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Transition Metal Complexes of Expanded Porphyrins

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Transition Metal Complexes of Expanded Porphyrins

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Siamo chimici cioè cacciatori [...]. Non ci si deve mai sentire disarmati: la natura è immensa e complessa, ma non è impermeabile all'intelligenza; devi girarle attorno, pungere, sondare, cercare il varco o fartelo.

We are chemists, that is, hunters [...]. We must never feel unarmed: nature is immense and complex, but it is not impermeable to the intelligence; we must circle around it, poke and probe, find the passage or make it.

Primo Levi, *Il Sistema Periodico*, Einaudi: Torino, 1975

(Translated by E. Tomat)

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Transition Metal Complexes of Expanded Porphyrins

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Over the last three decades, the rapid development of efficient synthetic routes for the preparation of expanded porphyrin macrocycles has allowed the exploration of a new frontier involving “porphyrin-like” coordination chemistry. This doctoral dissertation describes the author’s exploratory journey into the area of transition metal cation complexation using oligopyrrolic macrocycles. The reported synthetic findings were used to gain new insights into the factors affecting the observed coordination modes and to probe the emerging roles of counter-anion effects, tautomeric equilibria and hydrogen-bonding interactions in regulating the metalation chemistry of expanded porphyrins.

The first chapter provides an updated overview of this relatively young coordination chemistry subfield and introduces the idea of expanded porphyrins as a diverse family of ligands for metalation studies. Chapter 2 details the synthesis of a series of binuclear complexes and illustrates the importance of metal oxidation state, macrocycle protonation and counter-anion effects in terms of defining the final structure of the observed metal complexes. The binding study reported in Chapter 3 demonstrates a

strong positive allosteric effect for the coordination of silver(I) cations in a Schiff base expanded porphyrin. Chapter 4 introduces the use of oligopyrrolic macrocycles for the stabilization of early transition metal cations. Specifically, the preparation of a series of vanadium complexes illustrates the bimodal (i.e., covalent and noncovalent) recognition of the non-spherical dioxovanadium(V) species within the macrocyclic cavities. Experimental procedures and characterization data are reported in Chapter 5.

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Chapter 1

Introduction and historical overview

1.1 GENERAL BACKGROUND

Living systems routinely synthesize tetrapyrrolic macrocycles, either in their metal free forms (e.g., pheophorbide) or, more commonly, as the corresponding metal complexes (e.g., chlorophyll, heme, vitamin B₁₂, etc.). The resulting species have been called “the pigments of life” because they perform a variety of fundamental biological functions that lie at the very core of life as we understand it.¹

Figure 1.1 Examples of naturally occurring metal complexes of tetrapyrrolic macrocycles. From left to right: chlorophyll *a*, heme, and vitamin B₁₂.

While the extraordinary chemistry of these tetrapyrrolic compounds continues to fascinate chemists, biologists and materials scientists, over the last few decades increasing attention has been devoted to the development of a new class of ligands termed “expanded porphyrins”.²⁻⁴ The defining feature of these oligopyrrolic macrocycles is a larger internal cavity as compared to those present in natural tetrapyrroles. More

specifically, expanded porphyrins are macrocyclic compounds containing five-membered heterocyclic units (pyrrole, furan, or thiophene-like) linked together, either directly or through spacers, so that the internal ring pathway contains at least 17 atoms.

Over the past three decades, the focus on expanded porphyrin chemistry has led to some remarkable synthetic advances and provided new insights into the fundamental features of aromaticity.⁵ More recently, the scope of expanded porphyrin chemistry has grown to encompass the field of anion binding and transport.⁶ However, one of the main motivating forces behind the synthesis of expanded porphyrins continues to be the promise to extend the frontiers of “porphyrin-like” coordination chemistry so as to provide new complexes with unprecedented features.

To date, some of this latter promise has been realized. For instance, expanded porphyrins have allowed for the generation of complexes containing multiple cations and for the stabilization of large cations such as those of the lanthanide and actinide series. These synthetic findings, combined with a wide range of spectroscopic and physical properties, have prompted the study of expanded porphyrin metal complexes as photosensitizers in photodynamic therapy,^{7,8} contrast agents in magnetic resonance imaging,⁹ building blocks in nonlinear optical materials,^{10,11} and enzyme models in bioinorganic chemistry.¹²

While a complete overview of the evolution of expanded porphyrin chemistry can be found in the comprehensive reviews authored by Sessler^{3,4} and by Dolphin,² this introductory chapter intends to provide the reader with a historical perspective on the coordination of transition metals in expanded porphyrins. As such, the well known coordination of the actinide oxocations in oligopyrrolic systems¹³ will not be included in the present introduction. Additionally, since the investigations reported in this Dissertation feature exclusively pyrrole-based systems, the metalation of core-modified

(i.e., furane- or thiophene-based) expanded porphyrins will not be extensively reviewed and the interested reader is referred to more specialized sources.¹⁴ Nonetheless, when instrumental to the discussion or needed to frame a comparative argument, such systems will be appropriately cited.

Although far from complete, this introduction does aim to highlight the diversity of the available expanded porphyrin ligands and the principal advances in the field over the past two decades. It is hoped that this first chapter will provide a useful underpinning for the research work reported by the author in the ensuing chapters of this Dissertation and it will allow the readers to obtain a glimpse into the expanded porphyrin coordination chemistry that remains to be explored.

1.2 CARBON-BRIDGED SYSTEMS

The expanded porphyrins that display the greatest resemblance to natural porphyrins are those that contain either *meso*-like bridging carbon atoms or direct links between the heterocyclic subunits. According to the nomenclature put forward by Franck and Nonn,¹⁵ the name of these systems consists of three parts: 1) the number of π -electrons in the shortest conjugation pathway (in square brackets), 2) a core name indicating the number of pyrroles or other heterocycles (e.g., pentaphyrin, hexaphyrin), 3) the numbers of bridging carbon atoms between each pyrrole subunit (in round brackets and separated by dots). For instance, according to this nomenclature, the classic porphyrin macrocycle featured in the heme group (Figure 1.1) would be named as [18]tetraphyrin(1.1.1.1).

1.2.1 [22]Pentaphyrin(1.1.1.1.0) (sapphyrin)

The aromatic pentapyrrolic macrocycle **1.1** represents the first reported example of an expanded porphyrin and was discovered serendipitously by Woodward and coworkers in the early 1960s.¹⁶ Since this compound crystallizes as a dark blue solid, Woodward assigned it the name “sapphyrin” and thus began a trivial nomenclature for these macrocycles whose names end with the suffix “phyrin” or “rin” taken from porphyrin. Although limited to widely recognized systems, this unorthodox nomenclature will generally be used in this Dissertation.

The size of the cavity (ca. 5.5 Å vs. ca. 4.0 Å for porphyrins) and the presence of an additional nitrogen donor led Woodward and his group to envision the use of sapphyrins for metal coordination. Their early investigations showed that Co(II) and Zn(II) complexes could be isolated, but no structural information was obtained.¹⁶

The coordination chemistry of sapphyrin was reexamined by the Sessler group in the early 1990s. The difficulty in the characterization of the cobalt and zinc complexes was attributed to the small size of the coordinating cations and thus to inherent kinetic instability. In fact, the first fully characterized complexes of sapphyrin were prepared using rhodium and iridium dicarbonyl chloride salts in the presence of triethylamine (Scheme 1.1).^{17,18}

Scheme 1.1 Reactions of sapphyrin with rhodium and iridium carbonyl compounds.

In the resulting rhodium(I) and iridium(I) complexes, the metal carbonyl units are found above or below the mean macrocycle plane defined by the oligopyrrolic scaffold and each metal center is bound to a dipyrinato moiety of the sapphyrin scaffold. This coordination mode is reminiscent of the one reported for $[\text{Rh}(\text{CO})_2]_2(\text{octaethylporphyrin})$ and was later observed in several stable Rh(I) complexes of expanded porphyrins, such as Sessler's amethyrin¹⁹ (*vide infra*), Chandrashekar's core-modified smaragdyrin,²⁰ Furuta's N-confused pentaphyrin,²¹ and Osuka's N-fused pentaphyrin.²² Interestingly, the isolation of the *mono*-Rh(CO)₂ complex **1.2** and the *mono*-Ir(CO)₂ sapphyrin **1.3** allowed the preparation of the heterobimetallic species **1.6** by simple addition of Ir(CO)₂(py)Cl or Rh₂(CO)₄Cl₂, respectively (Scheme 1.1).

Analogous complexes of Rh and Ir with heterosapphyrins have been reported, including the structurally characterized monothiasapphyrin-*bis*[dicarbonylrhodium(I)]²³ **1.7** and monoselenasapphyrin-*bis*[dicarbonyliridium(I)]²⁴ **1.8** (Figure 1.2).

Figure 1.2 Structurally characterized complexes of heterosapphyrins.

The study of heterosapphyrins also led to the isolation of the *mono*-cobalt(II) complexes²³ **1.9a-c**, in which the metal centers are bound to two pyrrolic nitrogens (Figure 1.2). In contrast to what was seen in the case of Rh(I) and Ir(I), insertion of Co(II) cations was not accompanied by deprotonation of the ligand. Rather, a tautomeric rearrangement of the pyrrolic protons was found to take place. This allows the metal

center to retain its counter anions (Cl^- or OAc^-) and to coordinate to two iminic nitrogens on neighboring pyrrolic subunits.

To date, the metalation chemistry of sapphyrins has not displayed the diversity observed for other macrocycles (*vide infra*). However, the recent discovery of the biological activity of hydrophilic sapphyrins²⁵ as potential cancer therapeutics is likely to fuel new studies of this most venerable expanded porphyrin system.

1.2.2 [24]Hexaphyrin (1.0.0.1.0.0) (amethyrin)

Amethyrin, a 24 π -electron hexapyrrolic macrocycle, owes its name to the purple color (from Greek *amethus*) displayed by its protonated form in organic solution. This system was first reported by the Sessler group and was the first expanded porphyrin in which the in-plane coordination of two cations was established unequivocally.²⁶ In particular, it was found that reaction of the dichloride acid salt of amethyrin with ZnCl_2 in the presence of Et_3N afforded the *bis*-zinc complex **1.10** (Figure 1.3) after purification by column chromatography. X-ray diffraction analysis of the isolated product showed that each zinc center coordinates to a dipyrinato moiety and to two bridging counterions, namely a chloride and a hydroxyl anion (the latter presumably exchanged for chloride during chromatographic purification). The central pyrrole units in this complex do not contribute directly to the primary coordination spheres of the metal centers, but are engaged in hydrogen-bonding interactions with the bridging anions.

Figure 1.3 Transition metal complexes of amethyrin.

