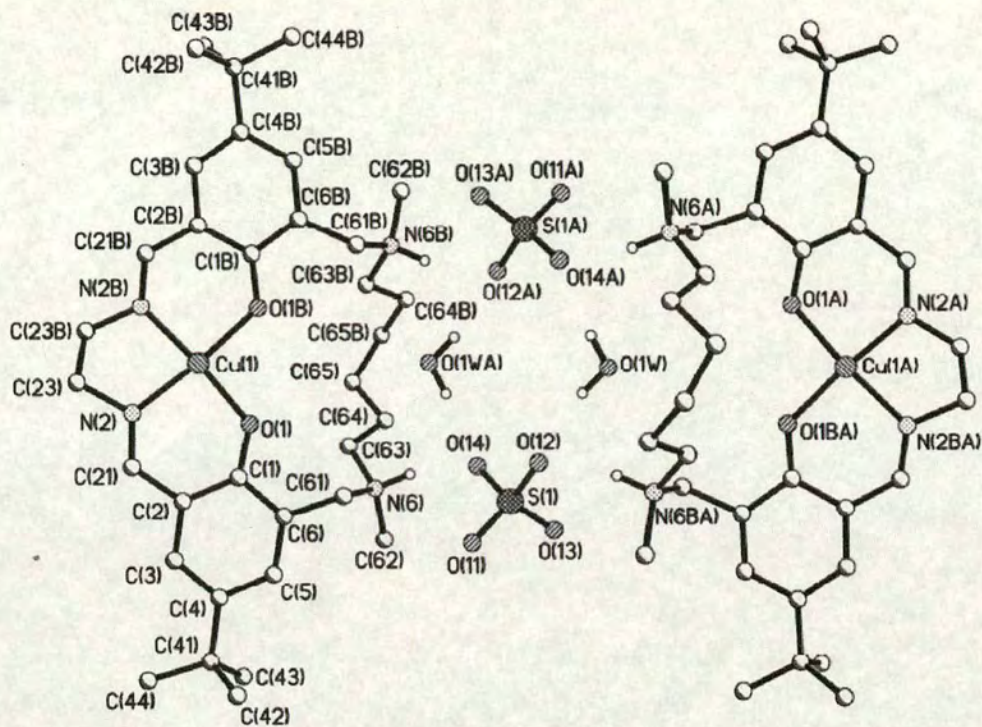


**Figure 5.19** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{HCl}$  uptake by **5** in  $\text{CHCl}_3/\text{H}_2\text{O}$  (triangles and circles) and also in  $\text{CHCl}_3 + 5\% \text{BuOH}/\text{H}_2\text{O}$  (diamonds and squares).

It can be seen that the  $\text{pH}_{1/2}$  of chloride-loading is approximately 7.8 in both solvent systems. The  $\text{pH}_{1/2}$  is slightly higher (6.2) for sulfate-loading in  $\text{CHCl}_3$  containing 5% butan-1-ol than in  $\text{CHCl}_3$  alone (5.9) but the ligand is still found to be selective for chloride over sulfate in both cases. The value for  $\Delta\text{pH}_{1/2}$  of 1.9 (1.6 when 5% BuOH is added to  $\text{CHCl}_3$ ) is comparable to the values obtained for the amide ligands so although the “strength” of sulfate-binding seems to have been improved by using the macrocyclic system there has been no advancement in sulfate selectivity.

## 5.6 X-Ray Crystallography

The X-Ray crystal structure of the copper sulfate complex **6** was obtained by Dr. Paul Plieger and found to exist as a dimer  $[\text{Cu}(\text{I})(\text{SO}_4)(\text{H}_2\text{O})]_2$  in the solid state (Figure 5.20).<sup>12</sup> The Cu-O distances and O-Cu-O angle (Table 5.2) were found to be greater than in related acyclic ligands<sup>16,17</sup> indicating that the copper is bound in a slightly different square planar arrangement. These differences may arise in part from the incorporation of the hexamethylene strap between the ammonium groups.



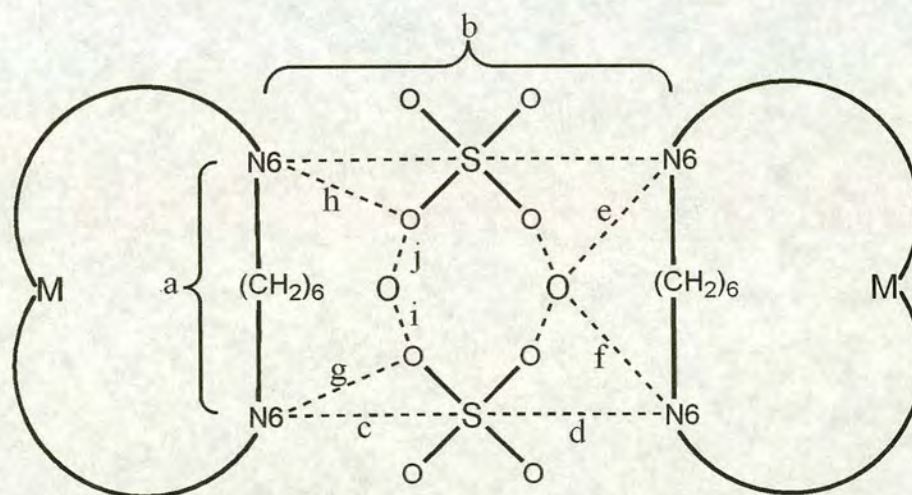
**Figure 5.20** The structure of the centrosymmetric  $[\text{Cu}(1)(\text{SO}_4)(\text{H}_2\text{O})_2]_2$  unit. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.<sup>12</sup>

**Table 5.2** Selected bond lengths (Å) and angles (°) for  $[\text{Cu}(1)(\text{SO}_4)]_2 \cdot \text{H}_2\text{O}$ .<sup>12</sup>

Cu(1)–O(1B)	1.926(4)	Cu(1)–N(2)	1.947(4)
Cu(1)–O(1)	1.912(4)	Cu(1)–N(2B)	1.950(4)
O(1)–Cu(1)–O(1B)	92.94(15)	O(1)–Cu(1)–N(2B)	174.71(17)
O(1)–Cu(1)–N(2)	91.66(17)	O(1B)–Cu(1)–N(2B)	92.04(17)
O(1B)–Cu(1)–N(2)	173.75(17)	N(2)–Cu(1)–N(2B)	83.50(18)
N(6B)–S(1)–N(6)	171.28(11)		

Symm. equiv. Cu structure: \$1 = x, y - 1, z\$; \$2 = 1 - x, -y, -z\$; \$3 = 1 - x, 1 - y, -z\$; \$4 = 1 - x, 2 - y, -z\$.

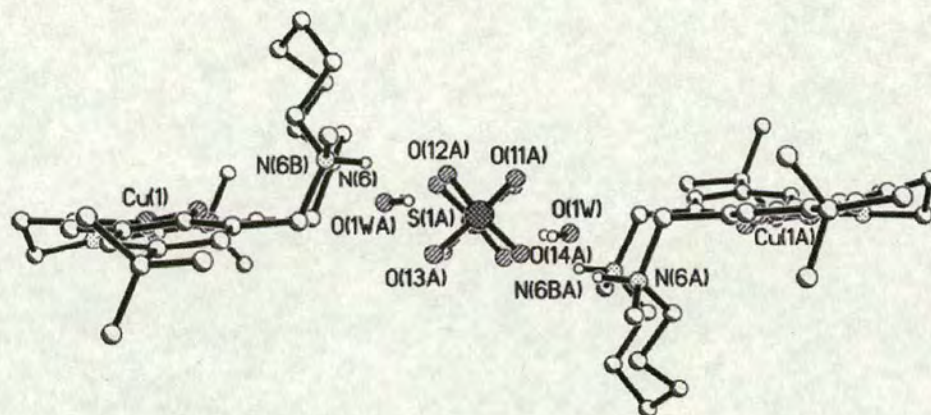
The centres of the dimeric units are composed of two sulfate anions bridged by hydrogen-bonded water molecules (Figure 5.21, distances *i* and *j*). This tetranionic unit interacts strongly with the protonated alkylammonium N(6) groups *via* a combination of electrostatic bonding (Figure 5.21, distances *c* and *d*) and hydrogen-bonding (Figure 5.21, distances *g* and *h*) between the ammonium nitrogen atoms and the sulfate anions. There is also weak hydrogen-bonding from the water molecules to the ammonium nitrogen atoms (Figure 5.21, distances *e* and *f*). On the basis of the distances shown in Figure 5.21 the sulfate anions appear to be equally strongly bonded to their neighbouring alkylammonium groups and water molecules. These interactions lead to an approximately linear *intermolecular* N(6)..S(1)..N(6) arrangement optimising the electrostatic component to bonding. This provides an explanation for the increased “strength” of sulfate-binding shown by the macrocyclic ligand, in comparison to related acyclic ligands, because in the dimeric CuSO<sub>4</sub> structures detailed in chapter 2 (section 2.6) the N..S..N bond angles were between 115° and 145° which would result in less efficient electrostatic binding. However as these interaction are in the solid state they can only be tentatively compared to the solution behaviour.



a	b	c	d	e	f	g	h	i	j
5.909(7)	7.364(6)	3.764(5)	3.622(4)	3.518(7)	3.221(7)	2.695(6)	2.751(6)	2.739(7)	2.786(7)

**Figure 5.21** Schematic diagram showing hydrogen-bonding interactions of the macrocyclic dimers with corresponding contact distances (Å).<sup>12</sup>

The hexamethylene strap sits above and below the macrocyclic plane (Figure 5.22) and if this conformation is retained in solution then it may help to screen the sulfate anion from its surrounding environment and therefore contribute to making sulfate-extraction more favourable.



**Figure 5.22** Side-on view of the  $[\text{Cu}(1)(\text{SO}_4)(\text{H}_2\text{O})_2]_2$  unit. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.<sup>12</sup>

## 5.7 Conclusions

This chapter describes the design, synthesis and analysis of ditopic zwitterionic macrocyclic metal *salt* extractants. It was anticipated that the pre-organisation in these ligands would induce a higher “strength” and selectivity in the extraction of  $\text{CuSO}_4$ .

It was hoped that the amide-functionalised macrocycle **3** would show a smaller tendency for intra-molecular hydrogen-bonding between the amides and therefore improve the “strength” of extraction relative to the acyclic amide ligands studied in chapter 4. However the  $\text{pH}_{1/2}$  for sulfate-binding was very similar to the values obtained for the acyclic ligands and the copper-binding “strength” was greatly reduced. The ligand also showed no improved selectivity for sulfate over chloride.

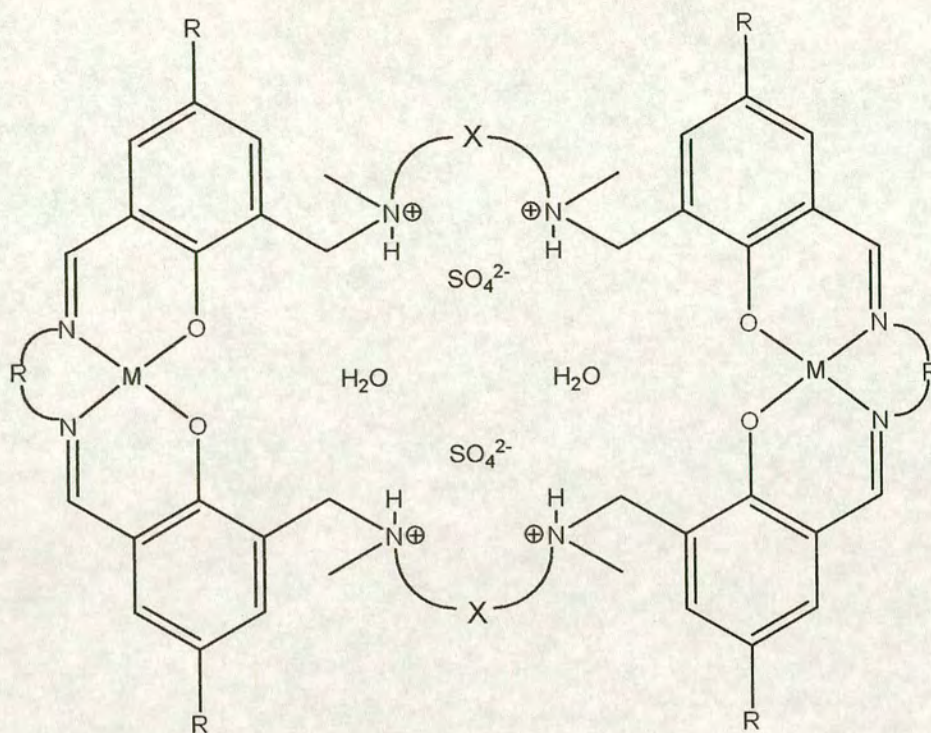


A possible reason for the weak copper-binding is that the long amide strap, between the nitrogen atoms, imposes a less favourable geometry on the  $N_2O_2^-$  donor set for binding Cu(II). It is also possible that a substantial fraction of the reagent is present as the 2 + 2 condensation product, detected in the FAB mass spectrum, which would form less stable copper complexes.

Ligand **1** and **2** were developed with hexamethylene straps between the pendant amine groups but only **2** was sufficiently soluble in chloroform (and then only with addition of 5% butan-1-ol) to obtain a complete loading profile. This profile is the most appropriate of all those determined in this thesis to treat high tenor sulfate feeds, after precipitation of iron(III), as these have a pH of approximately 4.5 which lies centrally in the range for which **2** shows > 90%  $CuSO_4$  loading.

The structure of the copper sulfate complex of ligand **1** contains the important feature of an approximately linear N...S...N arrangement of the protonated amines and the sulfate dianion. This will effectively maximise the electrostatic component to bonding. If this conformation is retained in solution then it may explain the high “strength” of sulfate-binding. Another interesting aspect of the structure is that the sulfate anions are hydrated in a tetranionic unit. This opens up the possibility of designing receptors to transport the hydrophilic sulfate anion as a water-bridged dimer (Figure 5.23).

Incorporation of additional hydrogen-bond donors into the sulfate-binding sites of preorganised structures such as that shown in Figure 5.23 may provide a tactic for the development of sulfate over chloride selectivity which is absent in all of the systems described in this thesis.



**Figure 5.23** Inclusion of hydrated sulfate dimers within a tetracationic macrocyclic cavity. X could be an alkyl chain or a strap containing additional hydrogen-bonding groups.

## 5.8 Experimental

### 5.8.1 Instrumentation

ES mass spectra were obtained on a Thermoquest LCQ spectrometer. Details of the other instrumentation used have been given in chapters 2 and 4.

### 5.8.2 Solvent and Reagent Pre-treatment

Unless stated to the contrary, commercial grade chemicals obtained from Aldrich or Acros were used without further purification.

### 5.8.3 Ligand Synthesis

2-Hydroxy-5-nonyl-benzaldehyde was synthesized by the method described by Levin and co-workers.<sup>10</sup> 3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-[(2-amino-ethyl)-amide] was prepared by a literature method and kindly supplied by Dr. P. Gale, University of Southampton.<sup>18</sup>

***N,N'*-Bis-ethoxymethyl-*N,N'*-dimethyl-hexane-1,6-diamine.**<sup>12</sup> *N,N'*-dimethyl-1,6-hexanediamine (30.0 g, 0.21 mol) was added dropwise to a stirred suspension of paraformaldehyde (12.5 g, 0.42 mol) and K<sub>2</sub>CO<sub>3</sub> (57.5 g, 0.42 mol) in ethanol (72 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred for 48 h. K<sub>2</sub>CO<sub>3</sub> was removed by filtration, the solvent was evaporated *in vacuo* and the resulting oil was purified by vacuum distillation to give *N,N'*-bis-ethoxymethyl-*N,N'*-dimethyl-hexane-1,6-diamine as a colourless oil (1.5 mmHg, 125°C) (39.3 g, 72%) (Found: C, 64.3; H, 12.3; N, 10.8. Calc. for C<sub>14</sub>H<sub>32</sub>N<sub>2</sub>O<sub>2</sub> C, 64.6; H, 12.4; N, 10.8%); δ<sub>H</sub> (CDCl<sub>3</sub>, 360 MHz): 3.89 (4 H, s, NCH<sub>2</sub>O), 3.28 (4 H, q, OCH<sub>2</sub>CH<sub>3</sub>), 2.36 (4 H, t, NCH<sub>2</sub>C<sub>2</sub>H<sub>4</sub>), 2.20 (6 H, s, NCH<sub>3</sub>), 1.29 (4 H, t, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.14 (4 H, s, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.00 (6 H, t, OCH<sub>2</sub>CH<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 87.6 (NCH<sub>2</sub>O), 63.3 (OCH<sub>2</sub>CH<sub>3</sub>), 53.4 (NCH<sub>2</sub>), 39.1 (NCH<sub>3</sub>), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.0 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 14.9 (OCH<sub>2</sub>CH<sub>3</sub>).

***N,N'*-Dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-*tert*-butylbenzylamine).**<sup>12</sup> A solution of 5-*tert*-butyl-2-hydroxybenzaldehyde (35 g, 0.2 mol) (prepared as outlined in section 2.8.3) and *N,N'*-bis-ethoxymethyl-*N,N'*-dimethyl-hexane-1,6-diamine (26 g, 0.1 mol) in acetonitrile (400 ml) was refluxed under dinitrogen for 72 h. After cooling to room temperature the solvent was removed *in vacuo* to give a pale yellow oil which was triturated with pentane to give *N,N'*-dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-*tert*-butylbenzylamine) as a pale yellow powder (41.7 g, 81 %). (Found: C, 73.3; H, 9.3; N, 5.4. Calc. for C<sub>32</sub>H<sub>48</sub>N<sub>2</sub>O<sub>4</sub> C, 73.2; H, 9.2; N, 5.3%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 11.95 (2 H, s, br) 10.35 (2 H, s, CHO), 7.61 (2 H, d, *J*(Ar-*H*) 2.6 Hz), 7.24 (2 H, d, *J*(Ar-*H*) 2.6 Hz), 3.70 (4 H, s, ArCH<sub>2</sub>N), 2.48 (4 H, t, *J*(NCH<sub>2</sub>) 7.2 Hz), 2.28 (6 H, s, NCH<sub>3</sub>), 1.57 (4

H, m,  $J(\text{NCH}_2\text{CH}_2\text{CH}_2)$  7.2 Hz), 1.34 (4 H, m,  $J(\text{NCH}_2\text{CH}_2\text{CH}_2)$  7.2 Hz), 1.26 (18 H, s,  $\text{C}(\text{CH}_3)_3$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 191.3 (CHO), 159.8 (COH), 141.5 (Ar C), 132.4 (Ar CH), 124.0 (Ar CH), 123.3 (Ar C), 122.2 (Ar C), 60.3 (ArCH<sub>2</sub>N), 57.0 (NCH<sub>2</sub>), 41.3 (NCH<sub>3</sub>), 34.0 (CCH<sub>3</sub>), 31.3 (CH<sub>3</sub>), 26.9 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 26.8 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\text{max}}/\text{cm}^{-1}$  2962s, 2862, 2846, 1678s, 1233s, 978, 889, 826;  $m/z$  525 ( $\text{M}^+$ ).

**10,25-Di-*tert*-butyl-14,21-dimethyl-3,6,14,21-tetraaza-tricyclo[21.3.1.18,12]**

**octacos-1(27),2,6,8,10,12(28),23,25-octaene-27,28,diol (1).**<sup>12</sup> Ethylenediamine (130  $\mu\text{l}$ , 1.94 mmol) in ethanol (20 ml) was added dropwise to *N,N'*-dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-*tert*-butylbenzylamine) (1.00 g, 1.94 mmol) in diethyl ether (200 ml). After stirring for 24 hr the solvent was removed *in vacuo* and the resulting orange residue was triturated with pentane (10 ml) to give **1** as a pale yellow powder (0.46 g, 44%). (Found: C, 73.8; H, 9.4; N 10.2. Calc. for  $\text{C}_{34}\text{H}_{52}\text{N}_4\text{O}_2 \cdot \frac{1}{4}\text{H}_2\text{O}$  C, 73.8; H 9.6; N 10.1%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 13.25 (2 H, s-br, Ar OH), 8.38 (2 H, s, N=CH), 7.36 (2 H, d,  $J(\text{Ph CH})$  2.5 Hz), 7.16 (2 H, d,  $J(\text{Ar-H})$  2.5 Hz), 3.89 (4 H, s, NCH<sub>2</sub>CH<sub>2</sub>N), 3.55 (4 H, s, ArCH<sub>2</sub>N), 2.49 (4 H, t, CH<sub>2</sub>CH<sub>2</sub>N), 2.22 (6 H, s, NCH<sub>3</sub>), 1.55 (4 H, m, CH<sub>2</sub>CH<sub>2</sub>N), 1.32 (4 H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N), 1.28 (18 H, s, C(CH<sub>3</sub>)<sub>3</sub>).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 166.3 (N=CH), 157.2 (Ar CH), 140.7 (Ar CH), 130.6 (Ar C), 126.3 (Ar C), 125.5 (Ar C), 118.0 (Ar C), 60.0 (NCH<sub>2</sub>CH<sub>2</sub>N), 57.7 (NCH<sub>2</sub>Ar), 55.9 (CH<sub>2</sub>N) 42.3 (NCH<sub>3</sub>), 33.9 (CCH<sub>3</sub>), 31.3 (CH<sub>3</sub>), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.2 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\text{max}}/\text{cm}^{-1}$  2952s, 2859s, 2788s, 1636s, 1466s, 1271, 1034, 823;  $m/z$  549 ( $\text{M}^+$ ), 1092 2( $\text{M}^+$ ).

***N,N'*-Dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-**

**nonylbenzylamine).** A solution of 5-nonyl-2-hydroxybenzaldehyde (3 g, 12.1 mmol) and *N,N'*-bis-ethoxymethyl-*N,N'*-dimethyl-hexane-1,6-diamine (1.57 g, 6 mmol) in acetonitrile (150 ml) was refluxed under dinitrogen for 72 h. The solution was cooled to room temperature, concentrated to 30 ml *in vacuo* and then heated to 60°C. An oil separated from a yellow solution on cooling which was collected, washed with acetonitrile (2 × 20 ml) and dried *in vacuo* to give *N,N'*-dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-nonylbenzylamine) as a *light brown oil* (2.3 g, 57 %) (Found: C, 74.4; H, 10.0; N, 4.4.  $\text{C}_{42}\text{H}_{68}\text{N}_2\text{O}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$  requires C, 74.8; H,

10.3; N, 4.2%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 10.36 (2 H, s, CHO), 7.56 (2 H, m, Ar-H), 7.20 (2 H, m, Ar-H), 3.70 (4 H, s, ArCH<sub>2</sub>N), 2.47 (4 H, t,  $J(\text{NCH}_2)$  7.2 Hz), 2.28 (6 H, s, NCH<sub>3</sub>), 1.56-1.38 (8 H, m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.25-0.86 (38 H, s, C<sub>9</sub>H<sub>19</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 191.4 (CHO), 159.4 (COH), 138.2 (Ar C), 133.0 (Ar CH), 124.7 (Ar CH), 123.2 (Ar C), 122.0 (Ar C), 60.1 (ArCH<sub>2</sub>N), 56.9 (NCH<sub>2</sub>), 41.2 (NCH<sub>3</sub>), 40-8 (C<sub>9</sub> mixed isomer chain);  $\nu_{\text{max}}/\text{cm}^{-1}$  2957s, 2859, 1681s, 1233s, 1014, 975, 747;  $m/z$  665 (M<sup>+</sup>).

**10,25-Di-nonyl-14,21-dimethyl-3,6,14,21-tetraaza-tricyclo[21.3.1.18,12]octacosan-1(27),2,6,8,10,12(28),23,25-octaene-27,28,diol (2).** Ethylenediamine (122  $\mu\text{l}$ , 1.83 mmol) in methanol (100 ml) was added dropwise to *N,N'*-dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-nonylbenzylamine) (1.22 g, 1.83 mmol) in chloroform (200 ml). After stirring for 24 hr the solvent was removed *in vacuo* to yield a yellow oil which was dissolved in chloroform (50 ml) and washed with water (2  $\times$  30 ml). The chloroform solution was dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **2** as a very viscous *yellow oil* (1.24 g, 98%). (Found: C, 77.3; H, 10.5; N, 8.4. C<sub>44</sub>H<sub>72</sub>N<sub>4</sub>O<sub>2</sub> requires C, 76.7; H, 10.5; N, 8.1%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 8.39 (2 H, s, N=CH), 7.15-7.07 (4 H, m, Ar-H), 3.88 (4 H, s, NCH<sub>2</sub>CH<sub>2</sub>N), 3.49 (4 H, s, ArCH<sub>2</sub>N), 2.31 (4 H, t,  $J(\text{NCH}_2\text{CH}_2)$  7.2 Hz), 2.23 (6 H, s, NCH<sub>3</sub>), 1.60-1.37 (8 H, m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.25-0.55 (38 H, s, C<sub>9</sub>H<sub>19</sub>).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 166.4 (N=CH), 157.3 (Ar C), 137.0 (Ar C), 131.7 (Ar CH), 127.8 (Ar CH), 125.0 (Ar C), 118.1 (Ar C), 60.0 (NCH<sub>2</sub>CH<sub>2</sub>N), 57.7 (NCH<sub>2</sub>Ar), 55.9 (CH<sub>2</sub>N) 45-8 (C<sub>9</sub> mixed isomer chain);  $\nu_{\text{max}}/\text{cm}^{-1}$  2931s, 2791s, 1632s, 1466s, 1264, 1033, 740;  $\lambda_{\text{max}}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 264 (27990), 331 (11372).  $m/z$  689 (M<sup>+</sup>).

**Pentanedioic acid bis-[(3-amino-propyl)-amide].** Dimethyl glutarate (10 g, 0.062 mol) and 1,3-propanediamine (27.8 g, 0.38 mol) were heated together at 100°C for 5 days. The mixture was then cooled and the excess 1,3-propanediamine was removed *in vacuo* (1.5 mmHg, 40°C). The sticky white solid residue was recrystallised from dichloromethane and dried *in vacuo* to yield pentanedioic acid bis-[(3-amino-propyl)-amide] as a *white solid* (5.1 g, 34%). (Found: C, 43.9; H, 8.0; N, 16.9. C<sub>11</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>.CH<sub>2</sub>Cl<sub>2</sub> requires C, 43.8; H, 8.0; N, 17.0%);  $\delta_{\text{H}}$  (MeOH, 250 MHz): 3.23

(4H, q,  $J(\text{CONHCH}_2)$  7.3 Hz), 2.63 (4H, t,  $J(\text{NH}_2\text{CH}_2)$  7.0 Hz), 2.21 (4H, t,  $J(\text{COCH}_2)$  7.2 Hz), 1.89 (2H, m,  $\text{COCH}_2\text{CH}_2$ ), 1.65 (4H, quintet,  $J(\text{CONHCH}_2\text{CH}_2)$  6.9 Hz).  $\delta_{\text{C}}$  (MeOH, 60 MHz): 175.7 (CO), 40.1 (CONHCH<sub>2</sub>), 37.9 (NH<sub>2</sub>CH<sub>2</sub>), 36.6 (COCH<sub>2</sub>), 33.9 (CONHCH<sub>2</sub>CH<sub>2</sub>), 23.6 (COCH<sub>2</sub>CH<sub>2</sub>).  $m/z$  245 (M<sup>+</sup>).

**Pentanedioic acid bis-[(3-benzylamino-propyl)-amide].** A solution of pentanedioic acid bis-[(3-amino-propyl)-amide] (2 g, 8.26 mmol) in ethanol (200 ml) was added dropwise to a stirred solution of benzaldehyde (1.75 g, 0.0165 mol) in ethanol (100 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (1.55 g, 0.041 mol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (200 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane (2 × 100 ml) was then added to extract the product. The combined organic extracts were dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield pentanedioic acid bis-[(3-benzylamino-propyl)-amide] as a viscous *white liquid* (3.3 g, 94%). (Found: C, 70.8; H, 8.2; N, 12.7. C<sub>25</sub>H<sub>36</sub>N<sub>4</sub>O<sub>2</sub> requires C, 70.7; H, 8.6; N, 13.2%);  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.36-7.25 (10H, m, Ar-*H*), 7.01 (2H, br, NHCO), 3.76 (4H, s, NHCH<sub>2</sub>Ar), 3.28 (4H, q,  $J(\text{CONHCH}_2)$  6.1 Hz), 2.70 (4H, t,  $J(\text{CH}_2\text{CH}_2\text{NHCH}_2)$  6.4 Hz), 2.40 (2H, br, ArCH<sub>2</sub>NH), 2.16 (4H, t,  $J(\text{COCH}_2)$  6.8 Hz), 1.90 (2H, m, COCH<sub>2</sub>CH<sub>2</sub>), 1.70 (4H, quintet,  $J(\text{CH}_2\text{NHCH}_2\text{CH}_2)$  6.4 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 173.4 (CO), 141.8 (Ar C), 129.1 (Ar CH), 128.8 (Ar CH), 127.6 (Ar CH), 54.5 (ArCH<sub>2</sub>NH), 48.0 (CONHCH<sub>2</sub>), 39.1 (CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>), 36.2 (COCH<sub>2</sub>), 29.6 (CONHCH<sub>2</sub>CH<sub>2</sub>), 22.8 (COCH<sub>2</sub>CH<sub>2</sub>).  $\nu_{\text{max}}/\text{cm}^{-1}$  3314s, 3085, 3031, 2935s, 1636s, 1542s, 1454, 689;  $m/z$  425 (M<sup>+</sup>).