In a parallel metalation study, it was found that the reaction of amethyrin with CoCl_2 produced a complex wherein only a single metal cation is coordinated (**1.11**, Figure 1.3). In analogy to what was observed for the cobalt complexes **1.9a-c** of heterosapphyrins, the metal insertion proceeds with no deprotonation of the ligand and is accompanied by a tautomeric rearrangement that affects the conjugation pathway of the macrocycle. As a result, the cobalt(II) center appears to fill its coordination sphere with two iminic nitrogen atoms from neighboring pyrrolic units.

Amethyrin was also reported to form a *mono*- and a *bis*- $[\text{Rh}(\text{CO})_2]$ adduct (**1.12**);¹⁹ however, in contrast to what was seen for the *bis*- $[\text{Rh}(\text{CO})_2]$ complexes of octaethylporphyrin, sapphyrin, and various heterosapphyrins, in the case of amethyrin the two rhodium centers were found to lie on the same side of the convex, bowl-shaped macrocycle. Presumably, this reflects the greater size of amethyrin relative to, for example, sapphyrin.

Tests carried out with other late transition metals confirmed that amethyrin can stabilize the formation of bimetallic nickel(II) and copper(II) complexes. A *bis*-Ni complex was obtained by treating the free base form of the macrocycle with $\text{Ni}(\text{acetylacetonate})_2$; however, this complex was not characterized by X-ray diffraction analysis and thus the coordination mode of the metal centers could not be deduced.²⁷ Conversely, treatment of amethyrin with CuCl and subsequent exposure to air afforded a

bis-Cu(II) complex (**1.13**, Figure 1.3) which was structurally characterized. The divalent oxidation state for the copper centers in **1.13** was confirmed by EPR spectroscopy and SQUID magnetometry. Each of the cations, held at an unusually short Cu...Cu distance of 2.761(1) Å, is bound to three nitrogen donors, with the net result that all of the pyrrolic nitrogen atoms are engaged in metal coordination.²⁸

A recent investigation of main group expanded porphyrin chemistry further underscored the scope of amethyrin as a ligand in that stable, non-labile *mono*- and *bis*-BF₂ complexes were obtained.²⁹

Amethyrin was the first binucleating expanded porphyrin to show a diverse coordination chemistry and to provide access to multiple coordination modes. It thus demonstrated that expanded porphyrins had a role to play as novel nitrogen-rich ligands.

1.2.3 N-Confused, N-Fused and Inverted Expanded Porphyrins

The first examples of N-confused porphyrins were independently reported in 1994 by the groups of Furuta³⁰ and Latos-Grazynski.³¹ While in naturally-occurring porphyrins the pyrrole rings are connected to the *meso* carbon atoms at the α and α' positions, in these synthetic isomers, one of the pyrrole rings is connected to the *meso* carbon atoms at the α and β' positions (Figure 1.4).

Figure 1.4 From the left: classic, N-confused, inverted and N-fused connectivity as seen in oligopyrrolic macrocycles.

Since those first reports, the so-called “confusion approach” has led to the development of a new breed of porphyrinoid ligands.^{21,32} The remarkable structural diversity of these macrocycles features many cases of *inverted* pyrrole rings (i.e., with the NH group pointing outside the macrocycle cavity) and *N-fused* tripentacyclic rings, in which the nitrogen atom of a pyrrole ring is bound to a β carbon of a neighboring inverted pyrrole (Figure 1.4).

While the main focus of work in this area have concerned with the synthesis of new macrocycles, many transition metal complexes of confused porphyrin and expanded porphyrin analogues have been reported. Interestingly, as recently reviewed by Furuta,³² Ziegler³³ and Latos-Grazynski,³⁴ several examples of metal-carbon bond formation were observed in metalation studies of N-confused porphyrins (complexes **1.14-16**, Figure 1.5). Indeed, these ligands have been appropriately identified as new “macrocyclic platforms for organometallic chemistry”.³⁴

Figure 1.5 Examples of organometallic N-confused and doubly N-confused porphyrins.

The extension of the confusion approach to pentapyrrolic and hexapyrrolic systems was pioneered by Osuka and Furuta, who reported the first example of a binucleating N-confused macrocycle.³⁵ Specifically, the doubly N-confused hexaphyrin **1.17** (Scheme 1.2) allowed for the in-plane coordination of a series of late transition metals (i.e., Mn(III), Fe(III), Co(II), Ni(II), Cu(II), and Zn(II)).^{36,37}

Scheme 1.2 Preparation of a binuclear copper(II) complex of the doubly N-confused hexaphyrin **1.17**.

The photophysical properties of the Co(II), Cu(II), and Zn(II) complexes of **1.17** are currently the object of an ongoing investigation for their potential use in nonlinear optical devices.³⁷

Osuka and collaborators have extensively investigated the redox behavior and the metalation chemistry of doubly-inverted *meso*-aryl substituted hexaphyrins.²² Interestingly, it was found that the insertion of gold(III) cations in [26]hexaphyrin(1.1.1.1.1.1) **1.19** was accompanied by activation of the pyrrolic β C-H bonds and hence organometallic *mono*- and *bis*-Au(III) complexes were isolated (Scheme 1.3).³⁸ Reaction of the *mono*-Au(III) species **1.20** with a silver(I) salt then afforded the Au(III)/Ag(III) heterobimetallic complex **1.22**, for which it was proposed that the oxidation from Ag(I) to Ag(III) allows the silver cation to fit in the macrocyclic core.³⁸

The ¹H NMR spectra of the gold complexes **1.20** and **1.21** showed resonances that are characteristic of aromatic macrocycles; for instance, the inner β -CH and NH proton peaks in **1.20** were observed at δ_{H} -2.93 and -2.08 ppm, respectively. The planar macrocyclic scaffold of **1.20** and **1.21**, rigidified by coordination to the gold centers, proved to be an ideal framework to investigate the factors that regulate aromaticity. Indeed, both complexes were reduced with NaBH₄ to give the 28 π -electron hexaphyrin complexes **1.23** and **1.24** without demetalation. Consistent with the Hückel rule as

extended to encompass heteroannulene systems, the ^1H NMR spectra of these complexes show a paratropic ring-current effect; for instance, the inner $\beta\text{-CH}$ and NH proton peaks in **1.23** were observed at δ_{H} 19.39 and 24.57 ppm, respectively.

Scheme 1.3 Preparation and reactivity of the gold(III) complexes of the doubly inverted hexaphyrin(1.1.1.1.1.1).

The coordination chemistry of N-confused, inverted, and N-fused expanded porphyrins, in which the pyrrolic units can act as both nitrogen donors and organometallic ligands, is one of the fastest moving areas in the generalized field of pyrrole-based macrocyclic chemistry.

1.2.4 Figure-eight octaphyrins and decaphyrins

In 1999, the Sessler group reported the preparation of [40]decaphyrin(0.0.1.0.1.0.0.1.0.1), a large conjugated system that was found to adopt a

“figure-eight” conformation both in solution and in the solid state.³⁹ This macrocycle, commonly known as turcasarin, featured two nitrogen-rich pentapyrrolic pockets. This structural feature led to the consideration that turcasarin might prove useful for anion transport and metal coordination. Indeed, preliminary metalation studies provided evidence the formation of uranyl⁴⁰ and copper⁴¹ complexes. However, these complexes were not fully characterized and the coordination chemistry of turcasarin remains largely unexplored. Nonetheless, the synthesis of turcasarin represented an important breakthrough in that it illustrated that full conjugation of heteroannulenes did not necessarily imply planarity. It thus paved the way for a number of other “twisted” oligopyrrolic macrocycles that were developed subsequently.

Vogel and coworkers reported the synthesis of a variety of figure-eight octaphyrins^{42,43} and they were the first to prepare and study a series of binuclear figure-eight metal complexes.^{44,45} Additionally, the successful separation of a racemic figure-eight octaphyrin mixture into its enantiomeric constituents was heralded as the first step towards the development of chiral expanded porphyrin catalysts.⁴⁴

In an example reported by the collaborating groups of Vogel and Houk,⁴⁶ the coordination chemistry of figure-eight octaphyrins revealed its most striking aspect (Scheme 1.4 A), namely the thermal splitting of the octapyrrolic macrocycle **1.25** into two tetrapyrrolic subunits directly connected through a *spiro* center (i.e., a tetrahedral quaternary carbon bridge in complex **1.26**).

Scheme 1.4 Thermal splitting of figure-eight octaphyrins into two tetrapyrrolic components. A: Preparation of a *spiro*-diporphyrin as reported by Vogel *et al.*⁴⁶ B: Total cleavage of a *bis*-Cu(II) octaphyrin complex as reported by Osuka *et al.*⁴⁷

More recently, Osuka and coworkers demonstrated that the ultimate step in the reactivity at the figure-eight crossing center is the total cleavage of the binuclear octaphyrin into two mononuclear tetrapyrrolic complexes. In this important contribution, the thermal splitting of the binuclear copper(II) [36]octapyrin(1.1.1.1.1.1) **1.27** is shown to generate two copper(II) [18]porphyrin(1.1.1.1) complexes (Scheme 1.4).⁴⁷

While unexpected, the peculiar transannular reactivity of octaphyrins has shown that the crossing center of figure-eight metal complexes represents a new chemical environment for the transformation of expanded porphyrins.

1.3 NITROGEN-BRIDGED SYSTEMS

Imine-containing pyrrolic macrocycles, or Schiff base expanded porphyrins, are systems wherein a *meso* carbon is formally substituted by a nitrogen atom. In many cases, the metal complexes of such systems have proved to be more stable than the metal-free forms. In other cases, the macrocycle is obtained most easily as the result of direct

metal-templating procedures, as has been appreciated by workers in the area since the first seminal studies of Schiff base pyrrolic macrocycles by the Fenton group in the mid-1980s.⁴⁸

As implied above, Fenton and coworkers were the first to use a pyrrolic precursor, namely pyrrole-2,5-dicarbaldehyde, for the preparation of a Schiff base macrocycle. Specifically, a copper(II) complex (**1.28**, Scheme 1.5) was prepared via the metal templated condensation of the 2,5-substituted pyrrole with an alkylamine in the presence of Cu(II) ethanoate.

Scheme 1.5 First example of a metal-templated preparation of a Schiff base oligopyrrolic macrocycle.