**Pentanedioic acid bis-[[3-(benzyl-ethoxymethyl-amino)-propyl]-amide].** A solution of pentanedioic acid bis-[(3-benzylamino-propyl)-amide] (2.5 g, 5.9 mmol) in ethanol (20 ml) was added dropwise to a stirred suspension of paraformaldehyde (0.36 g, 0.012 mol) and potassium carbonate (3.3 g, 0.024 mol) in ethanol (100 ml) at 0°C. The mixture was allowed to warm to room temperature and continually stirred for 48 hr. The solution was filtered to remove the potassium carbonate and the

solvent was evaporated in vacuo to yield pentanedioic acid bis- $\{[3-(\text{benzyl-ethoxymethyl-amino})\text{-propyl}]\text{-amide}\}$  as a *colourless liquid* which was used without further purification (3 g, 94%).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 7.35-7.26 (10H, m, Ar-H), 4.11 (4H, s,  $\text{NCH}_2\text{O}$ ), 3.76 (4H, s,  $\text{NCH}_2\text{Ar}$ ), 3.41 (4H, q,  $J(\text{OCH}_2\text{CH}_3)$  7.0 Hz), 3.22 (4H, m,  $\text{CONHCH}_2$ ), 2.70 (4H, t,  $J(\text{CH}_2\text{CH}_2\text{N})$  6.5 Hz), 2.07 (4H, m,  $\text{COCH}_2$ ), 1.85 (2H, m,  $\text{COCH}_2\text{CH}_2$ ), 1.63 (4H, m,  $\text{CH}_2\text{NHCH}_2\text{CH}_2$ ), 1.17 (6H, t,  $J(\text{CH}_2\text{CH}_3)$  7.0 Hz).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 172.9 (CO), 140.1 (Ar C), 129.6 (Ar CH), 129.0 (Ar CH), 127.8 (Ar CH), 85.1 ( $\text{NCH}_2\text{O}$ ), 64.1 ( $\text{ArCH}_2\text{N}$ ), 57.1 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 49.2 ( $\text{CONHCH}_2$ ), 38.2 ( $\text{NCH}_2\text{CH}_2$ ), 36.0 ( $\text{COCH}_2$ ), 30.4 ( $\text{CONHCH}_2\text{CH}_2$ ), 22.5 ( $\text{COCH}_2\text{CH}_2$ ), 16.0 ( $\text{CH}_3\text{CH}_2$ ).  $m/z$  449 (M – EtO – EtOH).

**Pentanedioic acid bis- $\{[3\text{-[benzyl-(5-tert-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}]\text{-amide}\}$ .** A solution of pentanedioic acid bis- $\{[3-(\text{benzyl-ethoxymethyl-amino})\text{-propyl}]\text{-amide}\}$  (1.6 g, 3 mmol) and 5-*tert*-butyl-2-hydroxybenzaldehyde (1.07 g, 6 mmol) in acetonitrile (80 ml) was refluxed under a dinitrogen atmosphere for 72 h. The reaction was then cooled to room temperature and the solvent was evaporated *in vacuo* to yield a viscous brown oil. The product was then purified by silica column chromatography (dichloromethane: methanol, 30:1) to yield pentanedioic acid bis- $\{[3\text{-[benzyl-(5-tert-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}]\text{-amide}\}$  as a *crispy light yellow solid* (0.2 g, 8%). (Found: C, 73.0; H, 7.9; N, 6.6.  $\text{C}_{49}\text{H}_{64}\text{N}_4\text{O}_6$  requires C, 73.1; H, 8.0; N, 7.0%);  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 10.20 (2H, s, CHO), 7.51-7.28 (14H, m, Ar-H), 5.98 (2H, br, NHCO), 3.74 (4H, s,  $\text{NCH}_2\text{CCOH}$ ), 3.61 (4H, s,  $\text{NCH}_2\text{Ar}$ ), 3.24 (4H, q,  $J(\text{CONHCH}_2)$  6.1 Hz), 2.55 (4H, t,  $J(\text{CH}_2\text{CH}_2\text{N})$  6.7 Hz), 2.02 (4H, t,  $J(\text{COCH}_2)$  6.6 Hz), 1.85-1.70 (6H, m,  $\text{CH}_2\text{CH}_2\text{NHCOCH}_2\text{CH}_2$ ), 1.30 (18H, s,  $\text{C}(\text{CH}_3)_3$ ).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 60 MHz): 194.4 (CHO), 173.1 (NHCO), 159.3 (Ar COH), 142.9 (Ar C), 138.5 (Ar C), 134.8 (Ar CH), 130.0 (Ar CH), 129.3 (Ar CH), 128.2 (Ar CH), 127.0 (Ar CH), 125.6 (Ar C), 122.0 (Ar C), 59.1 ( $\text{NCH}_2\text{CCOH}$ ), 55.4 ( $\text{NCH}_2\text{Ar}$ ), 51.6 ( $\text{CONHCH}_2$ ), 38.2 ( $\text{CH}_2\text{NCH}_2\text{CH}_2$ ), 36.0 (NHCOCH<sub>2</sub>), 34.8 ( $\text{C}(\text{CH}_3)_3$ ), 32.2 ( $\text{CONHCH}_2\text{CH}_2$ ), 32.0 ( $\text{C}(\text{CH}_3)_3$ ), 27.0 ( $\text{COCH}_2\text{CH}_2$ ).  $\nu_{\text{max}}/\text{cm}^{-1}$  3301, 3062, 3028, 2960s, 1658, 1647s, 1478, 1265, 735;  $m/z$  805 ( $\text{M}^+$ ).

**(2E,6E)-14,28-Dibenzyl-10,32-di-tert-butyl-34,35-dihydroxy-3,6,14,18,24,28-hexaaza-tricyclo[28.3.1.18,12]pentatriaconta-1(33),2,6,8(35),9,11,30(34),31-**

**octaene-19,23-dione (3).** Ethylenediamine (0.037 g, 0.62 mmol) dissolved in ethanol (100 ml) was added dropwise to a stirred solution of pentanedioic acid bis-({3-[benzyl-(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-amino]-propyl}-amide) (0.5 g, 0.62 mmol) in chloroform (300 ml). The reaction was stirred overnight and the solvent was then removed *in vacuo* to give a yellow oil. The product was dissolved in chloroform (50 ml) and washed with water (2 × 25 ml). The organic layer was subsequently dried with MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield **3** as a crispy yellow solid (0.49 g, 95%). (Found: C, 71.0; H, 8.4; N, 9.3. C<sub>51</sub>H<sub>68</sub>N<sub>6</sub>O<sub>4</sub>·2H<sub>2</sub>O requires C, 70.8; H, 8.4; N, 9.7%); δ<sub>H</sub> (CDCl<sub>3</sub>, 250 MHz): 8.44 (2H, s, N=CH), 7.48-7.02 (14H, m, Ar-H), 6.25 (2H, br, NHCO), 3.95 (4H, s, NCH<sub>2</sub>CCOH), 3.65-3.60 (8H, m, CH=NCH<sub>2</sub>, NCH<sub>2</sub>Ar), 3.20 (4H, m, CONHCH<sub>2</sub>), 2.53 (4H, m, CH<sub>2</sub>CH<sub>2</sub>N), 1.99 (4H, m, COCH<sub>2</sub>), 1.80-1.65 (6H, m, CH<sub>2</sub>CH<sub>2</sub>NHCOCH<sub>2</sub>CH<sub>2</sub>), 1.29 (18H, s, C(CH<sub>3</sub>)<sub>3</sub>). δ<sub>C</sub> (CDCl<sub>3</sub>, 60 MHz): 172.9 (NHCO), 167.5 (C=N), 158.0 (Ar COH), 141.8 (Ar C), 139.5 (Ar C), 132.9 (Ar CH), 129.8 (Ar CH), 128.9 (Ar CH), 128.9 (Ar CH), 127.6 (Ar CH), 126.7 (Ar C), 118.5 (Ar C), 60.7 (NCH<sub>2</sub>CCOH), 59.6 (CH=NCH<sub>2</sub>), 54.7 (NCH<sub>2</sub>Ar), 53.3 (CONHCH<sub>2</sub>), 39.4 (CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>), 36.2 (NHCOCH<sub>2</sub>), 34.6 (C(CH<sub>3</sub>)<sub>3</sub>), 32.2 (CONHCH<sub>2</sub>CH<sub>2</sub>), 32.0 (C(CH<sub>3</sub>)<sub>3</sub>), 26.0 (COCH<sub>2</sub>CH<sub>2</sub>). ν<sub>max</sub>/cm<sup>-1</sup> 3416s, 3338s, 3086, 3062, 3030, 2961s, 1635s, 1472, 1273, 909; m/z 829 (M<sup>+</sup>), 1658 2(M<sup>+</sup>).

**3,4-Diphenyl-1H-pyrrole-2,5-dicarboxylic acid bis-[(2-hexylamino-ethyl)-amide].** A solution of 3,4-diphenyl-1H-pyrrole-2,5-dicarboxylic acid bis-[(2-amino-ethyl)-amide] (0.19 g, 0.49 mmol) in ethanol (20 ml) was added dropwise to a stirred solution of hexanal (0.098 g, 0.98 mmol) in ethanol (40 ml). The reaction was refluxed for an hour and cooled to room temperature. Sodium borohydride (0.093 g, 2.46 mmol) was added portionwise to maintain a gentle effervescence. The reaction was refluxed for a further hour and cooled to room temperature. A solution of 10% sodium hydroxide (70 ml) was added, with caution, under a dinitrogen atmosphere. The ethanol was removed *in vacuo* and dichloromethane (2 × 50 ml) was added to extract the product. The combined organic extracts were dried over MgSO<sub>4</sub>, filtered



and evaporated *in vacuo* to yield 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-[(2-hexylamino-ethyl)-amide] as a viscous *colourless liquid* (0.25 g, 91%).  $\delta_{\text{H}}$  (CDCl<sub>3</sub>, 250 MHz): 7.34-7.17 (10H, m, Ar-*H*), 5.97 (2H, t, *J*(NHCO) 5.3 Hz), 3.33 (4H, q, *J*(CONHCH<sub>2</sub>) 5.6 Hz), 2.55 (4H, t, *J*(CH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>) 5.9 Hz), 2.38 (4H, t, *J*(NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>) 6.8 Hz), 1.29 (16H, m, NHCH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>), 0.90 (6H, t, *J*(CH<sub>2</sub>CH<sub>3</sub>) 6.4 Hz).  $\delta_{\text{C}}$  (CDCl<sub>3</sub>, 60 MHz): 161.1 (CO), 134.0 (Ar C), 131.4 (Ar CH), 129.3 (Ar CH), 128.5 (Ar CH), 126.5 (Ar C), 124.6 (Ar C), 50.1 (CONHCH<sub>2</sub>), 48.9 (CONHCH<sub>2</sub>CH<sub>2</sub>), 39.8 (NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 32.5 (NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 30.7 (NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.6 (NH(CH<sub>2</sub>)<sub>3</sub>CH<sub>2</sub>), 23.3 (NH(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>), 14.7 (CH<sub>2</sub>CH<sub>3</sub>). *m/z* 560 (M<sup>+</sup>).

**3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-({2-[(5-*tert*-butyl-3-formyl-2-hydroxy-benzyl)-hexyl-amino]-ethyl}-amide).** A two step Mannich reaction was performed on 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-[(2-hexylamino-ethyl)-amide] using the same procedure as before.<sup>11</sup> However the product could not be purified. *m/z* 940 (M<sup>+</sup>).

#### 5.8.4 Synthesis of Copper Sulfate Complex 4

[Cu(1)SO<sub>4</sub>].H<sub>2</sub>O (4).<sup>12</sup> A solution of 1 (0.100 g, 0.182 mmol) in methanol (25 ml) was mixed with a solution of CuSO<sub>4</sub>.5H<sub>2</sub>O (0.045 g, 0.182 mmol) in methanol (20 ml) for 24 hours. After removal of most of the solvent *in vacuo* the precipitates were purified by recrystallisation from ethanol/diethyl ether. Crushing and drying gave [Cu(1)SO<sub>4</sub>].H<sub>2</sub>O (0.050g, 39%), (Found C, 57.7; H, 7.7; N 7.9. Calc. for C<sub>34</sub>H<sub>52</sub>N<sub>4</sub>O<sub>2</sub>CuSO<sub>4</sub> C, 57.6; H, 7.4; N, 7.9%);  $\nu_{\text{max}}/\text{cm}^{-1}$  3418, 2954s, 2866, 2664, 1633s, 1546, 1452s, 1121s, 1089, 1042, 619;  $\lambda_{\text{max}}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) (CHCl<sub>3</sub>) 380 (23842), 566 (400). *m/z* 709 (M<sup>+</sup>), 611 (M – SO<sub>4</sub>), 1414 2(M<sup>+</sup>). Crystals of the monohydrate for X-ray structure determination were grown by the diffusion of diethyl ether into an ethanolic solution and were found also to contain ether and alcohol of solvation. These crystals were prepared and their structure solved by Dr. Paul G. Plieger.<sup>12</sup>

### 5.8.5 Synthesis of “Copper-only” Complexes

[Cu(2-2H)] (**5**). A solution of **2** (0.1 g, 0.182 mmol) in chloroform (20 ml) was added to a solution of  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  (0.036 g, 0.182 mmol) in methanol (70 ml) and stirred overnight. The solvent was then removed *in vacuo* to yield a black oil which was dissolved in chloroform (100 ml) and washed with a pH 9 ammonia solution ( $2 \times 50$  ml). The organic extract was dried with  $\text{MgSO}_4$ , filtered and concentrated *in vacuo* to yield **5** as a *black oil* (0.109 g, 80%) which was used without further purification in solvent extraction experiments. (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: Found 77.5 ppm,  $\text{C}_{44}\text{H}_{70}\text{N}_4\text{O}_2\text{Cu}$  requires 78.9 ppm);  $\nu_{\text{max}}/\text{cm}^{-1}$  3234, 2958s, 2870, 1625s, 1540, 1446s, 755;  $\lambda_{\text{max}}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 281 (20332), 382 (8114), 568 (310).  $m/z$  750 ( $\text{M}^+$ ).

[Cu(3-2H)] (**6**). A solution of ligand **3** (0.1 g, 0.12 mmol) in chloroform (10 ml) was added to a solution of  $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$  (0.024 g, 0.12 mmol) in methanol (40 ml) and stirred overnight. The solvent was then removed *in vacuo* to yield a black oil which was dissolved in chloroform (50 ml) and washed with a pH 9 ammonia solution ( $2 \times 30$  ml). The organic extract was dried with  $\text{MgSO}_4$ , filtered and concentrated *in vacuo* to yield a black oil. The product was triturated with hexane to produce **6** as a *crispy black solid* (0.1 g, 94%). (Cu-content by ICP-OES for a 0.001M solution in butan-1-ol: found 71.0 ppm,  $\text{C}_{51}\text{H}_{66}\text{N}_6\text{O}_4\text{Cu}$  requires 78.9 ppm);  $\nu_{\text{max}}/\text{cm}^{-1}$  3405s, 3296s, 3062, 3027, 2961s, 1627s, 1541, 1443, 1262, 802;  $\lambda_{\text{max}}/\text{nm}$  ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 282 (18004), 380 (7296), 570 (310).  $m/z$  890 ( $\text{M}^+$ ), 1783 2( $\text{M}^+$ ), 1658 2( $\text{M}^+ - \text{Cu}$ ).

### 5.8.6 The pH Dependence of Anion-loading

#### 5.8.6.1 The pH Dependence of Sulfate-loading

The “copper-only” complexes **5** and **6** were taken through the following procedure and then analysed for copper and sulfur content.