In general, the coordination chemistry of Schiff base expanded porphyrins has evolved in parallel with their synthetic development and, for a complete overview of the synthesis and coordination chemistry of such ligands, the reader is referred to a recent review article co-authored by two former Sessler group members, Wyeth Callaway and Jackie Veauthier.⁴⁹

1.3.1 Texaphyrin

Arguably the best studied of the Schiff base oligopyrrolic macrocycles, texaphyrin (**1.29**) represents the first expanded porphyrin for which a rich coordination

chemistry was described. It thus played an important historical role in terms of showcasing some of the advantages of “expanding” the porphyrin core. The lutetium(III) and gadolinium(III) complexes of a water-soluble texaphyrin have been the subject of clinical study as potential photosensitizers and radiation enhancers, respectively. To date, these two systems have been evaluated in a number of human clinical trials that have tested their use in the treatment of atherosclerotic disease and a number of cancers, including metastatic brain cancer, neuroblastoma, pediatric brain stem glioma, and non-small cell lung cancer. The biochemistry and physiology involved in these medical applications lies outside the scope of this introduction and it has, however, been reviewed elsewhere.⁸

The pentaaza core of texaphyrin is 20% larger than that of porphyrin and offers a “lone-star” pentagonal array of nitrogen donors that provide a single negative charge when the ligand is deprotonated. In the early 1990s this cavity was found to be suitable for the coordination of all non-radioactive lanthanide(III) cations;⁵⁰ however, it was not until 2002 that a series of first-row transition metal complexes (i.e., Mn(II), Fe(III), Co(II), Ni(II), and Zn(II)) of texaphyrin was reported.⁵¹ It was found that the metal insertion proceeds through a simultaneous oxidation/metalation analogous to the one previously observed in the preparation of lanthanide complexes. Specifically, the non-aromatic texaphyrin macrocycle, **1.29**, termed “sp³-texaphyrin” due to the hybridization state of the meso-like carbon bridges, undergoes oxidation to the aromatic form upon complexation of the metal cation (Scheme 1.6).

The Fe(III) texaphyrin complex **1.30** was isolated as a μ -oxo dimer, a common product in iron porphyrin chemistry.⁵² Conversely, the corresponding manganese and cobalt texaphyrin complexes, **1.31** and **1.32**, feature Mn(II) and Co(II) centers, respectively, even though these cations are typically stabilized in the +3 oxidation state in

porphyrin ligands. Presumably, the increased cavity size, as well as the decreased ligand charge, favors stabilization of the lower oxidation state complexes, which are found in rather uncommon six- or seven-coordinate geometries.

Scheme 1.6 Synthesis of transition metal complexes of texaphyrin.

Finally, the solid-state structure of the Zn(II) complex **1.34** provided the first example of texaphyrin acting as a tridentate ligand.[§] In fact, the relatively small zinc cation is seen to coordinate only to the tripyrrolyldimethene fragment. This stands in contrast to what is observed in the case of the largest lanthanide cations (e.g., La(III)), where the metal centers are found to sit above the plane of the pentadentate macrocycle. These two kinds of complexes thus represent opposite ends of the texaphyrin coordination “spectrum” (Table 1.1).

[§] A similar N3 binding mode was observed by Bröring and coworkers, who reported a series of open-chain transition metal complexes of the tripyrrolyldimethene fragment; see: Bröring, M.; Brandt, C. D.; Prikhodovski, S., *J. Porphyr. Phthaloc.* **2003**, 7, 17-24.

Table 1.1 Ionic radii* of selected metal cations coordinated by texaphyrins.

Cation	Ca ²⁺	Mn ²⁺	Zn ²⁺	La ³⁺	Gd ³⁺
Coordination number	6	6	4	7	7
Ionic radius (Å)	1.14	.89	.74	1.24	1.14

*[Source: Shannon, D. R. *Acta Crystallogr.* **1976**, A32, 751-767]

The availability of texaphyrin transition metal complexes provided an incentive to investigate their potential biomedical applications. In the context of this work, a water-soluble Mn(II) texaphyrin complex was prepared; it was found to act in vitro as a catalyst for the decomposition of peroxynitrite,⁵³ a reactive oxygen species whose cytotoxic effects have been implicated in numerous disorders, including cancer, amyotrophic lateral sclerosis, and atherosclerosis.

1.3.2 Dipyrromethane-based systems

The use of dipyrromethane derivatives for the synthesis of expanded porphyrins dates back to the mid-1980s, specifically to the seminal work of Mertes (now Bowman-James) and coworkers, who reported the preparation of the so-called “accordion porphyrins”. These macrocycles, with two accordion-like aliphatic chains bridging two dipyrromethane moieties, were initially isolated as binuclear lead and copper complexes.⁵⁴

Figure 1.6 Complexes of “accordion” porphyrins.

Later, the *bis*-Mn(II) accordion porphyrin complex **1.36**, in which the two manganese centers are held at a distance of 5.40 Å, was found to act as a functional model for metalloenzymes such as monooxygenases¹² and catalases.⁵⁵ As such, accordion porphyrins were the first expanded porphyrins to demonstrate the potential of these ligands in the field of enzyme modeling.[†]

In the mid-1990s, Dolphin and coworkers reported the first example of an aromatic dipyrromethane-based Schiff-base expanded porphyrin. “Porphyracine” **1.37** was found to coordinate ZnCl₂ to afford the mononuclear Zn(II) complex **1.38** (Scheme 1.7).⁵⁶ An X-ray diffraction analysis of **1.38** revealed that, as expected from an aromatic system, the macrocyclic core of porphyracine was fully planar.

Scheme 1.7 Metalation of the aromatic Schiff base porphyracine.

[†] Brooker and coworkers recently reported the synthesis of dicopper(II) and dinickel(II) complexes of accordion porphyrin analogues derived from dimethyldiformyldipyrromethane; see: Li, R.; Mulder, T. A.; Beckmann, U.; Boyd, P. D. W., Brooker, S. *Inorg. Chim. Acta* **2004**, 357, 3360-3368.

More recently, a dipyrromethane subunit, combined with a diamidopyridine fragment, was incorporated into the Schiff base hybrid macrocycle **1.39**. This ligand, which proved to be an effective anion binding receptor,⁵⁷ can be selectively oxidized to the conjugated diiminodipyrromethene system **1.40** (Scheme 1.8). A first metalation study of this macrocycle has shown that the Pd(II) cation binds preferentially to the pyrrolic moiety, both in the dipyrromethane system **1.41** and in the oxidized dipyrromethene system **1.42**.⁵⁸

Scheme 1.8 Oxidation and metalation reactions of a hybrid macrocycle that incorporates a dipyrromethane unit and a diamidopyridine moiety.

In recent years, binucleating dipyrromethane-based Schiff base macrocycles have appeared in a number of metalation studies carried out by the Sessler group, as well as the groups of Jason Love and Polly Arnold at the University of Nottingham, UK. These investigations resulted in the isolation of several transition metal complexes that will be compared to the ones reported by the author in Chapter 2 of this Dissertation. As such, the details of this chemistry will not be discussed in this introductory chapter, but rather postponed to that context.

1.4 OBJECTIVE AND OUTLINE OF THIS DISSERTATION

A major thrust of modern coordination chemistry is the engineering of nano-scaled spaces for the stabilization, activation, or recognition of metal ions. In the expanded porphyrin field, this has inspired the preparation of a number of novel pyrrole-based macrocyclic receptors. The main objective of this Dissertation is the exploration of expanded porphyrin cavities as novel chemical environments for transition metal coordination.

It is hoped that this first chapter has served as a useful summary of the state of the art in expanded porphyrin coordination chemistry. A portion of this introduction has been submitted for publication in *Accounts of Chemical Research* as a review article coauthored by Professor Jonathan L. Sessler and by the author of this Dissertation.

Chapter 2 describes the preparation of a series of late transition metal complexes of binucleating Schiff base expanded porphyrins. These synthetic findings illustrate the role of metal oxidation state, macrocycle protonation and counter-anion effects on the coordination modes of the resulting complexes. Part of this material has appeared on *Inorganic Chemistry* (as a communication⁵⁹ and as a full article⁶⁰) and was prepared in collaboration with Dr. Jacqueline M. Veauthier. The magnetic properties of the reported paramagnetic bimetallic species have been investigated thanks to a fruitful collaboration with the group of Professor John T. Markert of the Department of Physics of this University.

Chapter 3 presents a binding study that proves the cooperative behavior of silver(I) coordination in a binucleating Schiff base macrocycle. A portion of these findings, unprecedented in expanded porphyrin chemistry, has been reported in the *Journal of the American Chemical Society* as a Communication to the Editor.⁶¹

Chapter 4 details the first examples of early transition metal coordination in expanded porphyrin ligands. The bimodal recognition of the non-spherical dioxovanadium(V) cation, achieved through both covalent and noncovalent interactions, underscores a supramolecular aspect of this metalation chemistry and highlights the emerging roles of tautomeric equilibria and hydrogen bonding in expanded porphyrin coordination chemistry. While part of this material has appeared in *Chemical Communications* as a cover feature article,⁶² the latest findings described in this chapter have been recently reported in *Dalton Transactions* as a Communication to the Editor.⁶³

The experimental procedures for all the synthetic work described in this Dissertation are detailed in Chapter 5. The crystal structure refinements for all novel complexes were performed by Dr. Vincent M. Lynch of the X-ray Diffraction Laboratory of this Department. The resulting X-ray diffraction analysis data and refinement parameters are included in Appendix A. The magnetic measurements and data analyses, conducted in collaboration with Dr. Utkur Mirsaidov and Professor John T. Markert of the Department of Physics of this University, are detailed in Appendix B.

Chapter 2

Binuclear Transition Metal Complexes of Schiff Base Expanded Porphyrins

2.1 INTRODUCTION

A considerable effort has been devoted in recent years to the preparation of binuclear complexes of expanded porphyrins.^{12,22,49,64}

The fast-growing interest in this field reflects a confluence of several factors. First, several polypyrrolic macrocycles have been found to act as ligands for a range of larger cations (i.e., cations of the lanthanide⁵⁰ and actinide¹³ series), which has led to the consideration that more than a single metal center could be coordinated in appropriate systems. Second, in contrast to the relatively rigid scaffold provided by porphyrin and other naturally occurring tetrapyrrolic macrocycles, the size and functionalities of expanded porphyrins can be varied to allow access to a larger number of coordination modes. Third, the preorganization of two or more metals centers at short separations (2.5 - 6.0 Å) could pave the way to studies involving cooperativity in catalysis and enzyme mimicking.

Given the number of expanded porphyrin macrocycles prepared to date and the relatively small number of well characterized metal complexes that have been reported (see Chapter 1), it appears that many aspects of expanded porphyrin coordination chemistry remain to be explored.

This Chapter describes the preparation and structural characterization of a series of binuclear complexes of oligopyrrolic octaaza macrocycles with late first-row transition metals. Aside from their peripheral substitution patterns, the two ligands chosen for this

investigation (Figure 2.1) differ substantially with regard to the dipyrrolic precursor used for the macrocycle preparation, namely a dipyrromethane for **2.1** and a bipyrrrole for **2.2**. The metal complexes described in the present Chapter will demonstrate that, at least for these two systems, the difference of one methylene bridge in the macrocycle scaffold has a significant influence on the observed coordination modes.