### 5.8.6.1.1 Preparation of Acid and “Copper-only” Complex Solutions

Acid solutions were prepared as described in chapter 2 (appendix 7.2.1). 0.01 M chloroform stock solutions (250 ml) of “copper-only” complexes **5** and **6** and a 0.005 M “copper-only” complex of **5** in chloroform containing 5% butan-1-ol (250 ml) were also prepared.

### 5.8.6.1.2 Extraction Experiments on “Copper-only” Complexes

The extraction experiments were performed in the same way as chapter 2 (section 2.8.5). It should be noted that in these extractions a 1 ml aliquot of the CHCl<sub>3</sub> layer was removed, dried *in vacuo* and re-dissolved in butan-1-ol (10 ml) for analysis of copper and sulfur content by ICP-OES in each case (appendix 7.3.4).

### 5.8.6.2 The pH Dependence of Chloride-loading

Extraction experiments were carried out using the procedure defined in chapter 4 (section 4.10.5.3). The only notable difference was that in the experiments performed in CHCl<sub>3</sub> containing 5% butan-1-ol a 4 ml aliquot of the contacted organic phase, rather than 2 ml, was removed for chloride analysis (appendix 7.3.4).

### 5.8.7 X-Ray Structure Determination of [Cu(1)(SO<sub>4</sub>)]·H<sub>2</sub>O

Data was collected at 150 K on a Bruker SMART APEX diffractometer using Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The structure was solved<sup>12</sup> by Dr. Paul Plieger using direct methods (SHELXS 97)<sup>19</sup> and refined on  $F^2$  by full-matrix least squares (SHELXL 97)<sup>19</sup>. All hydrogen atoms were placed at calculated positions and refined using a riding model. An anisotropic model was used for all non-H atoms except S1. A 0.75/0.25 disorder model was applied to one *tert*-butyl group and one ethanol solvent molecule was refined with a partial occupancy of 0.75. The C–C bond distance in ethanol was restrained. The final refinement statistics are presented in Table 5.3.

**Table 5.3** Crystallographic data for [Cu(1)(SO<sub>4</sub>)]·H<sub>2</sub>O<sup>12</sup>

	[Cu(1)SO <sub>4</sub> ]·H <sub>2</sub> O
Emp. Formula	CuC <sub>42.5</sub> H <sub>78.5</sub> N <sub>4</sub> O <sub>10.75</sub> S
<i>M</i>	913.19
Crystal System	Monoclinic
Space group	P2 <sub>1</sub> /c
<i>a</i> /Å	18.500(3)
<i>b</i> /Å	18.493(3)
<i>c</i> /Å	14.850(3)
$\alpha$ /°	90
$\beta$ /°	104.677(2)
$\gamma$ /°	90
<i>V</i> /Å <sup>3</sup>	4914.5(14)
<i>Z</i>	4
$\rho_{\text{calcd}}$ /g cm <sup>-3</sup>	1.234
$\mu$ /mm <sup>-1</sup>	0.543
<i>T</i> /K	150
Unique data ( <i>R</i> <sub>int</sub> )	12084 (0.0709)
Unique data with $F_o > 4\sigma(F_o)$	10422
<i>R</i> <sub>1</sub> , $\omega R_2$	0.1205, 0.2929

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## **Chapter 6 : Conclusions and Further Work**

## Conclusions and Further Work

The main objective of the research presented for this thesis was to increase our understanding of the criteria needed to develop *selective* extractants for transition metal sulfates. Such reagents could be used in new flowsheets for the hydrometallurgical processing of metal sulfide ores which would overcome some of the environmental problems associated with the conventional pyrometallurgical treatments.

Although prototype extractants had been developed at The University of Edinburgh which are capable of transporting metal sulfates in the zwitterionic form of ditopic ligands with separated binding sites for the metal cation and sulfate dianion, detailed solution studies were required on these ligands to assess their suitability for use in commercial recovery processes. Extraction experiments were performed on some simple derivatives, containing 3-dialkylaminomethylsalicylaldimine units. The sulfate-loading in a two-phase  $\text{CHCl}_3/\text{H}_2\text{O}$  system, as expected, decreased with increasing pH, corresponding to the deprotonation of the tertiary amine arms in the anion-binding site. At low pH ( $< 1.5$ ) monocharged  $\text{HSO}_4^-$  anions were extracted but the complexes showed selectivity for  $\text{SO}_4^{2-}$  over  $\text{HSO}_4^-$ . The advantage of using a ditopic ligand was demonstrated by 4,4'-di-*tert*-butyl-6,6'-bis(dihexylaminomethyl)-2,2'-(1,2-phenylenedinitrilodimethylidyne)diphenol (ligand **4**, chapter 2) as the ligand on its own was found to be a poor sulfate extractant (loading was only observed at  $\text{pH} < 2$ ) but the metal complex of the ligand  $[\text{Cu}(\mathbf{4}\text{-2H})]$  showed a much higher affinity for the anion (loading sulfate only at  $\text{pH} < 5$ ). However, this ligand would not be effective in copper sulfate recovery because the metal cation cannot be removed from the rigid *o*-phenylene-bridged binding at a practicable pH.

An ideal profile for a metal sulfate ( $\text{MSO}_4$ ) extractant was defined as having a conveniently accessible pH-region where  $\text{M}^{2+}$  and  $\text{SO}_4^{2-}$  are loaded  $> 90\%$  and both  $\text{M}^{2+}$  and  $\text{SO}_4^{2-}$  can be recovered by pH adjustment. This was achieved, for the extraction of  $\text{CuSO}_4$ , with ligand **1**, chapter 2, which has a 1,2-ethane link in the “salen”-type metal binding site. This gave a plateau region of pH (2 – 4) in which

$\text{Cu}^{2+}$  and  $\text{SO}_4^{2-}$  loading was maximised. Although this extractant satisfied the initial requirement for a metal salt extractant, of an ideal extraction profile, commercial reagents also need to meet a number of other criteria.

The long-term stability of an extractant is particularly important as a ligand needs to be recycled many times. The hydrolytic stability of the ligands developed in chapter 2 were analysed, over a range of pH, in  $\text{CHCl}_3/\text{H}_2\text{O}$ . In general their hydrolytic stability was low. This problem would be likely to be less severe if kerosene, the solvent of choice in industry, was used instead of  $\text{CHCl}_3$  as there would be negligible solubility of sulfuric acid in the organic phase. Ligand **1**, the most successful extractant identified in chapter 2, has the poorest resistance to hydrolytic attack. Extractants which have aromatic substituents attached directly to the imine bond were found to be more stable to hydrolysis. Ligand **5** (chapter 3), which was developed with a 1,2-ethane-bridged metal binding site and phenyl substituents at the azomethine carbon atoms, showed similar extraction behaviour to ligand **1** but it also displayed an improved resistance to acid attack, attributed to the steric blocking effect of the azomethine carbon atom by the phenyl rings. The tests in  $\text{CHCl}_3$  are very useful as they allow insights into the structural features affecting stability. However the tests need to be extended to kerosene to confirm that a practicable reagent can be developed, and for this “greasier” hydrocarbon soluble ligands are required.

Selectivity is also of key importance for a metal sulfate extractant as other anions, such as chloride, are often contained in the leach solutions generated when processing metal sulfide ores. This is a challenging task as sulfate is very hydrophilic (Hofmeister series, section 1.8) so is generally more difficult to transport into an organic phase. It was hoped that incorporating well-placed amide hydrogen-bond donors into the ligand framework used in previous chapters, would help improve the affinity for sulfate. However, these amide ligands were found to have a lower “strength” of extraction than those in chapters 2 and 3. This is attributed to intramolecular hydrogen-bonding between adjacent amide groups which could inhibit the formation of a favourable binding cavity for anions. The synthesis of thiourea and

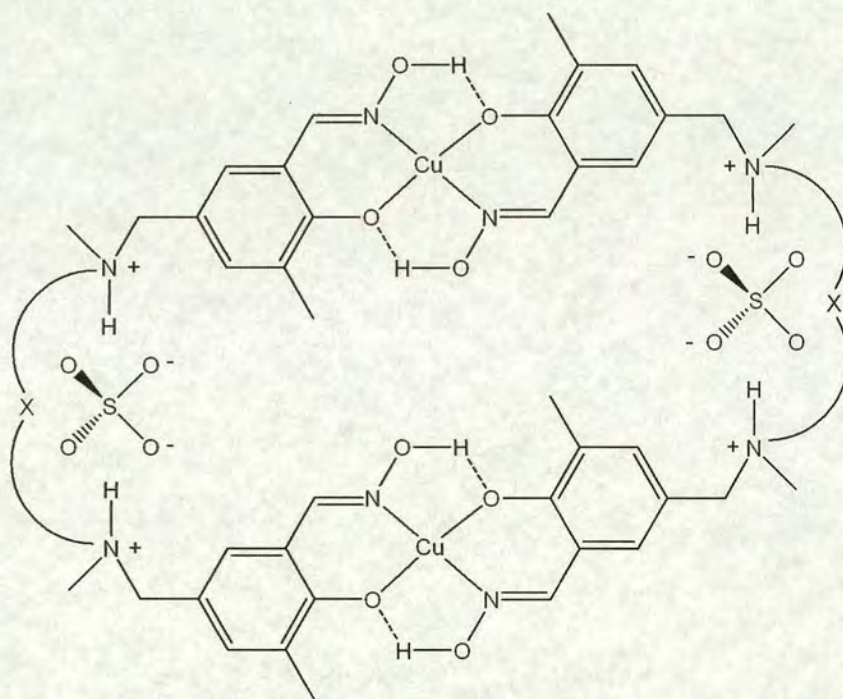


thioamide functionalised ligands was attempted to try to reduce any self-association occurring between the pendant groups. However all Mannich reactions on thioamide and thiourea substituted secondary amines failed. A future research target is to identify a successful route to these ligands.

The amide ligands all show selectivity for chloride over sulfate although this effect was notably reduced as the linkage between the tertiary amine nitrogen and amide group was shortened ( $C_6H_{12} \rightarrow C_3H_6 \rightarrow C_2H_4$ ). This suggests that a potential approach to achieving sulfate over chloride binding could be to restrict the size of the binding cavity so that it is unfavourable to bind *two* chloride anions in close proximity. Pre-organised macrocyclic ditopic ligands were synthesised to try and accomplish this target and the “strength” of sulfate-binding is significantly improved by the incorporation of a hexamethylene strap between the tertiary amine groups (ligand **2**, chapter 5) to create such a macrocycle. The crystal structure of the  $CuSO_4$  complex of the analogue with  $Bu^t$  sidearms instead of nonyl chains, (ligand **1**, chapter 5) exists as a dimer  $[Cu(1)(SO_4)(H_2O)]_2$  in the solid state. The centres of the dimeric units contain two sulfate anions bridged by hydrogen-bonded water molecules and this tetranionic unit interacts strongly with the protonated alkyl ammonium groups. This is an interesting result as it opens up the possibility of transporting the very hydrophilic sulfate anion as a partially hydrated dimer. The problems associated with this approach are that large supramolecular structures would have to be designed to accommodate this unit, increasing the cost of the extractant and lowering the mass transport ratio (mass of copper extracted per unit mass of extractant). A similar macrocycle, containing a longer amide-functionalised strap between the tertiary amines, was not found to be successful because it showed a sulfate binding “strength” similar to that of acyclic analogues. Both macrocycles showed a selectivity for chloride over sulfate, and although the “strength” of sulfate-binding was improved in ligand **2** (chapter 5) the extraction of chloride was still favoured.

The copper-binding by the amide macrocycle (ligand **3**, chapter 5) is very weak and it is possible that the amide-functionalised strap between the tertiary amines is too

long and imposes a distortion from the square planar geometry which is preferred by Cu(II). Consequently improvements to anion selectivity, such as incorporating additional anion binding groups into the strap between the tertiary amines, may be difficult if based on the current framework as there appears to be limitations to the length of the chain. New ligand designs could be achieved, without affecting the geometry of the metal binding site, if the functionalised straps were attached *para* to the phenol group rather than *ortho* as in this thesis. Combining this approach with using hydrolytically stable phenolic-oxime metal-binding units, e.g. as in Figure 6.1, could be used to create a *pseudo*-macrocyclic structure. This could give “strong” and selective copper-binding and also may provide the necessary supramolecular architecture to attempt to achieve the difficult and challenging task of selective sulfate-extraction.



**Figure 6.1** A *pseudo*-macrocyclic complex for the extraction of  $\text{CuSO}_4$ . X = hydrogen-bond donor.

In this thesis a novel approach was used to assess the anion selectivity of the ligands which involved comparing the measured  $\text{pH}_{1/2}$  values of anion extraction (see section 1.6). However this technique has some limitations since well-defined methods of analysis (eg. ICP-OES, ion selective electrode) are needed for each anion. My next

aim, by means of a Royal Society Fellowship at the University of Sydney, is to develop a potentiometric titration method, in a single phase of 95% MeOH/H<sub>2</sub>O, which can be used to quickly and conveniently assess the selectivity of these ligands for a number of anions which have varying sizes and geometries (eg. NO<sub>3</sub><sup>-</sup>, F<sup>-</sup>, I<sup>-</sup>, ClO<sub>4</sub><sup>-</sup>).

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## Cooperative sulfate binding by metal salt extractants containing 3-dialkylaminomethylsalicylaldimine units

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Received (in Cambridge, UK) 30th August 2002, Accepted 1st October 2002

First published as an Advance Article on the web 14th October 2002

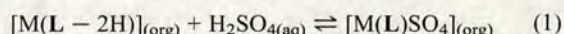
The pH-dependence of simultaneous metal- and sulfate-loading of simple salen derivatives demonstrates the feasibility of their application as extractants for recovery of base metals from the leaching of sulfidic ores. The efficacy of the ligands depends on the templating of the sulfate binding site by the attendant metal ion.

We have recently demonstrated the viability of using simple, inexpensive salen-derivatives **L** to extract both metal cations and their attendant anions from aqueous solutions.<sup>1–4</sup> Appending appropriate tertiary amine groups to the salen framework allows the metal salt to be transported in a zwitterionic form of the ligand (as in  $[M(L)SO_4]$  Scheme 1). In a solvent-extraction based process this leaves the pH of the aqueous 'feed' unchanged and removes the need for inter-stage neutralisation in a metal recovery circuit.<sup>5</sup>

The predominant anion in pregnant leach solutions from new hydrometallurgical processes to treat sulfidic ores is sulfate.<sup>6,7</sup> Commercial extraction is undertaken at low pH (<3) where there is a predominance of  $HSO_4^-$  over  $SO_4^{2-}$ . An extractant

capable of selectively removing  $SO_4^{2-}$  from the aqueous feed solution is a key requirement to obtain good materials balances and a high purity electrolyte for the reduction step. To date, there are only a few systems tailored to bind  $SO_4^{2-}$ ; the most successful are guanidinium-based ligands<sup>8,9</sup> that have shown selectivity for  $SO_4^{2-}$  over  $HPO_4^-$ .

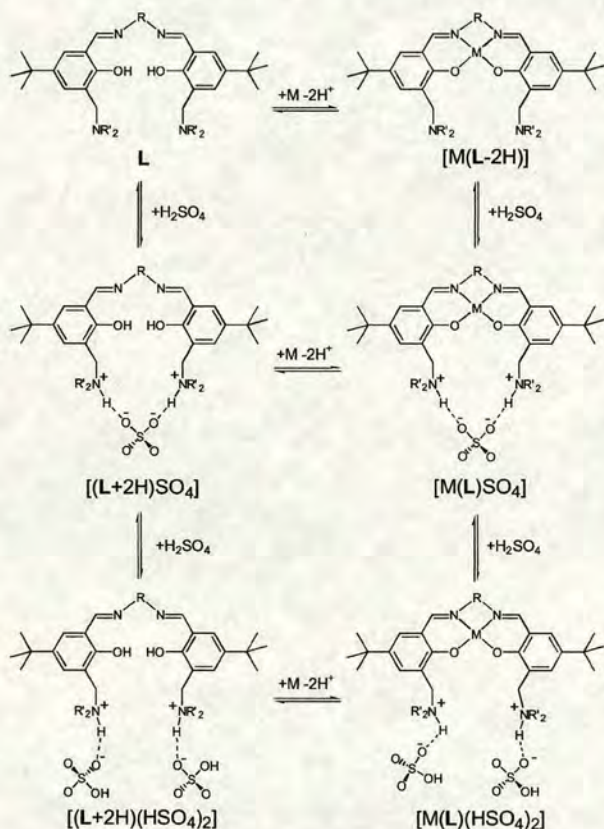
Direct addition of Ni(II) or Cu(II) sulfate to the ditopic ligands **L** in methanol yields the metal sulfate complexes  $[M(L)SO_4]$  which have been described previously.<sup>3</sup> The availability of the 'metal-only'  $[M(L-2H)]$  complexes from reaction with metal(II) acetates<sup>3</sup> has allowed us to study the uptake of sulfuric acid by these complexes in solvent extraction experiments, e.g.



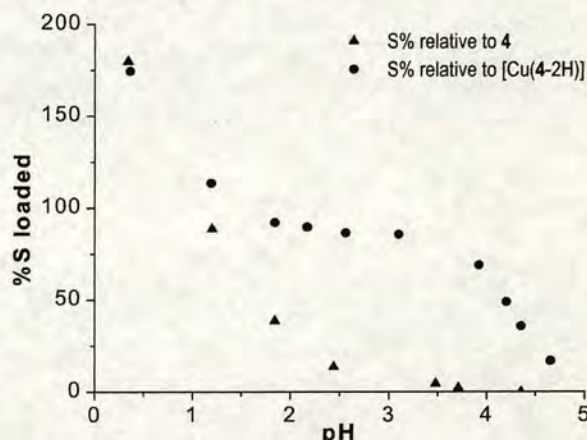
as a function of pH, and to determine how this depends on preorganisation of the ligands. Good chloroform solubility of both free ligands and complexes is shown by systems 1–4 with pendant di-*n*-hexylaminomethyl groups which are readily prepared by adaption of methods reported previously.<sup>† 3</sup>

The sulfate uptake by the *o*-phenylene-bridged ligand **4** and its copper complex  $[Cu(4-2H)]$  are compared in Fig. 1. The uptake by the free ligand is typical, with curves for 1–4 being almost superimposable.<sup>‡</sup> Very little transfer of sulfate to the organic phase is observed at pH > 2.0. As the pH is dropped below this value the uptake increases rapidly, approaching 200% at pH < 0.5, which can be attributed to the extraction of two mono-charged  $HSO_4^-$  anions which are present<sup>10</sup> in the aqueous phase in an excess at pH < 1. The  $SO_4^{2-}$  ion is present in a similar excess at pH > 3. No loading was seen in this region.

In contrast, the 'copper-only' complex  $[Cu(4-2H)]$  loads sulfate at pH values below 4.5, and the loading curve suggests that the 1:1:1 complex  $[Cu(4)SO_4]$  predominates in the pH range 1.5–3.5. This increase in apparent basicity of the pendant di-*n*-hexylaminomethyl groups in the copper complex favouring protonation and transport of sulfate is consistent with



**Scheme 1** Some of the equilibria associated with metal- and sulfate-loading of the ditopic Schiff base ligands **L**.  $R' = n-C_6H_{13}$  for the  $CHCl_3/H_2O$  solvent extraction studies reported here, and  $R = -(CH_2)_2-, 2,2'$ -biphenyl, ( $\pm$ )-*trans*-1,2-cyclohexyl, *o*- $C_6H_4$  for 1, 2, 3, 4, respectively.

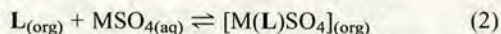


**Fig. 1** The pH dependence of  $H_2SO_4$  uptake by ligand **4** and  $[Cu(4-2H)]$ .

the copper ion templating the pendant tertiary amine groups to assemble a good sulfate-binding site which is dicationic with two H-bond donors and a hydrophobic exterior.

An important feature of this loading behaviour is that the copper complex of **4** is effectively selective for  $\text{SO}_4^{2-}$  over  $\text{HSO}_4^-$ ; in contact with an aqueous sulfate solution at pH = 1.92 where the  $\text{SO}_4^{2-}:\text{HSO}_4^-$  ratio is 1:1 the organic phase contains only the 1:1:1 complex  $[\text{Cu}(\mathbf{4})\text{SO}_4] \cdot \text{H}_2\text{O}$ .<sup>§</sup>

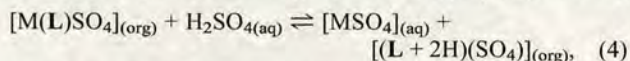
The pH dependence of sulfate-loading by the ditopic ligands **L** in  $\text{CHCl}_3$  is close to ideal for base metal recovery from sulfate feeds (Fig. 2). At pH  $\approx$  3.3, >90% loading of  $\text{MSO}_4$  is possible without pH adjustment.



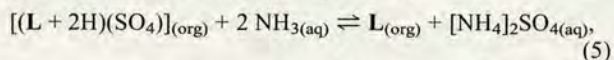
A very efficient materials balance for a circuit will result if the  $\text{pH}_{1/2}$  for the formation of the salen complex,



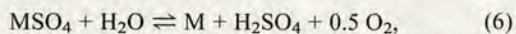
were ca. 2.0 (as shown in Fig. 2). Acid stripping at pH  $\leq$  1.5,



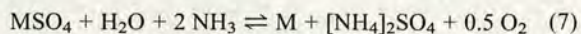
ligand regeneration with base to pH  $\approx$  3.0,



and electrolytic recovery of the metal,



regenerates the acid for stripping and gives a materials balance.



Any commercially viable extractant must show high stability towards hydrolysis or oxidation under operating conditions. The free ligands **1–4** were almost completely hydrolysed when  $\text{CHCl}_3$  solutions were contacted with  $\text{H}_2\text{SO}_4$  at pH  $\leq$  1 for 16 h, but at pH  $\approx$  3.0 the ligands were largely intact. This implies that at very low pH the transfer of sulfate to the chloroform phase involves the  $\text{HSO}_4^-$  salt of the protonated 5-*tert*-butyl-3-dihexylaminomethyl-2-hydroxybenzaldehyde, rather than  $[(\text{L} + 2\text{H})(\text{HSO}_4)]_2$  as indicated in Scheme 1.

Development of more hydrophobic hydrocarbon soluble analogues of **1–4** with enhanced hydrolytic stability is in hand.¶ The favourable 'strength' of sulfate extraction and selectivity for  $\text{SO}_4^{2-}$  over  $\text{HSO}_4^-$  demonstrated in this paper provides the basis for very efficient recovery of base metals from sulfidic

ores. The 'subtractive' removal of both the metal and its attendant sulfate anion could also open up an effective approach to treating acid mine drainage streams and other effluents prior to discharge.

We thank Mr J. Millar and Mr W. Kerr for obtaining NMR spectra, Mr A. Taylor and Mr H. Mackenzie for mass spectra. We gratefully acknowledge the Christina Miller Bequest and the EPSRC (GRM/R21653) for support and Mr R Swart (Avecia plc) and Dr B Harris (Hatch Ltd) for helpful discussions.

## Notes and references

† Example preparation of ligand **4**: to a stirred solution of 5-*tert*-butyl-3-dihexylaminomethyl-2-hydroxybenzaldehyde (3 g, 0.0080 mol) in ethanol (30 ml) was added a solution of phenylene-1,2-diamine (0.43 g, 0.0040 mol) in ethanol (25 ml). The orange solution was stirred overnight and then concentrated *in vacuo* to yield an orange oil. The product was then dissolved in dichloromethane (50 ml) and extracted with water ( $3 \times 25$  ml). The organic fraction was dried with  $\text{MgSO}_4$ , filtered and then evaporated *in vacuo* to yield **4** as a viscous orange oil (3.2 g, 98%). This was used without further purification. Calc. for  $\text{C}_{54}\text{H}_{86}\text{N}_4\text{O}_2$ : C, 78.78; H, 10.53; N, 6.81; Found: C, 78.30; H, 10.54; N, 6.92%.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 250 MHz): 0.89 (t, 12H,  $J$  6.6 Hz,  $\text{N}(\text{CH}_2)_5\text{CH}_3$ ), 1.29 (m, 24H,  $\text{NCH}_2\text{CH}_2(\text{CH}_2)_3\text{CH}_3$ ), 1.33 (m, 18H,  $(\text{CH}_2)_3\text{C}$ ), 1.53 (m, 8H,  $\text{NCH}_2\text{CH}_2$ ), 2.54 (t, 8H,  $J$  6.8 Hz,  $\text{NCH}_2\text{CH}_2$ ), 3.73 (s, 4H, Ar-CH<sub>2</sub>N), 6.78 (m, 2H, Ar-H), 7.08 (m, 2H, Ar-H), 7.46 (m, 2H, Ar-H), 7.64 (d, 2H, Ar-H), 8.83 (s, 2H, N=CH).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 14.4 ( $\text{N}(\text{CH}_2)_5\text{CH}_3$ ), 22.9 ( $\text{N}(\text{CH}_2)_4\text{CH}_2\text{CH}_3$ ), 26.6 ( $\text{N}(\text{CH}_2)_3\text{CH}_2\text{CH}_2\text{CH}_3$ ), 27.1 ( $\text{N}(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$ ), 31.9 ( $\text{C}(\text{CH}_3)_3$ ), 32.2 ( $\text{NCH}_2\text{CH}_2$ ), 34.4 ( $\text{C}(\text{CH}_3)_3$ ), 53.9 ( $\text{NCH}_2\text{CH}_2$ ), 54.4 (ArCCH<sub>2</sub>N), 115.8 (Ar-C), 118.4 (Ar-C), 119.8 (Ar-CH), 125.4 (Ar-CH), 127.1 (Ar-CH), 130.3 (Ar-CH), 141.4 (Ar-C), 141.7 (Ar-C), 157.8 (Ar-C), 161.1 (N=CH).  $\nu_{\text{max}}/\text{cm}^{-1}$  2954s (C-H), 1619s (N=CH), 1205s (C-N), 822m, 748s. MS (FAB, NOBA):  $m/z$  823 ( $\text{MH}^+$ , 56.9%).

‡ 10 ml aliquots of  $\text{H}_2\text{SO}_4/\text{Na}_2\text{SO}_4$  with pH values in the range 0–6 and a constant  $\text{SO}_4^{2-}$  concentration (0.8 mol  $\text{dm}^{-3}$ ) were intimately mixed for 16 h with  $\text{CHCl}_3$  solutions of metal-only complexes (10 ml, 0.01 M). The organic layer was separated, a 2 ml aliquot removed, evaporated *in vacuo*, and then redissolved in butan-1-ol (10 ml). Analysis for M and S was performed on a Thermo Jarrell Ash IRIS ICP-AES spectrometer. Extraction experiments on the free ligands used the same procedure with 10 ml of a 0.01 M ligand solution in  $\text{CHCl}_3$  and the degree of hydrolysis was determined by comparison of the intensities of the azomethine and aldehyde  $^1\text{H}$  NMR signals.

§ On the basis of analytical data it is not possible to distinguish this from the complex  $[\text{Cu}(\mathbf{4} - \text{H})\text{HSO}_4]$ . However, this is of no consequence to the materials balances, the ligand still effectively transports  $\text{CuSO}_4$ .

¶ Marked improvements in hydrolytic stability are observed when imine extractants are used in hydrocarbon solvents, e.g. 5-nonyl-derivatives of salicylaldehyde show long lifetimes when used in kerosene as extractants from acidic media.<sup>11</sup>

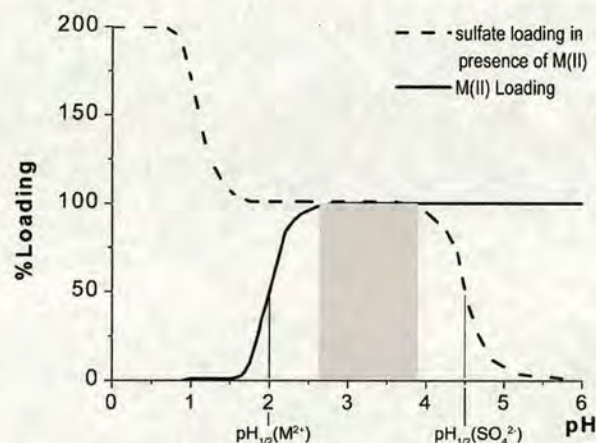


Fig. 2 Idealised pH profile for the loading and stripping of Cu(II) and  $\text{SO}_4$

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# Zwitterionic macrocyclic metal sulfate extractants containing 3-dialkylaminomethylsalicylaldimine units

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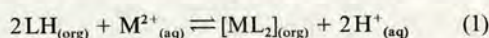
Received 17th October 2003, Accepted 19th November 2003

First published as an Advance Article on the web 5th December 2003

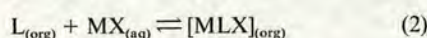
10,25-Di-*tert*-alkyl-14,21-dimethyl-3,6,14,21-tetraazatricyclo[21.3.1.18,12]octacos-1(27),2,6,8,10,12(28),23,25-octaene-27,28-diol macrocycles form Ni(II) and Cu(II) complexes in which the metal cation and the sulfate anion are bound in separated sites in a zwitterionic form of the ligand. The nonyl-substituted macrocycle shows a higher affinity for  $\text{SO}_4^{2-}$  and a lower binding strength for  $\text{Cu}^{2+}$  than open chain analogues, the pH-dependences for which fall in ranges which allow loading of  $\text{CuSO}_4$  at  $\text{pH} \approx 4$  and easy stripping to recycle the ligand. X-Ray structure determinations of the Cu(II) and Ni(II) sulfate complexes of the *tert*-butyl substituted ligand suggest that the de-tuning of  $\text{M}^{2+}$ -binding results from a distortion from planarity of the "salen"  $\text{N}_2\text{O}_2^{2-}$  donor set imposed by the incorporation of the hexamethylene strap in the ligand and reveal that the sulfate is bound as a hydrate in a 2 : 2 : 2 : 2, ligand- $\text{M}^{2+}$ - $\text{SO}_4^{2-}$ - $\text{H}_2\text{O}$ , assembly.