Figure 2.1 Schiff base octaaza macrocycles utilized as binucleating ligands for the preparation of late transition metal complexes.

The coordination ability of each ligand will be examined from several points of view, probing the influence of the metal oxidation state and of the anionic counterions on the metalation chemistry. Additionally, it will be shown that, under appropriate reaction conditions, both the free base and the diacid salt form of the macrocycles can be used as ligands for coordination studies.

2.2 COMPLEXES OF A DIPYRRROMETHANE-BASED MACROCYCLE

2.2.1 Background

The preparation of the dipyrromethane-based macrocycle **2.1** was reported by the Sessler group in 2003.⁶⁵ While **2.1** proved to be an efficient receptor for the chloride anion,⁶⁵ the wide nitrogen-rich cavity of this ligand motivated the investigation of its potential as a binucleating cation receptor.

The first metalation attempts were focused on the preparation of binuclear iron complexes. While reactions using simple iron salts (e.g., FeCl₃, Fe(acetylacetonate)₃, [Fe(CH₃CN)₆][AlCl₄]₂) failed to afford identifiable metal complexes, the organometallic Fe₂Mes₆ reagent proved to be an excellent iron source.⁶⁶ This organometallic species is a convenient deprotonating agent and, further, does not introduce any anionic counterion into the reaction mixture. Indeed, the use of transition metal mesityl compounds, unprecedented in the metalation chemistry of expanded porphyrins, provided a new strategy for the exploration of the reactivity towards metal cations of ligands such as **2.1** and **2.2**. The work on iron coordination, carried out by Dr. Jackie Veauthier in the Sessler labs, actually initiated a more general investigation, which developed in part into the copper coordination studies described in the present Chapter.

The μ -oxo *bis*-Fe(III) complexes **2.3** and **2.4** (Scheme 2.1) were the first examples of iron complexes in which a Fe(III)-O-Fe(III) bridge is stabilized within a single macrocyclic framework. Interestingly, the structures of the complexes obtained during the metal insertion reaction depended on the protonation state of the starting macrocycle. In complex **2.3**, obtained from the free base **2.1b**, the macrocycle behaves as a *bis*-tetradentate ligand. On the other hand, when the same reaction conditions are applied to the corresponding acid salt, **2.1b**·2HCl, the resulting complex **2.4** features a *bis*-tridentate ligand and retains two chloride anions.

Scheme 2.1 Synthesis of μ -oxo-bridged *bis*-iron(III) complexes.

The iron complexes **2.3** and **2.4** provided support for the notion that macrocycles such as **2.1** are able to stabilize a variety of coordination modes, which are affected by the protonation state of the ligand and by the presence of anionic counterions.

In an independent metalation study that was also reported in 2004, Love and coworkers described the preparation of a *bis*-Pd(II) complex (**2.5**, Figure 2.2) of macrocycle **2.1a**.⁶⁷ In complex **2.5**, the macrocycle was found to act as a *bis*-tetradentate ligand, with the two Pd(II) ions stabilized in a typical square planar geometry.

Additionally, work in the collaborating groups of Love and Arnold produced the first example of actinide coordination in macrocycle **2.1**.⁶⁸ Reaction of a uranyl trimethylsilylamido reagent with the free base form of the ligand resulted in the formation of the *mono*-UO₂²⁺ complex **2.6**, in which the oxocation is coordinated within one of the N₄-donor pockets of the macrocycle. Interestingly, the monouranyl complex **2.6** could be used as a substrate for the further coordination of Mn(II), Fe(II), and Co(II) cations to afford three different heterobimetallic complexes (**2.7-9**, Figure 2.2).⁶⁹

Figure 2.2 Metal complexes of macrocycle **2.1** reported by Love, Arnold and coworkers. Complexes **2.7-9** were the first examples of transition-metal uranyl binuclear complexes stabilized with this type of ligands.

The versatility of oligopyrrolic Schiff base macrocycles, such as **2.1**, was further highlighted by the work of Love and coworkers, who reported an unusual metal-directed expansion of the macrocycle scaffold (see Section 2.2.4),⁷⁰ as well as a series of binuclear transition metal complexes (including Cd(II), Ni(II), Cu(II), and Mn(II)) with analogous ligands.⁷¹

2.2.2 Synthesis and Magnetic Behavior of a *bis*-Cu(II) Complex

The interesting coordination chemistry of **2.1**, much of which was only on the horizon at the time this project was initiated, led us to consider a study of its reactivity towards copper species. Both Cu(I) and Cu(II) were expected to be stabilized within the macrocyclic cavity. Moreover, it was anticipated that the coordination geometry around each metal center would change with the oxidation state of the copper atoms (i.e., Cu(I) complexes are known to favor tetrahedral geometry, while Cu(II) complexes are generally observed to adopt square planar geometries). The work on copper coordination described in this Section was carried out in collaboration with Dr. Jackie Veauthier in the Sessler labs.

2.2.2.1 Preparation

As previously demonstrated by the iron coordination study, the use of a mesityl organometallic reagent, in this case Cu_5Mes_5 , proved appealing. This reagent was prepared, according to the literature procedure,⁷² from a transmetalation reaction between mesityl magnesium bromide and purified copper(I) chloride. The resulting air-sensitive organometallic species provided a readily available source of metal ion and a built-in deprotonating agent in the form of the highly basic mesityl residues. Additionally, unlike common metal salts, Cu_5Mes_5 did not introduce any anionic counterion in the reaction mixture; as such, the presence of anionic species in solution was determined by the choice of ligand substrate, namely the free base (no anions in solution) or the acid salt of the macrocycle (two anionic counterions per ligand).

Scheme 2.2 Preparation of a *bis*-Cu(II) complex of the dipyrromethane-based macrocycle **2.1**.

The bimetallic copper(II) complexes **2.10** (Scheme 2.2) was prepared by combining one equivalent of the free base macrocycle **2.1a** with excess Cu_5Mes_5 in THF at room temperature under argon. The resulting dark brown solution, presumably containing one or more coordinated Cu(I) species, was stirred overnight at room temperature. Subsequent air-oxidation then gave the *bis*-copper(II) complex **2.10** as a dark green crystalline solid in 45% yield after subjecting the crude product to

recrystallization (slow diffusion of hexanes into a methylene chloride solution). Elemental analysis, mass spectrometry, and X-ray crystallography (see below) proved consistent with the *bis*-copper(II) adduct depicted in Scheme 2.2.

Recently, Love *et al.* reported an alternative route for the synthesis of complex **2.10** that involves the reaction of the free base form of **2.1a** with $\text{Cu}^{\text{II}}(\text{BF}_4)_2 \cdot \text{H}_2\text{O}$ in the presence of triethylamine.⁷¹

2.2.2.2 Structural Characterization

The solid-state structure of **2.10** (Figure 2.3) is similar, in terms of connectivity, to that of the diferric complex **2.3**, as well as that of the dipalladium complex **2.5**. In all cases, the eight nitrogen atoms of the macrocycle coordinate the metal cations within two tetradentate binding pockets.

Figure 2.3 Two views of **2.10** showing partial atom labeling schemes. Displacement ellipsoids are scaled to the 50% probability level. The hydrogen atoms have been removed for clarity. The lattice contains 1.5 molecules of CH_2Cl_2 (not shown).

The geometry around each metal center in **2.10** is square planar (the sum of the N–Cu–N angles around is 358.92° for Cu1 and 359.14° for Cu2 and the largest deviation

from the mean plane defined by the nitrogen atoms is 0.078(2) Å for Cu1 and 0.128(2) for Cu2). Each copper(II) center is bound to the pyrrole nitrogen atoms from one of the dipyrromethane units and to one of the imine nitrogen atoms from each of the phenylenediimine units. The individual N–Cu–N bond angles for **2.10** are between 81.73–108.69°, with the largest angles being formed between a copper atom and two imine nitrogen atoms and the smallest angles occurring between a copper atom and two pyrrole nitrogen atoms. These angles compare well with those previously reported for bimetallic copper(II) dipyrromethane Schiff base macrocycles (N–Cu–N bond angles of 79.3–110.7°).^{55,73,74} In particular, the crystal structure for complex **2.10** is reminiscent of the *bis*-Cu(II) accordion porphyrin originally reported by Mertes (now Bowman-James) and coworkers (**2.11**, Figure 2.4)⁷³ and other dipyrromethane-based Schiff base macrocycles recently described by Brooker and coworkers (**2.12**, Figure 2.4).⁷⁴

Figure 2.4 Previously reported examples of *bis*-Cu(II) complexes of dipyrromethane-based Schiff base macrocycles ($n = 3$ or 4).

The Cu–N_{pyrrole} distances for **2.10** (1.897–1.925 Å) are slightly shorter than the Cu–N_{imine} (1.996–2.069 Å) distances within the same complex. Both distances are comparable to the ones seen in the Schiff base complexes reported by Mertes (complex **2.11**; Cu–N_{pyrrole}, 1.914–1.999 Å and Cu–N_{imine}, 2.034–2.150 Å)⁷³ and Brooker (complex **2.12**; Cu–N_{pyrrole}, 1.881–1.934 Å and Cu–N_{imine}, 1.986–2.068 Å).⁷⁴ On the other hand,

complex **2.10** differs significantly from the previously characterized bimetallic copper(II) complexes of dipyrromethane-based macrocycles with regard to the distance between the two Cu(II) metal centers. In **2.10**, the Cu1...Cu2 distance is 3.473(3) Å, while the corresponding inter-copper distance is 5.393(2) Å in the Mertes system (Figure 2.4, complex **2.11**, $n = 3$). Both sets of distances are shorter than those reported by Brooker for her somewhat analogous systems, namely 6.5063(19) Å and 8.3235(12) Å, respectively, for the separation between the two Cu(II) centers in complexes **2.12**, $n = 3$ and $n = 4$, of Figure 2.4.[§]

2.2.2.3 Magnetic Properties

The relatively short Cu...Cu distance (3.473 Å) found in the X-ray crystal structure of **2.10** led us to examine the magnetic properties of this complex. The experimental details associated with these magnetic measurements are reported in Appendix B.

First, we determined the room temperature, spin-only magnetic moment (μ_{eff}) of complex **2.10** in deuterated chloroform using the Evans method.⁷⁵⁻⁷⁷ Measurements were performed at two different concentrations to give values of $\mu_{\text{eff}} = (2.0 \pm 0.1) \mu_{\text{B}}$ for **2.10**. These values are lower than the expected magnetic moment ($\mu_{\text{eff}} = 2.45 \mu_{\text{B}}$) for two isolated Cu(II) metal centers ($S = 1/2$).

In order to investigate the magnetism of this complex further, SQUID magnetometry was used to measure the solid-state magnetic susceptibility, χ , for **2.10**. All the SQUID measurements reported in the present Chapter were carried out in

[§] A shorter Cu...Cu distance has however been observed in the *bis*-Cu(II) amethyryn complex **1.13** described in Chapter 1 (Cu...Cu, 2.761(1) Å).

collaboration with the group of Professor John Markert in the Department of Physics of this university.