## Introduction

Solvent extraction has proven to be a robust and efficient technology to achieve the concentration and separations in hydrometallurgy.<sup>1</sup> Whilst ion exchange based processes, typically using kerosene-soluble acidic reagents to transport metal ions,



give very good materials balances in certain processes, there are flowsheets which require transport of metal salts to achieve an efficient process<sup>2</sup>



When processing aqueous streams containing coordinating anions it is possible to generate neutral, hydrocarbon soluble, complexes with the anion in the inner coordination sphere. This strategy has been deployed extensively in chloride hydrometallurgy,<sup>3</sup> but is less likely to succeed for processing streams containing weakly coordinating anions such as sulfate. This is unfortunate because new leaching technology for sulfidic ores<sup>4</sup> generates such streams and there is also a need to remove metal sulfates from acid mine drainage streams. These requirements have led us to consider the development of reagents such as **1** (Scheme 1) to transport metal sulfates. In these reagents the base metal dication and its sulfate counter-ion are bound in separated charged sites generated in a zwitterionic form of the ligand. The zwitterionic nature of the carrier allows the transported ions to be stripped by pH adjustment and the free ligand to be regenerated and recycled. The design of ditopic ligands to

function as strong sulfate extractants represents a challenge because the hydrophilicity of sulfate makes extraction into low polarity organic solvents difficult and obtaining selectivity over other anions such as chloride is especially challenging, given the well established order of hydrophobicity  $\text{Cl}^- \gg \text{SO}_4^{2-}$  (the Hofmeister order).<sup>5</sup>

Sulfate binding in the prototype open chain reagents (Scheme 1) has been shown to be templated by incorporation of the metal dication into the "salen"  $\text{N}_2\text{O}_2^{2-}$  donor set.<sup>6</sup> In this paper we present work on macrocyclic analogues in which a hexamethylene strap has been inserted between the pendant amine groups in order to preorganise the sulfate binding site. It was also hoped that this strap would screen the complexed ion, increasing solubility in non polar, water immiscible solvents.

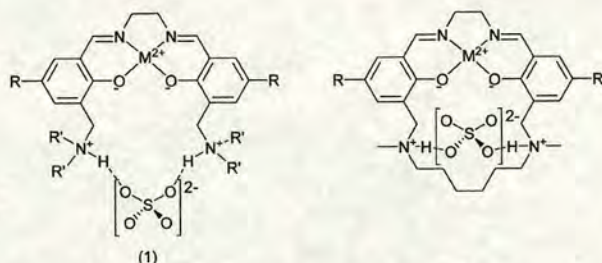
## Experimental

### Instrumentation

Nuclear magnetic resonance spectra were obtained on Bruker AC 250 and 300 instruments, FAB mass spectra on a Kratos MS 50 machine, EI mass spectra on a Kratos Profile instrument, FTIR spectra on a Perkin-Elmer paragon 1000 spectrometer as KBR discs and electronic absorption spectra on a Perkin-Elmer  $\lambda$ -900 spectrometer. Inductively coupled plasma optical emission spectroscopy (ICP-OES) analysis was performed on a Thermo Jarrell Ash IRIS ICP-OES spectrometer. The measurement of pH was carried out using a Fisher Scientific AR50 pH meter.

### Ligand synthesis

*N,N'*-Bis(ethoxymethyl)-*N,N'*-dimethylhexane-1,6-diamine. *N,N'*-Dimethyl-1,6-hexanediamine (30.0 g, 0.21 mol) was added dropwise to a stirred suspension of paraformaldehyde (12.5 g, 0.42 mol) and  $\text{K}_2\text{CO}_3$  (57.5 g, 0.42 mol) in ethanol (72 ml) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 48 h.  $\text{K}_2\text{CO}_3$  was removed by filtration, the solvent was evaporated *in vacuo* and the resulting oil was purified by vacuum distillation to give **1** as a colourless oil (125 °C, 1.5 mmHg) (39.3 g, 72%) (Found: C, 64.3; H, 12.3; N, 10.8.  $\text{C}_{14}\text{H}_{32}\text{N}_2\text{O}_2$  requires C, 64.6; H, 12.4; N, 10.8%);  $\delta_{\text{H}}$  (360 MHz; solvent  $\text{CDCl}_3$ ; reference  $\text{CDCl}_3$ ) 3.89 (4H, s,  $\text{NCH}_2\text{O}$ ), 3.28 (4H, q,  $\text{OCH}_2\text{Me}$ ), 2.36 (4H, t,  $\text{NCH}_2\text{C}_2\text{H}_4$ ), 2.20 (6H, s,  $\text{NCH}_3$ ), 1.29 (4H, t,  $\text{NCH}_2\text{CH}_2\text{CH}_2$ ), 1.14 (4H, s,  $\text{NCH}_2\text{CH}_2\text{CH}_2$ ), 1.00 (6H, t,  $\text{OCH}_2\text{CH}_3$ );  $\delta_{\text{C}}$  (360 MHz; solvent



**Scheme 1** Metal(II) sulfate complexes of open chain and macrocyclic zwitterionic ligands containing "salen" metal-binding sites. **1a**, R = *t*-Bu, R' = *n*-C<sub>2</sub>H<sub>5</sub>, **1b**, has the 1,2-ethane link between the imine nitrogen atoms replaced by an 1,2-phenylene unit.

CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 87.6 (NCH<sub>2</sub>O), 63.3 (OCH<sub>2</sub>Me), 53.4 (NCH<sub>2</sub>), 39.1 (NMe), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.0 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 14.9 (OCH<sub>2</sub>Me); *m/z* 189, 173, 157.

***N,N'*-Dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-*tert*-butylbenzylamine) (2a).** A solution of 5-*tert*-butyl-2-hydroxybenzaldehyde (35 g, 0.2 mol) and **1** (26 g, 0.1 mol) in acetonitrile (400 ml) was refluxed under dinitrogen for 72 h. After cooling to room temperature the solvent was removed *in vacuo* to give a pale yellow oil which was triturated with pentane to give **2a** as a pale yellow powder (41.7 g, 81%), mp 90 °C (from hexane) (Found: C, 73.3; H, 9.3; N, 5.4. C<sub>32</sub>H<sub>48</sub>N<sub>2</sub>O<sub>4</sub> requires C, 73.2; H, 9.2; N, 5.3%);  $\nu_{\max}/\text{cm}^{-1}$  2962s, 2862, 2846, 1678s (C=O), 1233s, 978, 889, 826 (KBr);  $\delta_{\text{H}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 11.95 (2H, s, br) 10.35 (2H, s, CHO), 7.61 (2H, d, *J* 2.6 Hz, Ph), 7.24 (2H, d, *J* 2.6 Hz, Ph), 3.70 (4H, s, PhCH<sub>2</sub>N), 2.48 (4H, t, *J* 7.2 Hz, NCH<sub>2</sub>), 2.28 (6H, s, NCH<sub>3</sub>), 1.57 (4H, m, *J* 7.2 Hz, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.34 (4H, m, *J* 7.2 Hz, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.26 (18H, s, *t*-Bu);  $\delta_{\text{C}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 191.3 (CHO), 159.8 (CHOC), 141.5 (COH), 132.4 (Ph CH), 124.0 (Ph CH), 123.3 (Ph), 122.2 (Ph), 60.3 (PhCH<sub>2</sub>N), 57.0 (NCH<sub>2</sub>), 41.3 (NMe), 34.0 (CMe<sub>3</sub>), 31.3 (Me), 26.9 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 26.8 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); *m/z* 525 (M<sup>+</sup>).

***N,N'*-Dimethyl-*N,N'*-hexamethylenedi(3-formyl-2-hydroxy-5-nonylbenzylamine) (2b).** A solution of 5-nonyl-2-hydroxybenzaldehyde (3 g, 12.1 mmol) and **1** (1.57 g, 6 mmol) in acetonitrile (150 ml) was refluxed under dinitrogen for 72 h. The solution was cooled to room temperature, concentrated to 30 ml *in vacuo* and then heated to 60 °C. An oil separated from a yellow solution on cooling which was collected, washed with acetonitrile (2 × 20 ml) and dried *in vacuo* to give **2b** as a light brown oil (2.3 g, 57%) (Found: C, 74.4; H, 10.0; N, 4.4. C<sub>42</sub>H<sub>68</sub>N<sub>2</sub>O<sub>4</sub>·½H<sub>2</sub>O requires C, 74.8; H, 10.3; N, 4.2%);  $\nu_{\max}/\text{cm}^{-1}$  2957s, 2859, 1681s (C=O), 1233s, 1014, 975, 747;  $\delta_{\text{H}}$  (250 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 10.36 (2H, s, CHO), 7.56 (2H, m, Ph), 7.20 (2H, m, Ph), 3.70 (4H, s, PhCH<sub>2</sub>N), 2.47 (4H, t, *J* 7.2 Hz, NCH<sub>2</sub>), 2.28 (6H, s, NCH<sub>3</sub>), 1.56–1.38 (8H, m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.25–0.86 (38H, s, C<sub>9</sub>H<sub>19</sub>);  $\delta_{\text{C}}$  (250 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 191.4 (CHO), 159.4 (CHOC), 138.2 (COH), 133.0 (Ph CH), 124.7 (Ph CH), 123.2 (Ph), 122.0 (Ph), 60.1 (PhCH<sub>2</sub>N), 56.9 (NCH<sub>2</sub>), 41.2 (NMe), 40–8 (C<sub>9</sub>, mixed isomer chain); *m/z* 665 (M<sup>+</sup>).

**10,25-Di-*tert*-butyl-14,21-dimethyl-3,6,14,21-tetraazatricyclo[21.3.1.18,12]octacosane-1(27),2,6,8,10,12(28),23,25-octaene-27,28-diol (3a).** 1,2-Ethanediamine (130 µl, 1.94 mmol) in ethanol (20 ml) was added dropwise to **2a** (1.00 g, 1.94 mmol) in diethyl ether (200 ml). After stirring for 24 hr the solvent was removed *in vacuo* and the resulting orange residue was triturated with pentane (10 ml) to give **3a** as a pale yellow powder (0.46 g, 44%), mp 94–96 °C (Found: C, 73.8; H, 9.4; N 10.2. C<sub>34</sub>H<sub>52</sub>N<sub>4</sub>O<sub>2</sub>·½H<sub>2</sub>O requires C, 73.8; H 9.6; N 10.1%);  $\nu_{\max}/\text{cm}^{-1}$  2952s, 2859s, 2788s, 1636s (C=N), 1466s, 1271, 1034, 823 (KBr);  $\delta_{\text{H}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 13.25 (2H, s-br, Ph OH), 8.38 (2H, s, N=CH), 7.36 (2H, d, *J* 2.5 Hz, Ph), 7.16 (2H, d, *J* 2.5 Hz, Ph), 3.89 (4H, s, NCH<sub>2</sub>CH<sub>2</sub>N), 3.55 (4H, s, PhCH<sub>2</sub>N), 2.49 (4H, t, CH<sub>2</sub>N), 2.22 (6H, s, NCH<sub>3</sub>), 1.55 (4H, m, CH<sub>2</sub>CH<sub>2</sub>N), 1.32 (4H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N), 1.28 (18H, s, *t*-Bu);  $\delta_{\text{C}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 166.3 (N=CH), 157.2 (Ph CH), 140.7 (Ph CH), 130.6 (Ph), 126.3 (Ph), 125.5 (Ph), 118.0 (Ph), 60.0 (NCH<sub>2</sub>CH<sub>2</sub>N), 57.7 (NCH<sub>2</sub>Ph), 55.9 (CH<sub>2</sub>N), 42.3 (NMe), 33.9 (CMe<sub>3</sub>), 31.3 (Me), 27.5 (NCH<sub>2</sub>CH<sub>2</sub>), 27.2 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); *m/z* 549 (M<sup>+</sup>), 1092 (2M<sup>+</sup>).

**10,25-Dinonyl-14,21-dimethyl-3,6,14,21-tetraazatricyclo[21.3.1.18,12]octacosane-1(27),2,6,8,10,12(28),23,25-octaene-27,28-diol (3b).** 1,2-Ethanediamine (122 µl, 1.83 mmol) in methanol (100 ml) was added dropwise to **2b** (1.22 g, 1.83

mmol) in chloroform (200 ml). After stirring for 24 h the solvent was removed *in vacuo* to yield a yellow oil which was dissolved in chloroform (50 ml) and washed with water (2 × 30 ml). The chloroform solution was dried over MgSO<sub>4</sub>, filtered and evaporated *in vacuo* to yield a viscous yellow oil (1.24 g, 98%) (Found: C, 77.3; H, 10.5; N, 8.4%. C<sub>44</sub>H<sub>72</sub>N<sub>4</sub>O<sub>2</sub> requires C, 76.7; H, 10.5; N, 8.1%);  $\nu_{\max}/\text{cm}^{-1}$  2931s, 2791s, 1632s (C=N), 1466s, 1264, 1033, 740;  $\delta_{\text{H}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 8.39 (2H, s, N=CH), 7.15–7.07 (4H, m, Ph), 3.88 (4H, s, NCH<sub>2</sub>CH<sub>2</sub>N), 3.49 (4H, s, PhCH<sub>2</sub>N), 2.31 (4H, t, *J* 7.2 Hz, NCH<sub>2</sub>), 2.23 (6H, s, NCH<sub>3</sub>), 1.60–1.37 (8H, m, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.25–0.55 (38H, s, C<sub>9</sub>H<sub>19</sub>);  $\delta_{\text{C}}$  (360 MHz; solvent CDCl<sub>3</sub>; reference CDCl<sub>3</sub>) 166.4 (N=CH), 157.3 (Ph), 137.0 (Ph), 131.7 (Ph CH), 127.8 (Ph CH), 125.0 (Ph), 118.1 (Ph), 60.0 (NCH<sub>2</sub>CH<sub>2</sub>N), 57.7 (NCH<sub>2</sub>Ph), 55.9 (CH<sub>2</sub>N) 45–8 (C<sub>9</sub>, mixed isomer chain);  $\lambda_{\max}/\text{nm}$  (MeOH) 260 (13120), 328 (4732), 414 (1462); *m/z* 689 (M<sup>+</sup>).

#### Preparation of complexes of metal sulfates

Solutions of ligand (0.182 mmol) in methanol (25 ml) and the appropriate metal sulfate (1 mol equivalent) in methanol (20 ml) were mixed and stirred for 24 h. After removal of most of the solvent *in vacuo* the precipitates were purified as indicated.

**Nickel[10,25-di-*tert*-butyl-14,21-dimethyl-3,6-diaza-14,21-diazoniatricyclo[21.3.1.18,12]octacosane-(27),2,6,8,10,12(28),23,25-octaene-27,28-diolato[κN<sup>3</sup>,κN<sup>6</sup>,κO<sup>27</sup>,κO<sup>28</sup>] sulfate monohydrate, [Ni(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O.** Recrystallisation from methanol-diisopropyl ether, followed by crushing and drying gave [Ni(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O (0.074 g, 57%) (Found: C, 58.2; H, 8.0; N 8.0. C<sub>34</sub>H<sub>52</sub>N<sub>4</sub>O<sub>2</sub>NiSO<sub>4</sub> requires C, 58.0; H, 7.5; N, 8.0%);  $\nu_{\max}/\text{cm}^{-1}$  3409, 2957s, 2867, 1625s (C=N), 1548, 1455s, 1245s, 1128s, 609 (KBr);  $\lambda_{\max}/\text{nm}$  (MeOH) 435sh, 406 (8889), 334sh, 326 (11187); *m/z* 704 (M<sup>+</sup>), 606 (M<sup>+</sup> – SO<sub>4</sub>), 1403 (2M<sup>+</sup>), 1309 (2M<sup>+</sup> – SO<sub>4</sub>). Crystals of the monohydrate for X-ray structure determination were grown by the diffusion of diisopropyl ether into a methanolic solution and were found also to contain diisopropyl ether of solvation.

**Copper[10,25-di-*tert*-butyl-14,21-dimethyl-3,6-diaza-14,21-diazoniatricyclo[21.3.1.18,12]octacosane-(27),2,6,8,10,12(28),23,25-octaene-27,28-diolato[κN<sup>3</sup>,κN<sup>6</sup>,κO<sup>27</sup>,κO<sup>28</sup>] sulfate monohydrate, [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O.** Recrystallisation from ethanol-diethyl ether, followed by crushing and drying gave [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O (0.050 g, 39%) (Found: C, 57.7; H, 7.7; N 7.9. C<sub>34</sub>H<sub>52</sub>N<sub>4</sub>O<sub>2</sub>CuSO<sub>4</sub> requires C, 57.6; H, 7.4; N, 7.9%);  $\nu_{\max}/\text{cm}^{-1}$  3418, 2954s, 2866, 2664, 1633s (C=N), 1546, 1452s, 1121s, 1089, 1042, 619 (KBr);  $\lambda_{\max}/\text{nm}$  (MeOH) 363 (22040), 591, (680); *m/z* 709 (M<sup>+</sup>), 611 (M – SO<sub>4</sub>), 1414 (2M<sup>+</sup>), 1318 (2M<sup>+</sup> – SO<sub>4</sub>). Crystals of the monohydrate for X-ray structure determination were grown by the diffusion of diethyl ether into an ethanolic solution and were found also to contain ether and alcohol of solvation.

#### Preparation of “metal-only” complexes

**Copper[10,25-dinonyl-14,21-dimethyl-3,6,14,21-tetraazatricyclo[21.3.1.18,12]octacosane-1(27),2,6,8,10,12(28),23,25-octaene-27,28-diolato(2-)[κN<sup>3</sup>,κN<sup>6</sup>,κO<sup>27</sup>,κO<sup>28</sup>], [Cu(3b – 2H)].** Using the ligand **3b** and Cu(CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>·H<sub>2</sub>O as the source of copper in the procedure outlined above for the preparation of [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O gave a black oil which was dissolved in chloroform (30 ml) and washed with pH 9 ammonia solution (2 × 20 ml). The chloroform solution was dried over MgSO<sub>4</sub>, filtered, and on evaporation *in vacuo* gave a viscous black oil (0.109 g, 80%) which was used without further purification in solvent extraction experiments (copper content determined by ICP-OES for a 0.001 M solution in butanol: found 77.5 ppm, calc. for C<sub>44</sub>H<sub>70</sub>N<sub>4</sub>O<sub>2</sub>Cu 78.9 ppm).  $\nu_{\max}/\text{cm}^{-1}$  3234, 2958s, 2870,

**Table 1** Crystallographic data

	[Cu(3a)(SO <sub>4</sub> )]·H <sub>2</sub> O	[Ni(3a)(SO <sub>4</sub> )]·H <sub>2</sub> O
Emp. formula	CuC <sub>42.5</sub> H <sub>78.5</sub> N <sub>4</sub> O <sub>10.75</sub> S	NiC <sub>34</sub> H <sub>54</sub> N <sub>4</sub> O <sub>7</sub> S
<i>M</i>	913.19	721.58
Crystal system	Monoclinic	Monoclinic
Space group	<i>P</i> 2 <sub>1</sub> / <i>c</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>
<i>a</i> /Å	18.500(3)	14.447(3)
<i>b</i> /Å	18.493(3)	18.992(4)
<i>c</i> /Å	14.850(3)	33.985(7)
$\beta$ /°	104.677(2)	96.60(3)
<i>V</i> /Å <sup>3</sup>	4914.5(14)	9263(3)
<i>Z</i>	4	8
<i>D</i> <sub>c</sub> /g cm <sup>-3</sup>	1.234	1.035
$\mu$ /mm <sup>-1</sup>	0.543	0.504
<i>T</i> /K	150	150
Unique data ( <i>R</i> <sub>int</sub> )	12084 (0.0709)	12291 (0.0921)
Unique data with <i>F</i> <sub>o</sub> > 4σ( <i>F</i> <sub>o</sub> )	10422	10173
<i>R</i> <sub>1</sub> , <i>wR</i> <sub>2</sub>	0.1205, 0.2929	0.1268, 0.2669

1625s (C=N), 1540, 1446s, 755 (KBr);  $\lambda_{\text{max}}$ /nm (MeOH) 364 (7840), 585 (260); *m/z* 750 (M<sup>+</sup>).

### Solvent extraction studies

10 ml aliquots of H<sub>2</sub>SO<sub>4</sub>/Na<sub>2</sub>SO<sub>4</sub> with pH values in the range 0–7 and a constant SO<sub>4</sub><sup>2-</sup> concentration (0.8 mol dm<sup>-3</sup>) were intimately mixed for 16 h with CHCl<sub>3</sub> solutions (containing 5% butan-1-ol) of the “copper-only” complex [Cu(3b – 2H)] (10 ml, 0.005 M). The organic layer was separated, a 2 ml aliquot removed, evaporated *in vacuo*, and then redissolved in butan-1-ol (10 ml). The copper and sulfur content was subsequently analysed using ICP-OES. Solutions of the free ligand 3b (10 ml, 0.005M) were treated similarly and the sulfur content was determined.

### X-Ray structure determinations of [Ni(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O and [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O

Data were collected at 150 K on a Bruker SMART APEX diffractometer using Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å). The structures were solved by direct methods (SHELXS 97)<sup>7</sup> and refined on *F*<sup>2</sup> by full-matrix least squares (SHELXL 97).<sup>7</sup> All hydrogen atoms were placed at calculated positions and refined using a riding model. For [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O an anisotropic model was used for all non-H atoms except S1. A 0.75/0.25 disorder model was applied to one *tert*-butyl group and one ethanol solvent molecule was refined with a partial occupancy of 0.75. The C–C bond distance in ethanol was restrained. The final refinement statistics are presented in Table 1. For [Ni(3a)(SO<sub>4</sub>)] an isotropic model was applied for all C, H and N atoms and diffuse solvent equivalent to eight diisopropyl ether molecules per unit cell was treated in the manner described by van der Sluis and Spek.<sup>8</sup> The final refinement statistics are presented in Table 1.

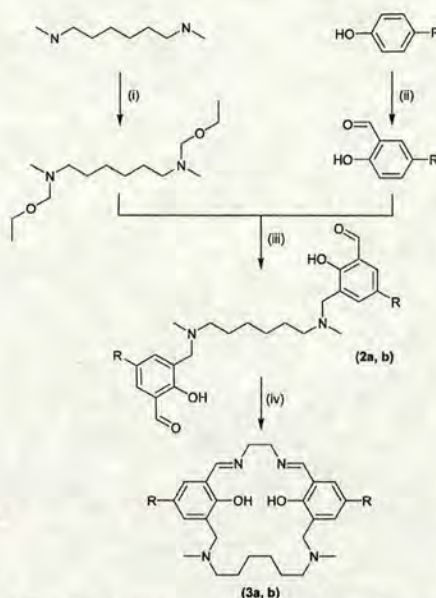
CCDC reference numbers 222180 and 222181.

See <http://www.rsc.org/suppdata/dt/b3/b313078a/> for crystallographic data in CIF or other electronic format.

## Results and discussion

### Synthesis of new Schiff base ligands

The 22-membered macrocycle 3a was prepared from 2-hydroxy-5-*tert*-butylbenzaldehyde,<sup>9</sup> paraformaldehyde, *N,N*-dimethyl-1,6-hexanediamine and 1,2-ethanediamine as outlined in Scheme 2. A two-step Mannich reaction<sup>10</sup> gave the parent dialdehyde 2a in 81% yield which was purified by first sonicating the oil in pentane and recrystallising the resulting pale yellow solid from hexane. The macrocycle was characterised by <sup>1</sup>H and <sup>13</sup>C NMR and elemental analysis. Mass spectrometry indicated that some of the related 44-membered macrocycle



**Scheme 2** Ligand synthesis. Reagents and conditions: (i) paraformaldehyde, ethanol, distillation; (ii) MgOMe, MeOH–toluene, reflux 3 h; (iii) MeCN, N<sub>2</sub>, reflux 66 h; (iv) 1,2-ethanediamine, Et<sub>2</sub>O–EtOH (10 : 1), r.t. 24 h.

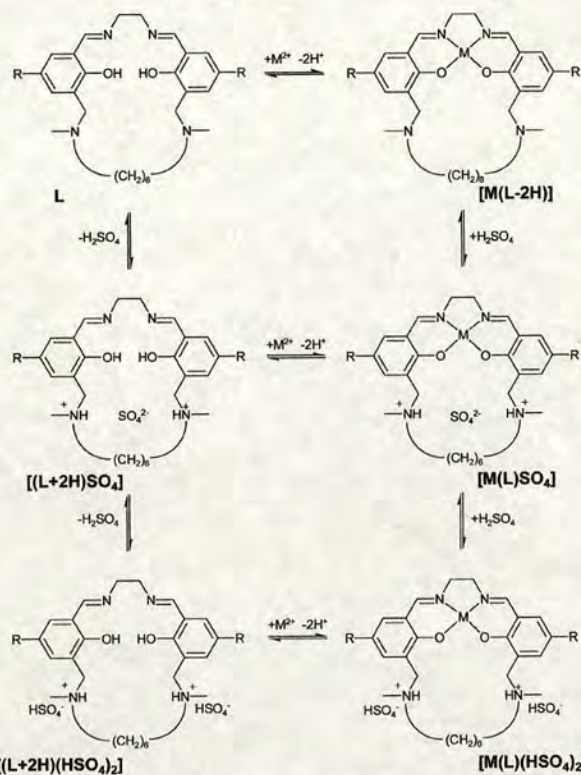
resulting from a 2 + 2 condensation of 2a and 1,2-ethanediamine had been formed. No attempt was made to remove this component before the preparation of the metal complexes of 3a (see below). The related macrocycle (3b) with two multiply branched, mixed isomer, nonyl substituents and its copper sulfate complexes have sufficient solubility in chloroform + 5% butan-1-ol to allow copper and sulfate loadings from aqueous solutions to be investigated. Whilst FAB mass spectra showed only very weak peaks with *m/z* greater than that of 3b, it is probable that, as in the case of the *tert*-butyl-substituted macrocycle 3a, some large-ring 2 + 2 condensation product is present in the material used in the solvent extraction experiments (see below).

### Formation of metal salt complexes

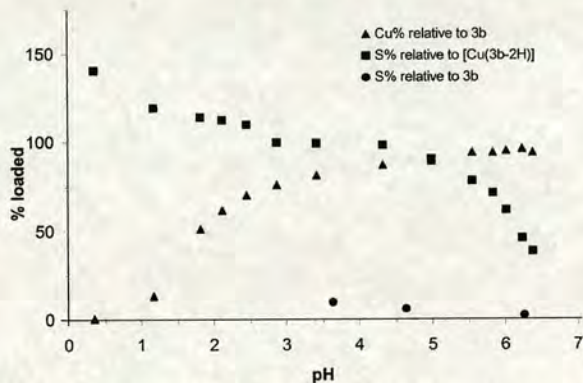
Ni(II) and Cu(II) sulfate complexes [M(L)(SO<sub>4</sub>)] of the ligand 3a were readily isolated from methanol. Microanalysis and FAB mass spectrometry and X-ray structure determination (see below) confirmed the formation of complexes containing a zwitterionic form of the ligand in which the phenolic protons have been transferred to the nitrogen atoms in hexamethylene diamine strap, and that the sulfate ion is “complexed” to these cationic sites rather than the metal centre.

A practicable solvent extraction system to transport metal(II) sulfates should be capable of loading both metal dications and sulfate (or bisulfate) anions from an aqueous solution with pH values typical of pregnant leach solutions or other process streams or effluents. Whilst a complex series of equilibria is needed to define the relative concentrations of species involved in transport, titration of an organic solution of the “metal only” complex, [M(L – 2H)] (top right, Scheme 3), with aqueous sulfuric acid and monitoring the metal and sulfate content in the organic phase provides useful information on the “strengths” of metal and sulfate binding.

The pH-dependence of sulfate loading of the “copper-only” complex [Cu(3b – 2H)] and the free ligand 3b is compared in Fig. 1. The copper complex binds sulfate when contacted with aqueous solutions of pH < 7, and the plateau region pH 3–5 is consistent with more than 90% of the copper complex being present in the form [Cu(3b)(SO<sub>4</sub>)] in the organic phase. In contrast, the free ligand is less than 10% sulfate-loaded, as [(3b + 2H)(SO<sub>4</sub>)] or [(3b + H)(HSO<sub>4</sub>)] in this region, indicating that



**Scheme 3** Some of the equilibria involved in transporting metal(II) sulfates in zwitterionic forms of ligands 3.



**Fig. 1** The pH dependence of  $\text{H}_2\text{SO}_4$  and  $\text{CuSO}_4$  uptake by ligand **3b** in a chloroform–5% butanol solvent system.

the copper centre is needed to “template” the tertiary amine groups to provide an effective receptor for  $\text{H}_2\text{SO}_4$  in chloroform–butanol. Such cooperativity of  $\text{M}^{2+}$  and  $\text{SO}_4^{2-}$  binding is potentially of great significance for tuning reagents to show high selectivities of metal sulfate transport.

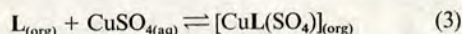
Sulfate-loading corresponding to formation of the mono-sulfato complexes  $[\text{Cu}(\text{L})(\text{SO}_4)]$  occurs at higher pH values for the macrocyclic system **3b** than for linear analogues such as **1a** and **1b** (Scheme 1). The pH values for 50% sulfate uptake by  $[\text{Cu}(\mathbf{3b}-2\text{H})]$  and of  $[\text{Cu}(\mathbf{1b}-2\text{H})]$  under identical conditions† are 5.9 and 4.2, respectively.

Whilst the incorporation of the hexamethylene strap enhances sulfate binding *cf.* the linear analogues **1**, the “strength” of metal-binding is decreased slightly. More than 85% of the copper is stripped when a chloroform solution of

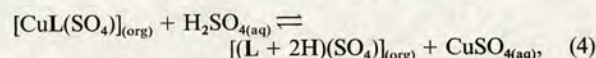
† These values are for 0.01 M solutions in neat  $\text{CHCl}_3$ . Data for **1** were generated using a 0.005 M solution in  $\text{CHCl}_3$  containing 5% butan-1-ol because solid material separated from a 0.01 M solution in neat  $\text{CHCl}_3$  in the pH region 2–5.5. The  $\text{pH}_{50}$  in Fig. 1 is 6.2 which is slightly higher.