The solid-state magnetic susceptibility of the *bis*-Cu(II) complex **2.10** was measured over the (4–300 K) temperature range in a 1 kOe field (Figure 2.5). As the temperature is lowered, χ increases until a maximum is reached at approximately 38 K, indicating an antiferromagnetic interaction between the Cu(II) centers.

Figure 2.5 SQUID data for the bimetallic Cu(II) complex **2.10**. Measurement of the magnetic susceptibility χ over the (4–300 K) temperature range indicates an antiferromagnetic coupling between the metal centers.

The data were fit to a modified Bleaney-Bowers equation (see Appendix B for more details). The fit of the data resulted in a J value of $-41.0 \pm 0.2 \text{ cm}^{-1}$ indicative of weak antiferromagnetic coupling between the metal centers in complex **2.10**.

The small $-J$ value observed for **2.10** is as predicted given the absence of a Cu–Cu bond or a direct single atom bridge between the Cu(II) metal centers in this complex. Indeed, the only connection between the copper(II) centers is via a four atom (N–C–C–N) π -conjugated bridge.

A similar observation has been made by Brooker *et al.* for the bimetallic Cu(II) complex of a Schiff base macrocycle.⁷⁸ Indeed, they reported a J value of -13.2 cm^{-1} for a *bis*-Cu(II) species wherein the Cu(II) metal centers are connected by five-atom (N-N-C-C-N) pyridazine-linked bridges and the distance between the two Cu(II) metal centers is $5.874(2)\text{ \AA}$.

2.2.3 Synthesis of *bis*-Cu(I) Complexes

Unfortunately, as yet, no well-defined Cu(I) species from the initial reaction mixture leading to complex **2.10** were characterized. However, as noted above, previous work with iron mesityl reagents demonstrated that the protonation state of macrocycle **2.1** had a profound influence on the coordination environment of the iron centers in the isolated μ -oxo Fe(III) complexes **2.3** and **2.4**. Thus, the metalation chemistry of the *bis*-HCl salts of macrocycles **2.1a** and **2.1c** was examined.

2.2.3.1 Preparation

In a typical reaction (Scheme 2.3), two equivalents of hydrochloric acid were added to one equivalent of the free base macrocycle in CH_2Cl_2 to form what was presumed to be the *bis*-HCl salt of the ligand as a red-orange solution. Next, the solvent was removed under reduced pressure and the flask was charged with one equivalent of Cu_5Mes_5 and dry oxygen-free THF to give a yellow-brown solution that was stirred overnight at room temperature. After removal of the solvent, the brown powder was redissolved in THF and layered with *n*-pentane to give air-sensitive yellow-brown crystals of the resulting bimetallic copper(I) complex, **2.13** or **2.14**, in 30–55 % yield.

Complexes **2.13** and **2.14** were characterized by elemental analysis, ^1H and ^{13}C NMR spectroscopy, and X-ray crystallography (see below).

The room temperature ^1H NMR spectrum of **2.13** contains seven unique proton resonances and that of **2.14** contains eight unique proton resonances. Both spectra are consistent with the structures proposed in Scheme 2.3 and reveal that the two Cu(I) complexes are highly symmetric in solution. Consistent with metal coordination to the iminic nitrogens only (and not to the pyrrolic nitrogens), the ^1H NMR spectra (400 MHz, CD_2Cl_2) also confirm the presence of four pyrrolic NH's in **2.13** and **2.14** (i.e., δ_{H} 11.11 and 10.99 ppm, respectively, each integrating to four protons).

Scheme 2.3 Preparation of *bis*-Cu(I) complexes of macrocycle **2.1**.

2.2.3.2 Structural Characterization

The structures of the copper(I) complexes **2.13** and **2.14** indicate that the presence of hydrochloric acid in the reaction mixture has a strong effect of the binding mode of the copper centers.

In both structures, each copper atom is bound to two nitrogen atoms from a single phenylenediimine unit and to at least one chlorine atom. However, the X-ray crystal structure for complex **2.13** contains significant disorder around one of the Cu atoms (Cu2, Figure 2.6) and although this disorder has been modeled, a definitive characterization of the structure for **2.13** cannot be provided (see Appendix A for crystallographic details). Thus, the quantitative discussion of the metal geometries will be limited to complex **2.14**.

Figure 2.6 Two views of **2.13** showing partial atom labeling schemes. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms and two THF solvent molecules have been removed for clarity. The disorder for Cu2 is not shown (see Appendix A for details).

The *bis*-Cu(I) complex **2.14** contains two bridging Cl atoms that lie on a crystallographic two-fold rotation axis bisecting the macrocycle. The geometry around each metal center is a distorted tetrahedron (the angle between the N3–N2–Cu1 plane and the Cl1–Cl2–Cu1 plane is 96.3(1)°) with a N–Cu–N angle of 81.03(11)°, a Cl–Cu–Cl angle of 92.16(3)°, and N–Cu–Cl angles of 129.95(8)° and 118.88(8)°. The Cu–N_{imine} distances for **2.14** are 2.084(3) Å and 2.059(3) Å and the Cu–Cl distances are 2.333(1) Å and 2.412(1) Å. The observed Cu–Cl distances compare well with those found in a similar chloride-bridged copper complex of amethyrin (**1.13**) described in Chapter 1, (Cu–Cl, 2.366–2.476 Å).²⁸

Finally, the flexibility of the macrocycle in **2.14** allows the ligand to fold and bring the two copper(I) centers close together resulting in a Cu···Cu distance of 3.290 Å. This separation is shorter than that seen in the *bis*-Cu(II) complex **2.10** (3.473 Å), as well as in the *bis*-Cu(I) complex **2.20** of the bipyrrrole-based macrocycle described in Section 2.3 of this Chapter (Cu···Cu, 5.296 Å).

Figure 2.7 Two views of **2.14** showing partial atom labeling schemes. Displacement ellipsoids are scaled to the 50% probability level. The complex resides on a crystallographic two-fold rotation axis at 0, y , $\frac{3}{4}$. The chloride ions lie on the two-fold rotation axis, which bisects the macrocycle. Most hydrogen atoms and two regions of disordered solvent have been removed for clarity. One of the ethyl substituents is disordered about two orientations as shown.

2.2.3.3 Air-oxidation of the Cu(I) Complexes

Once characterized, complexes **2.13** and **2.14** were dissolved in CH_2Cl_2 and exposed to air. Mass spectrometric analyses of the resulting solutions confirmed that the copper atoms present in both complexes remained coordinated to the macrocycles after air oxidation.

Interestingly, crystals isolated from the oxidation reaction of **2.13** were characterized by elemental analysis and X-ray diffraction and found to correspond to a complex similar to **2.10**. Despite some minor differences (possibly due to different

crystallization conditions), the complex obtained from air oxidation of **2.13** contains exactly the same connectivity found in complex **2.10**.

In complex **2.13**, the macrocycle supports the coordination of two Cu(I) cations by acting as a *bis*-bidentate ligand through the two phenylenediimine units. However, upon air oxidation, the macrocycle becomes a *bis*-tetradentate ligand and coordinates each Cu(II) cation through the pyrrole nitrogen atoms of a dipyrromethane unit and one imine nitrogen atom from each phenylenediimine unit. This dramatic change in the coordination mode upon oxidation of the coordinated cations from Cu(I) to Cu(II), parallels what was seen in the case of the bipyrrrole-type Schiff base macrocycle **2.2** (see below, Section 2.3) and serves to highlight further the versatility of the oligopyrrolic Schiff base ligands described in the present Chapter .

2.2.4 Synthesis of a *bis*-Zn(II) Complex

The coordination ability of macrocycle **2.1** towards late transition metals was further investigated through a series of metalation experiments in the presence of several zinc sources.

Exposure of the free base **2.1a** to zinc acetate in THF (both at room temperature and under reflux conditions) appeared to afford one or more zinc-containing species. A mass compatible with a binuclear zinc complex was observed in the mass spectrum of the reaction mixture; however, this putative *bis*-Zn(II) species was poorly soluble and could not be crystallized or otherwise purified (as judged by the ¹H NMR spectra of the isolated solids).

While this work was in progress, Love and coworkers reported an independent study involving the insertion of zinc in macrocycle **2.1**.⁷⁰ It was found that reaction of the free base ligand with Zn(OAc)₂·2H₂O in boiling chloroform resulted in the formation of a

trinuclear zinc complex **2.15**, in which the original ligand has been expanded to form a new hexapyrrolic macrocycle (Scheme 2.4). In fact, while **2.1a** is the result of a [2+2] condensation between 1,2-phenylenediamine and dipyrromethane dialdehyde, the macrocyclic ligand in complex **2.15** appears to be the product of a [3+3] condensation between the same precursors.

Scheme 2.4 Preparation of a trinuclear zinc(II) complex as described by Love *et al.* A metal-directed ring-expansion of macrocycle **2.1a** is observed.

In complex **2.15**, each zinc center is bound to one of the phenylenediimine units of the ligand and to two acetate ions. Successful demetalation of this species was achieved in the presence of Na_2S and the metal-free [3+3] macrocycle was isolated. However, the latter product was found to be thermodynamically unstable, rapidly decomposing to give the [2+2] macrocycle **2.1a** or other open chain species.

Although the authors of this investigation did not propose a mechanism to explain the observed (and unusual) ring-expansion, it appears that, in the presence of zinc acetate, a putative hydrolytic cleavage of **2.1a** is followed by metal-templated recondensation and formation of a larger macrocycle of limited stability. Therefore, these findings offer a viable explanation for the difficulties encountered by the author of the present Dissertation during the zinc-insertion experiments using zinc acetate.

Further experiments using ZnCl_2 and the organometallic reagent diethylzinc as metal sources only afforded preliminary evidence of complex formation; however, the low solubility of the obtained products precluded purification and isolation of any zinc-containing species.

In contrast to the above difficulties, it was found that treatment of the free base **2.1a** with $\text{Zn}(\text{BF}_4)_2 \cdot 5\text{H}_2\text{O}$ resulted in the formation of a new zinc complex, which could be fully characterized (Scheme 2.5). While initial mass spectrometric data indicated the formation of a binuclear zinc complex, the exact structure of **2.16** was elucidated through X-ray diffraction analysis.

Scheme 2.5 Preparation of a fluoride-bridged binuclear zinc complex of **2.1a**.

As previously observed for the *bis*-Cu(I) complexes **2.13** and **2.14**, as well as for the trinuclear zinc complex **2.15**, the zinc centers in **2.16** (Figure 2.8) are bound to the iminic nitrogens of the macrocycle, but do not coordinate to the pyrrolic nitrogen atoms. Additionally, each zinc center is bound to a tetrafluoroborate anion and to two bridging fluoride anions. The primary coordination sphere of both metal centers is completed by the bridging oxygen atom of an acetone molecule that resides within the wedged structure of the complex. As such, each zinc ion lies in a distorted octahedral geometry.

Figure 2.8 Top and side views of complex **2.16** showing a partial atom labeling scheme. In the top view on the left, the coordinated acetone molecule has been removed for clarity. Displacement ellipsoids are scaled to the 50% probability level. The dashed lines are indicative of H-bonding interactions. The macrocycle lies on a crystallographic two-fold rotation axis at $\frac{1}{2}, y, \frac{3}{4}$. Only one set of the disordered ZnBF_4 ion pairs is shown (see Appendix A for details).

Since no other fluoride source was present in the reaction mixture, the presence of two bridging fluoride ligands in **2.16** can be attributed to a fluoride abstraction from the tetrafluoroborate anions of the $\text{Zn}(\text{BF}_4)_2$ salt. Indeed, although serendipitous in the present case, such decomposition of the BF_4^- ion is well known in the coordination chemistry of late transition metals and has been employed for the intentional delivery of fluoride ligands.^{79,80} Additionally, Reger *et al.* recently reported on the juxtaposition of Lewis acidic centers (i.e., Fe(II), Zn(II), and Cd(II)) as a means to mediate fluoride abstraction.⁸¹ In the case of complex **2.16**, the coordination of two Lewis acidic zinc

centers within the macrocycle scaffold resulted in the activation of a B-F bond in the tetrafluoroborate anions and ultimately in the abstraction of a fluoride ion. It appears that the presence of the bridging fluorides stabilizes the coordination geometries of the divalent cations within the macrocycle framework, thus allowing the isolation of a hitherto elusive *bis*-Zn(II) complex.[‡]

During the X-ray diffraction analysis of complex **2.16**, the two Zn-BF₄ units were found to be disordered about two orientations of equal weight (see Appendix A for the refinement details); however, for the sake of clarity, only one set of these disordered units is shown in the crystal structure depicted in Figure 2.8.

The Zn-F_{bridge} distances in **2.16** (1.938–2.187 Å) fall within the range for those observed in other fluoride-bridged zinc complexes⁸¹⁻⁸³ and are longer than those between zinc and terminal fluoride ligands (ca. 1.85 Å).^{84,85} The rather long Zn-O distance of 2.254 Å indicates that the acetone molecule in **2.16** is loosely bound to the metal centers. All of the pyrrolic NH's of the macrocycle are engaged in hydrogen bonding interactions with the bridging fluoride anions.

The ¹H and ¹³C NMR spectra (400 MHz, CD₃COCD₃) of **2.16** are similar to the ones of the other diamagnetic complexes of **2.1** described in this Chapter (i.e., the *bis*-Cu(I) species **2.13** and **2.14**). However, the NMR spectroscopic data for **2.16** were characterized by significant peak broadening, possibly indicating a slow exchange between two or more conformational states of the complex.

[‡] Love and coworkers reported the preparation of a different *bis*-Zn(II) complex of **2.1a** using Zn(BF₄)₂ as a zinc source. This species was not structurally characterized; however, combustion analysis of the isolated product was found to be compatible with the presence of four tetrafluoroborate anions and no fluoride bridges. The reasons for such different reactivity are not clear at present and will likely require a detailed study of the experimental conditions for the reaction of **2.1** with Zn(BF₄)₂.

While fully consistent with the known fluoride coordination chemistry, the fluoride abstraction by a binuclear zinc complex observed in the present case was unprecedented in the metalation chemistry of expanded porphyrins.

2.3 COMPLEXES OF A BIPYRROLE-BASED MACROCYCLE

2.3.1 Background

The appearance of the bipyrrrole subunit in a Schiff base expanded porphyrin dates back to the early 1990s, namely to the synthesis of the tetrapyrrolic octaaza macrocycle **2.2**, which was carried out by Dr. Tarak D. Mody in the Sessler labs.⁸⁶

The first investigations on the chemistry of this macrocycle revealed that **2.2** binds methanol within its cavity; it thus provided the first example of neutral substrate complexation by an expanded porphyrin.⁸⁶ Additionally, early metalation studies showed that macrocycle **2.2** reacts readily with simple metal salts to give binuclear Ni(II), Cu(II) and Zn(II) complexes (Scheme 2.6).⁸⁷

Scheme 2.6 Initial metalation studies with macrocycle **2.2** provided evidence for the formation of binuclear complexes with divalent late transition metals.

The crystal structure of the *bis*-Ni(II) complex **2.17** showed that the two metal centers coordinate to the macrocycle via the iminic nitrogen atoms (Figure 2.9). As observed for the copper(I) and zinc(II) complexes of **2.1** described earlier in this Chapter, the pyrrolic nitrogens in **2.17** do not participate in metal complexation; rather, the hydrogen atoms of these nitrogens are hydrogen-bound to the donor oxygens of the four acetate counter-ions. The acetate ions also coordinate to the nickel(II) centers and do so in three distinct binding modes. First, a bidentate acetate group coordinates to Ni1 through donor atoms O1A and O3A. Second, a bridging acetate group binds to Ni1 and Ni2 through atoms O1B and O3B, respectively. Finally, two monodentate acetates bind to Ni2 through oxygen donors O1C and O1D. Each nickel(II) ion is also coordinated to a water molecule (i.e., Ni1-O1W and Ni2-O2W). The Ni $\cdots$ Ni distance in this complex is 5.375 Å.

Figure 2.9 Crystal structure of the *bis*-Ni(II) complex **2.17** reported by Dr. Tarak D. Mody.⁸⁷ Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity.

Consistent with what was observed for **2.17**, the combustion analyses of the *bis*-Cu(II) complex **2.18** and of the *bis*-Zn(II) complex **2.19** indicated that each metal center retains two acetate anions and, on this basis, it was inferred that the macrocycle acts as a *bis*-bidentate neutral ligand. Additionally, the ^1H NMR spectrum (400 MHz, CD_2Cl_2) of the diamagnetic *bis*-Zn(II) species **2.19**, recorded by the author of the present Dissertation, confirmed the presence of four hydrogen-bound pyrrolic NH protons. These were found to resonate at δ_{H} 11.5 ppm and appear as one singlet integrating to four protons.

2.3.2 Synthesis of a *bis*-Cu(I) Complex

The ability of macrocycle **2.2** to coordinate readily nickel, copper, and zinc in their divalent oxidation states provided an incentive to study the coordination of a typical monovalent metal cation, namely copper(I). For the reasons described earlier in this Chapter (see Section 2.2.2), the organometallic Cu(I) species Cu_5Mes_5 was used as the metalation reagent of choice for this investigation.

The diprotonated nitrate salt **2.2**·(HNO_3)₂ was reacted with Cu_5Mes_5 in THF at room temperature under an argon atmosphere (Scheme 2.7). Initial mass spectrometric data indicated the formation of a binuclear copper complex, but did not provide interpretable information about the oxidation state of the coordinated metal ions.

The formation of a *bis*-Cu(I) complex (**2.20**), as opposed to a *bis*-Cu(II) or mixed valent species, was inferred from ^1H NMR spectroscopic measurements and subsequently confirmed by X-ray diffraction analysis (Figure 2.10).

Scheme 2.7 Preparation of a *bis*-Cu(I) complex of macrocycle **2.2**.

The ^1H NMR spectrum (400 MHz, CD_2Cl_2) of **2.20** was found to be rather similar to the one of the *bis*-Zn(II) complex **2.19**. For instance, in the down-field region, a singlet at δ_{H} 11.00 ppm is ascribable to the pyrrolic NH protons. On this basis, in accord with what was previously observed for **2.19**, it is concluded that the pyrrolic nitrogens are not engaged in metal coordination. Furthermore, the overall ^1H NMR spectrum, containing seven unique proton resonances, supports the notion that **2.20** be highly symmetric in solution.

Figure 2.10 Top and side view of the *bis*-Cu(I) complex **2.20** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. The macrocycle lies around a crystallographic inversion center at 1, $\frac{1}{2}$, $\frac{1}{2}$.

Consistent with the solution spectroscopic data, the crystal structure of **2.20** revealed that the complex lies around a crystallographic inversion center and that each copper(I) ion coordinates two iminic donors of the macrocycle and one oxygen atom of a nitrate counterion. The copper centers lie in a distorted T-shaped planar geometry, with a N-Cu-N angle of 84.50(17)°, and N-Cu-O angles of 109.65(17)° and 165.80(18)°. The Cu-N bond distances of 1.944(4) Å and 2.116(4) Å compare well with those observed for the *bis*-Cu(I) complex **2.14** described in Section 2.2.3.

The two coordination planes in **2.20**, containing the Cu ions and the nitrate anions, are tilted above and below the mean plane defined by the nitrogen atoms of the macrocycle, such that each counterion interacts with only one metal center. Additionally, all of the pyrrolic NH protons of the macrocycle are engaged in hydrogen-bonding interactions with the nitrate oxygen atoms. Perhaps as a consequence of these interactions, each bipyrrrolic moiety is characterized by an “up-down” conformation of the two pyrrole rings.

The Cu(I)⋯Cu(I) distance of 5.296 Å in **2.20** is significantly longer than the one observed in the Cu(I) complex **2.14** (Cu(I)⋯Cu(I), 3.290 Å) described earlier in this Chapter. This difference in the metal-metal separation of the two complexes is arguably due to the higher rigidity of the macrocyclic ligand **2.2** when compared with its dipyrromethane-based congener **2.1**.

2.3.3 Preparation of a new *bis*-Cu(II) complex through air-oxidation of the *bis*-Cu(I) complex **2.20**

It was expected that the air-oxidation of the *bis*-Cu(I) complex **2.20** (Scheme 2.8) would provide new insights into the coordination chemistry of macrocycle **2.2**. Thus,

crystals of **2.20** were exposed to air, dissolved in CH_2Cl_2 , and layered with *n*-pentane. As a result, a crystalline solid, which proved to be a novel *bis*-Cu(II) complex, was isolated and characterized by mass spectrometry, elemental analysis, and X-ray diffraction analysis (Figure 2.11).

Scheme 2.8 Air-oxidation of the *bis*-Cu(I) complex **2.20**.

Figure 2.11 View of the *bis*-Cu(II) complex **2.21** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity.

As previously observed for complex **2.20**, the crystal structure of **2.21** shows that each copper center is bound to the two nitrogen atoms of each phenylenediimine moiety of the macrocycle. However, the two additional anionic ligands, which are required by the charge balance of the *bis*-Cu(II) complex **2.21**, are provided by the macrocycle itself. Indeed, the ligand undergoes a dramatic distortion in order to coordinate to each copper(II) ion not only via the two iminic nitrogen atoms but also through a pyrrolic nitrogen. As a consequence, the metal ions lie in a highly distorted square pyramidal environment that includes a bridging nitrate ion. The fifth coordination site is occupied by the second nitrate counterion for Cu1 and by a water molecule for Cu1A.