$[\text{Cu}(\mathbf{3b})(\text{SO}_4)]$  is contacted with dilute sulfuric acid of pH 1.2. The  $\text{pH}_{0.5}$  for the copper stripping in this macrocycle is 1.9.‡  $[\text{Cu}(\mathbf{1a})(\text{SO}_4)]$  under the same conditions has a  $\text{pH}_{0.5}$  value for copper-stripping of 1.4 and at pH 1.2 less than 70% of the copper had been stripped. This slight de-tuning of the metal binding site may arise from the hexamethylene strap imposing a distortion from a square planar arrangement of the  $\text{N}_2\text{O}_2^{2-}$  “salen” donor set preferred by Cu(II). This is suggested by the X-ray structure determinations (see below).

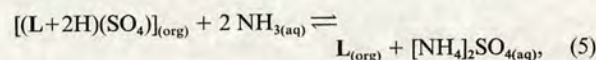
The pH profiles for  $\text{Cu}^{2+}$  and  $\text{SO}_4^{2-}$  loading, and in particular the overlapping plateaux in the region pH 3–5 are close to ideal for base metal recovery from sulfate feeds. At pH  $\approx$  4, >90% loading of  $\text{CuSO}_4$  is possible without pH adjustment,



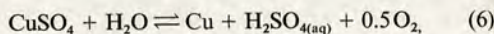
and an efficient materials balance for a circuit will result if the copper is stripped with sulfuric acid at pH < 1.0,



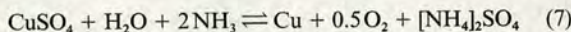
followed by reagent regeneration with base to pH  $\approx$  5.0,



and electrolytic recovery of the metal,



which will regenerate the acid for stripping and gives overall:



The slow rise of copper loading with increase of pH and the failure to load fully until the pH is > 5.5 may be a feature of the reagent containing a significant quantity of the larger ring 2 + 2 condensation product. It is quite probable that this will not so readily form the desired  $\text{CuSO}_4$  complex, and 100% metal loading can only be achieved in the “metal only” form by deprotonation of the ligand at pH > 5.5.

#### X-Ray structure determination

$[\text{Ni}(\mathbf{3a})(\text{SO}_4)] \cdot \text{H}_2\text{O}$  and  $[\text{Cu}(\mathbf{3a})(\text{SO}_4)] \cdot \text{H}_2\text{O}$  are solvated differently in the solid state and the copper complex shows some minor disorder of one of the *tert*-butyl substituent. Apart from this, structural features associated with the assembly of sulfate complexes are remarkably similar. Both are dimers  $[\text{M}(\mathbf{3a})(\text{SO}_4)(\text{H}_2\text{O})]_2$ , Figs. 2–4, with approximately planar  $\text{M}(\text{II})(\text{salen})$  units. The  $\text{N}_2\text{O}_2^{2-}$  donor set is more distorted from planarity and has a larger O–M–O angle (see Table 2) than the related open-chain ligands. This is more pronounced in the nickel complex  $[\text{Ni}(\mathbf{3a})(\text{SO}_4)] \cdot \text{H}_2\text{O}$  with O–Ni–O values of 88.5(3) and 88.8(3)° compared with 83.2(1) to 86.4(1)° for a range of open chain analogues<sup>11</sup> and 82.7(1)° for the related mononickel(II) macrocycle complex of Okawa and co-workers.<sup>12</sup> These distortions may arise in part from the incorporation of the hexamethylene strap and account for the weaker binding of  $\text{Cu}^{2+}$  shown in the solvent extraction experiments (above).

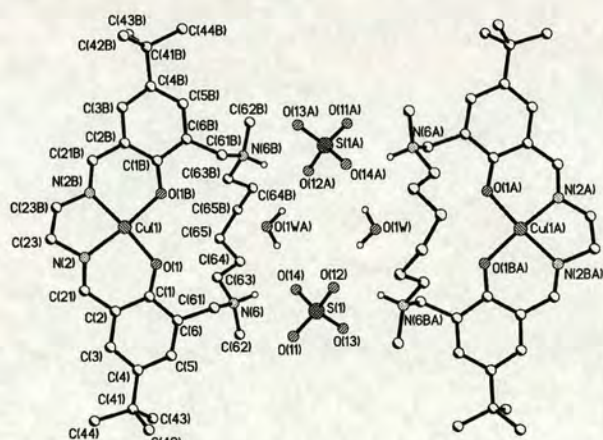
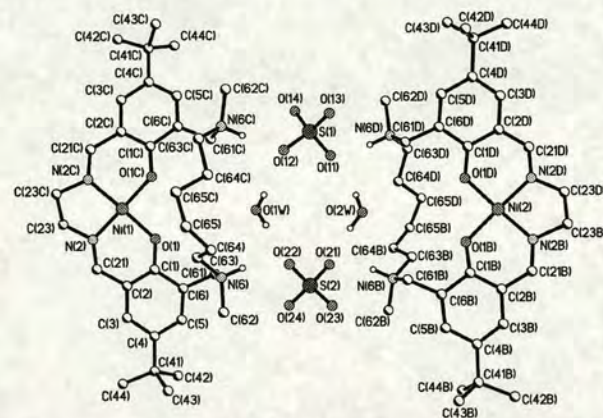
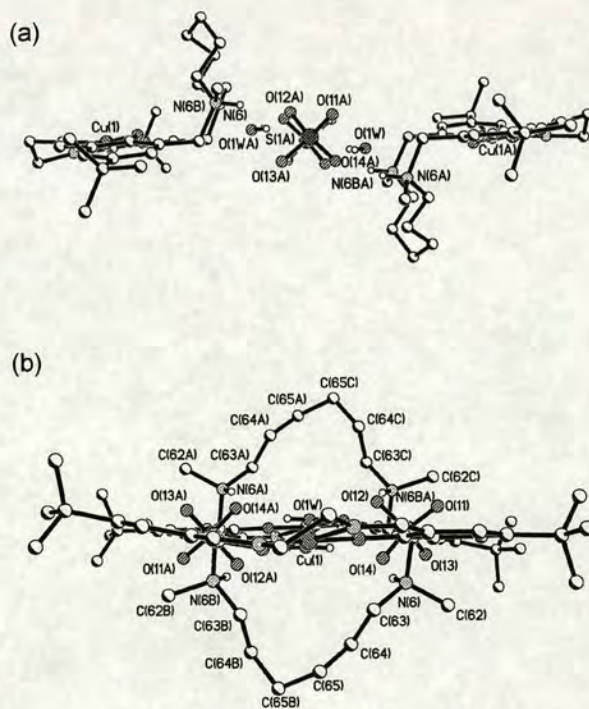
The centres of the dimeric units are composed of two sulfate anions bridged by H-bonded water molecules, see Fig. 5, distances *i* and *j*. This tetranionic unit interacts strongly with the protonated alkylammonium N(6) groups *via* a combination of electrostatic bonding (distances *c* and *d* in Fig. 5) and

‡ This value for  $[\text{Cu}(\mathbf{3b})(\text{SO}_4)]$  is for a 0.01 M solution in chloroform, under the same conditions used for  $[\text{Cu}(\mathbf{1a})(\text{SO}_4)]$ , whilst the value calculated from Fig. 1 of 1.8 is for chloroform containing 5% butan-1-ol.

**Table 2** Selected bond lengths (Å) and angles (°) for [Cu(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O and [Ni(3a)(SO<sub>4</sub>)]·H<sub>2</sub>O

Cu(1)–O(1B)	1.926(4)	Cu(1)–N(2)	1.947(4)
Cu(1)–O(1)	1.912(4)	Cu(1)–N(2B)	1.950(4)
O(1)–Cu(1)–O(1B)	92.94(15)	O(11)–S(1)–O(14)	110.0(3)
O(1)–Cu(1)–N(2)	91.66(17)	O(13)–S(1)–O(14)	108.1(3)
O(1B)–Cu(1)–N(2)	173.75(17)	O(11)–S(1)–O(12)	109.5(3)
O(1)–Cu(1)–N(2B)	174.71(17)	O(13)–S(1)–O(12)	109.0(2)
O(1B)–Cu(1)–N(2B)	92.04(17)	O(14)–S(1)–O(12)	108.3(2)
N(2)–Cu(1)–N(2B)	83.50(18)	N(6B)–S2–S(1)–S1–N(6)	171.28(11)
O(11)–S(1)–O(13)	111.8(3)		
Ni(1)–O(1)	1.862(6)	Ni(2)–O(1B)	1.870(6)
Ni(1)–O(1C)	1.881(6)	Ni(2)–O(1D)	1.849(5)
Ni(1)–N(2)	1.877(7)	Ni(2)–N(2B)	1.845(7)
Ni(1)–N(2C)	1.864(7)	Ni(2)–N(2D)	1.846(7)
O(1)–Ni(1)–N(2C)	178.2(3)	O(11)–S(1)–O(14)	109.1(4)
O(1)–Ni(1)–N(2)	92.7(3)	O(13)–S(1)–O(14)	112.7(5)
N(2C)–Ni(1)–N(2)	85.5(3)	O(11)–S(1)–O(12)	107.7(4)
O(1)–Ni(1)–O(1C)	88.5(3)	O(13)–S(1)–O(12)	109.3(4)
N(2C)–Ni(1)–O(1C)	93.3(3)	O(14)–S(1)–O(12)	108.9(5)
N(2)–Ni(1)–O(1C)	177.9(3)	O(24)–S(2)–O(23)	112.3(5)
N(2B)–Ni(2)–N(2D)	86.0(3)	O(24)–S(2)–O(22)	110.2(4)
N(2B)–Ni(2)–O(1D)	176.4(3)	O(23)–S(2)–O(22)	108.8(4)
N(2D)–Ni(2)–O(1D)	92.9(3)	O(24)–S(2)–O(21)	107.4(4)
N(2B)–Ni(2)–O(1B)	92.3(3)	O(23)–S(2)–O(21)	109.3(4)
N(2D)–Ni(2)–O(1B)	178.3(3)	O(22)–S(2)–O(21)	108.8(4)
O(1D)–Ni(2)–O(1B)	88.8(3)	N(6)–S(2)–N(6B)–S1	170.3(2)
O(11)–S(1)–O(13)	109.0(4)	N(6B)–S(1)–N(6D)–S1	177.5(2)

Symm. equiv. Cu structure: S1 =  $x, y - 1, z$ ; S2 =  $1 - x, -y, -z$ ; S3 =  $1 - x, 1 - y, -z$ ; S4 =  $1 - x, 2 - y, -z$ . Symm. equiv. Ni structure: S1 =  $x - 1, y, z$ .

**Fig. 2** The structure of the centrosymmetric [Cu(3a)(SO<sub>4</sub>)(H<sub>2</sub>O)<sub>2</sub>]<sub>2</sub> unit. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.**Fig. 3** The structure of the pseudo-centrosymmetric [Ni(3a)(SO<sub>4</sub>)(H<sub>2</sub>O)<sub>2</sub>]<sub>2</sub> unit. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.**Fig. 4** Side-on and end-on views of the [Cu(3a)(SO<sub>4</sub>)(H<sub>2</sub>O)<sub>2</sub>]<sub>2</sub> unit. Note the hydrogen bonding arrangement of the sulfate and water molecules with the ammonium nitrogens, and the long alkyl chains above and below the macrocyclic plane. The coordinated nickel structure is very similar. Molecules of solvation and H-atoms attached to C-atoms have been removed for clarity.

H-bonding (distances *g* and *h*) between the ammonium nitrogen atoms and the sulfate ions and also weak H-bonding from the water molecules to the ammonium nitrogen atoms (distances *e* and *f*). On the basis of the distances shown in Fig. 5 the sulfate ion appears to be equally strongly bonded to each of its neighbouring alkylammonium groups and water molecules.

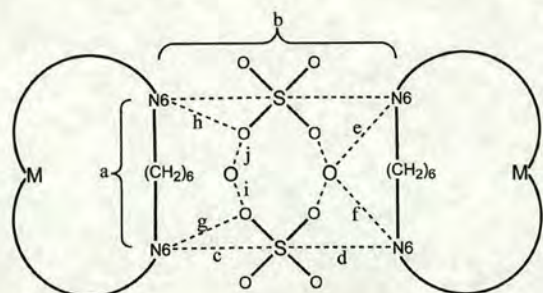


Fig. 5 Schematic diagram showing the hydrogen bonding interactions of the macrocycle dimers with corresponding contact distances.

	Cu	Ni	
a	5.909(7)	6.057(11)	6.009(10)
b	7.364(6)	7.292(11)	7.299(10)
c	3.764(5)	3.685(7)	3.587(8)
d	3.622(4)	3.706(8)	3.640(8)
e	3.518(7)	3.170(11)	3.641(11)
f	3.221(7)	3.783(12)	3.220(11)
g	2.695(6)	2.776(10)	2.701(10)
h	2.751(6)	2.694(10)	2.747(10)
i	2.739(7)	2.720(12)	2.785(10)
j	2.786(7)	2.765(10)	2.717(10)

These interactions lead to an approximately linear intermolecular N(6) ... S(1) ... N(6) arrangement optimising the electrostatic component to bonding. The short intra-molecular N(6) ... N(6) separations (distances *a* in Fig. 5 of 5.909–6.067 Å) make it impossible for a sulfate ion to be included within the macrocyclic cavity defined by the hexamethylene strap as implied in Fig. 1, but point the way towards the design of systems which could incorporate sulfate dimers within the cavity of a related 2 + 2 macrocycle with longer, functionalised, straps between the benzylamino nitrogen atoms (see Fig. 6).

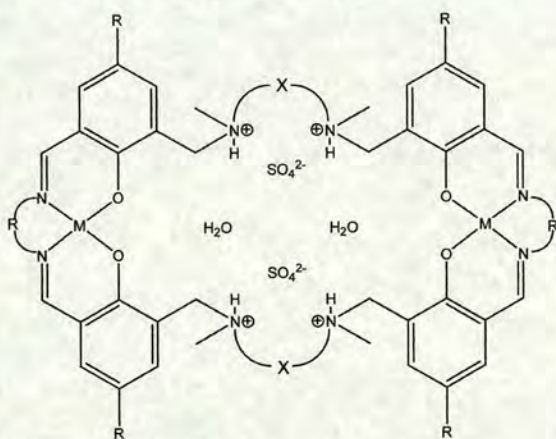


Fig. 6 Inclusion of sulfate dimers within a tetracationic macrocycle cavity.

## Conclusion

Formation of metal sulfate complexes in the zwitterionic forms of the macrocyclic ligands **3a** and **3b** occurs in pH regions which allow loading and stripping under convenient operating conditions. The formation of assemblies with water-bridged

dimers opens up the possibility of transporting the very hydrophilic  $\text{SO}_4^{2-}$  and  $\text{HSO}_4^-$  ions as dimers, the geometries of which are well defined, see for example the recently published<sup>13</sup> studies of  $[\text{Et}_4\text{N}][\text{HSO}_4]$  and references therein.

## Acknowledgements

We thank Mr J. Millar and Mr W. Kerr for obtaining NMR spectra, Mr A. Taylor and Mr H. Mackenzie for mass spectra and Ms S Djurdjevic for elemental analysis. We acknowledge the EPSRC for support under grant GR/R21653 and a studentship (SGG).

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