Both the Cu-N_{imine} (1.947(4) Å and 2.037(4) Å) and the Cu-N_{pyrrole} (1.956(5) Å) bond distances are similar to the ones observed for the dipyrromethane-based Cu(II) complex **2.10**.

The Cu(II)⋯Cu(II) distance of 5.289 Å in **2.21** is quite similar to the one seen in the parent complex **2.20** (5.296 Å). The slight shortening of the metal-metal separation in **2.21** is likely explained by the different conformation of the macrocycle, which has effectively adjusted so as to accommodate the new oxidation state of the coordinated cations.

The structures of the binuclear complexes **2.17** (Figure 2.9) and **2.20** (Figure 2.10) indicated that macrocycle **2.2** can support both monovalent and divalent cations in a similar coordination mode that involves the imine nitrogens but not the pyrrolic nitrogens. However, the successful formation of **2.21** (Figure 2.11) provides *prima facie* evidence that this is not the only binding mode available to ligand **2.2**. In fact, the macrocycle was shown to change its denticity, conformation, and overall charge in response to a change in the oxidation state of the coordinated cations (i.e., from Cu(I) to Cu(II)).

2.3.4 Magnetic Measurements

The magnetic behavior of the binuclear nickel(II) complex **2.17** and the binuclear copper(II) complexes **2.18** and **2.21** was investigated.

As expected from the large separation between the metal centers in complexes **2.17**, **2.18** and **2.21**, no evidence of a magnetic coupling was seen in solution at room temperature (Evans method).⁷⁵⁻⁷⁷ Additionally, magnetic susceptibility SQUID data were consistent with these complexes acting in a paramagnetic manner over the temperature range (4-300 K), as would be expected in the absence of a magnetic interaction between the two Ni(II) centers in **2.17** or between the two Cu(II) centers in **2.18** and **2.21**. Indeed, the susceptibility data per mole formula unit of the three bimetallic complexes were found to fit well to the Curie law. All experimental details for the magnetic measurements performed in support of this conclusion are reported in Appendix B of this Dissertation.

2.3.5 Additional coordination studies

As described in Section 2.3.1, the binuclear copper complexes **2.20** and **2.21** were prepared from the acid salt **2.2**·(HNO₃)₂. When similar experimental conditions were applied to the free base macrocycle **2.2**, a multinuclear copper-containing species was obtained. In particular, mass spectrometric data and a low-resolution X-ray crystal structure indicated the formation of a dimeric species containing two macrocyclic ligands and six copper ions. However, this putative complex proved to be rather unstable and could not be fully characterized.

Preliminary investigations on the coordination of heavier transition metals in **2.2** indicated that this macrocycle can serve as a versatile ligand for the complexation of a variety of cations, including silver(I), gold(I), rhodium(I), and palladium(II). Only the first of these cations was explored in detail.

An in-depth study on the binding of silver(I) cations in **2.2** revealed a new and intriguing aspect of the coordination chemistry of this macrocycle, namely the cooperative coordination of metal ions.

The description of the cooperative effects influencing the silver coordination in **2.2** will require specific background information on allostereism in artificial organic systems, as well as an appropriate set of technical tools for the study of substrate binding events. This material constitutes a new story line of this Dissertation and hence is illustrated as a separate topic. Therefore, the syntheses of Ag(I) complexes of **2.2** and the corresponding studies of cooperative silver binding are the subject of Chapter 3 of the present Dissertation.

2.4 SCHIFF BASE OLIGOPYRROLIC MACROCYCLES OF INCREASED HYDROPHILICITY

One of the leading goals that motivate the study of expanded porphyrin chemistry is the widely recognized potential of these ligands in biomedical applications such as photodynamic therapy and other cancer therapeutic treatments. Indeed, the biological activity of lutetium and gadolinium texaphyrin complexes have been extensively studied in a number of human clinical trials that have mainly focused in testing their efficacy in the treatment of arteriosclerosis and several types of cancer.⁸

More recently, a hydrophilic sapphyrin analogue was identified as showing promise in cancer chemotherapy.⁸⁸

The evaluation and employment of expanded porphyrins and their metal complexes for biomedical applications require high hydrophilicity, and possibly water solubility. Indeed, the solubilization of expanded porphyrins in biological media requires substantial changes in the character of these typically organic-soluble compounds. As a consequence, the preparation of new oligopropiolic macrocyclic scaffolds is often followed or accompanied by functionalization efforts aimed at tuning the hydrophilicity of the ligands.

The present Section describes the author's initial efforts directed towards the preparation of water-soluble analogues of macrocycles **2.1** and **2.2**, and of their metal complexes.

Over the past two decades, a successful approach towards hydrophilicity has involved the introduction of polyethyleneglycol (PEG) chains, which typically impart amphiphilic solubility to organic ligands. Unfortunately, in many cases, the presence of the hydrophilic PEG groups makes the isolation of the target compounds more challenging. The presence of these or other water-solubilizing groups can sometimes preclude a satisfactory purification of either a targeted ligand or its metal complexes.

A PEG-containing version of macrocycle **2.1** was first isolated by Dr. Jackie Veauthier in the Sessler labs.⁴¹ Although not fully water-soluble, macrocycle **2.23** (Figure 2.12) shows good hydrophilicity and does not precipitate in a dimethylsulfoxide/water mixture (ca. 5% v/v DMSO). As such, this ligand was used for the preparation of two new water-compatible metal complexes (Scheme 2.9).

Figure 2.12 An analogue of macrocycle **2.1** in which four polyethylene glycol (PEG) chains impart higher hydrophilicity to the ligand scaffold.

The experimental conditions previously described for the preparation of the *bis*-Cu(II) complex **2.10** were applied to macrocycle **2.23** to yield the corresponding copper complex **2.24**. This species was characterized by mass spectrometry and elemental analysis. Additionally, treatment of **2.23** with ZnCl_2 afforded the new *bis*-Zn(II) complex **2.25** that was characterized by mass spectrometry, NMR spectroscopy and combustion analysis.

Scheme 2.9 Preparation of binuclear Cu(II) and Zn(II) of increased hydrophilicity.

Unfortunately, a similar “PEGylation” approach was not successful in the case of macrocycle **2.2**. The acid-catalyzed condensation of 2,2'-diformyl-3,3',4,4'-tetramethyl-5,5'-bipyrrole with 4,5-*bis*(2-[2-(2-methoxyethoxy)ethoxy]ethoxy)benzene-1,2-diamine afforded the [2+2] condensation product and several open-chain side products. Although mass spectrometric and NMR spectroscopic data indicated that the desired compound was in fact the major product, a satisfactory purification of the PEG-containing analogue of **2.2** could not be achieved.

As an alternative approach towards attaining enhanced water-solubility, attempts were made to prepare a hydrophilic analogue of **2.2** using a protection/deprotection strategy (Scheme 2.10). In this case, the target molecule was **2.26**, a tetra-hydroxyl version of **2.2**, a product that was expected to display good hydrophilicity due to the hydroxyl substituents on the two phenyl rings of the macrocycle. Additionally, it was recognized that the OH groups of **2.26** could be further functionalized with appropriate solubilizing groups as needed to meet higher or lower water-solubility requirements.

In order to avoid unwanted condensation reactions at the OH groups, a protected phenylenediamine was used for the macrocyclization reaction. Specifically, the hydroxyl substituents on the benzene ring were protected using triisopropylsilyl (TIPS) groups. Condensation of 4,5-*bis*(triisopropylsilyloxy)benzene-1,2-diamine with 2,2'-diformyl-3,3',4,4'-tetramethyl-5,5'-bipyrrole then afforded a TIPS-protected analogue of **2.2**, which was isolated and characterized (**2.27**, Scheme 2.10).

Scheme 2.10 A proposed route for the preparation of a hydrophilic analogue of **2.2**.

Unfortunately, initial deprotection attempts have failed to afford the desired macrocycle **2.26**. Both fluoride-based (tetrabutylammonium fluoride, 4 equiv.) and acidic (HCl , 4 equiv.) conditions led to the decomposition of the macrocycle. As such, the deprotection step of this synthetic scheme will require further investigations.

In general, it is likely that the rich coordination chemistry of macrocycles **2.1** and **2.2** will fuel future synthetic efforts aiming at tuning the solubility of these ligands and hence at expanding the range of their potential applications.

2.5 FUTURE DIRECTIONS

The findings described in this Chapter show that binucleating oligopyrrolic macrocycles such as **2.1** and **2.2** can be used for the preparation of a wide variety of late transition metal complexes. The influence of the macrocycle protonation state (i.e., free base vs. acid salt) and of the metal oxidation state (i.e., Cu(I) vs. Cu(II)) are illustrated by the copper coordination chemistry of both ligands **2.1** and **2.2**. Conversely, the importance of the chosen metal source (i.e., Zn(OAc)₂ vs. Zn(BF₄)₂) is demonstrated by the zinc insertion studies on macrocycle **2.1**.

In general, the ability to juxtapose two metal centers within a macrocyclic ligand and to control the separation distance between the cations and their coordination environments provides a promising direction for future studies. Within the context of these efforts, a particularly appealing idea is to engineer binuclear complexes wherein the two metal ions act in a concerted way on a given reaction substrate. In favorable cases, this could give rise to new catalytic systems. For instance, binuclear copper(II) and zinc(II) complexes of expanded porphyrins could be tested as functional mimics of a number of enzymes that catalyze the hydrolysis of phosphate diesters (e.g., RNA or DNA) or triesters (such as those found in nerve gas and numerous pesticides). Additionally, the fluoride abstraction observed during the formation of the *bis*-Zn(II) complex **2.16** leads the author of this Dissertation to propose a new potential application of expanded porphyrin metal complexes, namely the activation of fluorine-containing compounds and ultimately the scission of C-F bonds.

Finally, it is safe to predict that the chemistry of bimetallic expanded porphyrin complexes will continue to provide new opportunities to investigate magnetic interactions. In particular, the preparation of new homo- and heterobimetallic complexes

with unprecedented coordination geometries will surely provide interesting systems for magnetic studies.

Chapter 3

Cooperative binding of silver(I) cations in a Schiff base expanded porphyrin

3.1 BASIC PRINCIPLES AND BACKGROUND

3.1.1 Definitions

Allosteric interactions play a critical role in a number of well-recognized biological processes.⁸⁹ In *allosteric* systems, the binding of a controlling substrate to a receptor affects the affinity of the system towards subsequent substrates, thus efficiently modulating the binding of multiple guests in a nonlinear fashion. In the most cited example of allosteric behavior in Nature, the binding of a first dioxygen molecule to the oxygen-carrier protein hemoglobin enhances the affinity towards O₂ of the other three oxygen binding sites in the protein.

When the effect of the first substrate binding is an increased affinity of the system for subsequent substrates (such as is observed in hemoglobin), the allosteric behavior is termed *positive*; on the other hand, if the first substrate decreases the affinity in subsequent binding events, the allosterism is *negative*.

Additionally, a given allosteric system is termed *homotropic* when all the binding substrates are chemically identical, or *heterotropic* when the binding of one chemical species influences the binding of a different chemical species.

As such, allosteric systems can be classified into four categories, namely (i) positive homotropic, (ii) negative homotropic, (iii) positive heterotropic, and (iv) negative heterotropic. Homotropic allosteric systems are also termed *cooperative*.

The cooperativity between the dioxygen-binding subunits of hemoglobin was first analyzed by Archibald V. Hill, who reported, in 1910, a simple and effective method to assess cooperative behavior.⁹⁰ The so-called *Hill plot* is a plot of $\log(Y/(1-Y))$ versus $\log[S]$, where Y is the fractional saturation of the host and $[S]$ is the concentration of the binding substrate. The association constant K and the *Hill coefficient* n_H of the system are derived from a linear regression analysis of the Hill-plot data points according to the equation:

$$\log(Y/(1-Y)) = n_H \log[S] + \log K ,$$

where $\log K$ and n_H are the intercept and the slope of the regression line, respectively.⁹¹ The value of the Hill coefficient is a measure of the cooperativity of the system.⁹² Specifically,

- (i) $n_H = 1$ for non-cooperative systems with independent binding sites,
- (ii) $n_H > 1$ in the case of positive cooperativity, and
- (iii) $n_H < 1$ in the case of negative cooperativity.

The study of cooperative systems, in which chemically equivalent binding sites respond differently to identical substrates, continues to be a central theme in biochemistry and enzymology, as well as a novel challenge in molecular engineering and biomimetic chemistry.

3.1.2 Cooperative Effects in Organic Chemistry

A desire to reproduce the key features of allostery in artificial systems has long been a goal within the chemical community, since it is appreciated that such efforts can lead to new advances in biomimetic design or contribute to the interpretation of natural regulated machinery.^{93,94} Additionally, the steep bound-unbound transitions of

cooperative systems allow one to envision the generation of on-off devices that respond to small changes in the input signal (i.e., concentration of the substrate). As a consequence, artificial cooperative systems are attracting increasing attention as potential molecular machines.

As noted above, in the case of positive homotropic allosterism, the binding of a guest causes the receptor to bind a subsequent identical guest with a higher affinity. This effect has proven to be much more difficult to reproduce than either negative or heterotropic allosterism.⁹⁵

The pioneering work reported by Rebek and coworkers in the 1980s provided some of the earliest examples of artificial positive cooperativity in a synthetic system. For instance, the macrobicyclic biphenyl *bis*-crown ether system **3.1** was shown to bind $\text{Hg}(\text{CN})_2$ with a Hill coefficient n_H of 1.5 (Scheme 3.1).⁹⁶

Scheme 3.1 Positive cooperativity between two crown ether binding pockets connected through a biphenyl skeleton [$M = \text{Hg}(\text{CN})_2$].

The positive cooperativity observed for this system was explained in terms of a binding-induced conformational change. While the free receptor has access to a range of dihedral angles between the phenyl rings, the binding of one substrate restricts the conformation of the system to the specific dihedral angle that is optimal for binding. As such, a sort of binding information is passed to the second binding pocket that is preorganized for complexation of a subsequent substrate.

During the last decade, Shinkai and coworkers developed a relatively large family of allosteric systems using functionalized double-decker porphyrinato complexes.⁹⁷⁻¹⁰¹ Since the allosteric effects in these systems are based on the influence of the guest upon the rotation of the porphyrin planes, these receptors are also called *double-wheel allosteric systems*.

One of the early molecular designs utilized by the Shinkai group was based on a cerium(IV) *bis*(porphyrinato) double-decker scaffold and has now become a classic example of elegant supramolecular chemistry.

Scheme 3.2 Positive cooperative binding of a chiral dicarboxylic acid by a double-wheel cerium(IV) tetrakis(4-pyridyl)porphyrinato receptor.

The cerium(IV) double-decker tetrakis(4-pyridyl)porphyrin **3.3** was shown to bind *trans*-1,2-cyclohexanedicarboxylic acid to form a 1:4 complex with a Hill coefficient of 4.0 (Scheme 3.2).^{100,102}

Such strong positive homotropic allostereism was attributed to a guest-induced suppression of the rotation of the porphyrin planes in **3.3**. When the diacid engages two pyridyl groups in hydrogen-bonding interactions, the free rotation of the receptor is inhibited and three binding sites are aligned in a way that favors interactions with subsequent guests.¹⁰³ Interestingly, the binding of the chiral guest (R,R)-1,2-cyclohexanedicarboxylic acid was followed by monitoring changes in the circular dichroism of the system. Such an approach allowed a facile means of following a process wherein chiral information is transferred from the guest to the overall supramolecular complex **3.4**.¹⁰⁴

In recent years, the design of systems featuring the rotation of two subunits about an axle has allowed Shinkai and others to prepare allosteric systems for the binding of a range of substrates, including anions,^{105,106} metal cations,¹⁰⁷ and saccharides.¹⁰⁸

This chapter describes the synthesis and characterization of binuclear silver(I) complexes of macrocycle **2.2** that are formed as the result of homotropic cooperative ion pair insertions wherein the receptor binds two metal cations and two anions. UV-visible and ¹H NMR spectroscopic binding studies are reported along with a hypothesis advanced to explain the observed cooperative effect.

3.2 BINUCLEAR SILVER(I) COMPLEXES OF A SCHIFF BASE OLIGOPYRROLIC MACROCYCLE

3.2.1 Synthesis

The preparation of binuclear complexes of the Schiff base oligopyrrolic macrocycle **2.2** with late first-row transition metals has been described in Chapter 2 of this Dissertation. The versatility of **2.2** as a receptor, as well as its ability to stabilize different coordination modes for copper(I) and copper(II), provided an incentive to study its coordination chemistry using second-row transition metal cations. Because of the homology of Ag(I) to Cu(I), the second-row coinage metal was elected as the test substrate for this work.

The binuclear silver(I) complex **3.5** was readily prepared in 92% yield by treatment of the free base macrocycle **2.2** with Ag(I) acetate at room temperature in an argon atmosphere (Scheme 3.3).

Scheme 3.3 Preparation of *bis*-silver(I) complexes of the Schiff base ligand **2.2**.

The coordination mode depicted in Scheme 3.3 was deduced from the ^1H NMR spectrum (400 MHz, CD_2Cl_2) of the isolated product **3.5**, which included singlet resonances for four pyrrolic NH protons (i.e., $\delta_{\text{H}} = 11.55$ ppm) and for six protons ascribed to the acetate counteranions (i.e., $\delta_{\text{H}} = 1.62$ ppm). Additionally, consistent with

silver coordination to the Schiff base nitrogen atoms, the iminic proton resonance at $\delta_{\text{H}} = 8.37$ ppm appeared as a doublet with a coupling constant $^3J(^1\text{H}, ^{109,107}\text{Ag})$ of 7.1 Hz.

An analogous binuclear silver(I) complex (**3.6** in Scheme 3.3), showing similar NMR spectroscopic and mass spectrometric characterization data, was prepared using a *para*-toluenesulfonate salt as a silver source.

3.2.2 Structural characterization

Solid state structural information on the specific coordination mode and conformation of complexes **3.5** and **3.6** was obtained from single-crystal X-ray diffraction analyses.

As shown in Figure 3.1, each Ag(I) ion in **3.5** lies in a distorted square planar geometry and coordinates to two iminic nitrogen atoms of the macrocycle and to two oxygen atoms of the acetate counterion.

Figure 3.1 Top view of the *bis*-Ag(I) complex **3.5** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. The macrocycle lies around a crystallographic inversion center at (1, 0, $\frac{1}{2}$).

The observed Ag-N bond distances (Ag1-N2, 2.338(3) Å, and Ag1-N3, 2.282(3) Å) and Ag-O distances (Ag1-O1A, 2.498(4) Å and Ag1-O2A, 2.387(3) Å) are similar to those reported for silver complexes featuring iminic¹⁰⁹⁻¹¹² and carboxylate ligands,^{113,114} respectively.

The two acetate anions in **3.5** participate in hydrogen-bonding interactions with the pyrrolic NH hydrogen atoms (e.g., O1A⋯H-N4 and O2A⋯H-N1 in Figure 3.1) and the two coordination sites on each side of the ligand are tilted such that they are above and below the mean plane of the macrocycle nitrogen atoms, respectively.

The side view shown in Figure 3.2 illustrates the “up-down” conformation of the bipyrrolic units, as well as a close intermolecular interaction between two adjacent complexes, which is mediated by a silver-silver contact.

Figure 3.2 Side view of two *bis*-Ag(I) complexes as seen in the crystal packing diagram of **3.5** (the top complex is represented in wireframe style for clarity). The intermolecular silver-silver separation of 3.1444(5) Å (dashed line) between the two complexes is indicative of an argentophilic interaction.

The separation between silver ions on neighboring complexes (3.1444(5) Å, dashed line in Figure 3.2) is less than twice the van der Waals radius for silver (3.44

Å).¹¹⁵ Hence, the observed d¹⁰-d¹⁰ contact represents an example of intermolecular *argentophilic* interaction¹¹⁶ in which the two closed-shell ions are not held together by a multidentate ligand.

The argentophilic silver-silver distance in **3.5** is slightly longer than the ones typically observed in Ag-O bonding clusters (2.77-3.01 Å),¹¹³ wherein the presence of bridging ligands forces the Ag(I) ions in close proximity. However, the observed silver-silver contact of 3.1444(5) Å in **3.5** falls within the range of the more recently reported examples of unsupported argentophilic interactions (3.07-3.37 Å) whose existence could not be attributed to evident coulombic or ligand-packing effects.¹¹⁷

The metallophilic interactions that characterize the solid-state chemistry of coinage metals continue to be the object of theoretical investigations due to their implications on the nature of chemical bonding.¹¹⁶ However, in spite of this interest and some emerging theories, no cogent rationalization for argentophilic interactions such as the one in **3.5** is available at present time.

The crystal structure of the tosylate *bis*-Ag(I) derivative **3.6** is depicted in Figure 3.3. Each silver center, found within a distorted tetrahedral geometry, is bound to two iminic nitrogen atoms of the macrocycle and to two oxygen atoms of the bridging tosylate anions. The bond distances in the first coordination sphere of the metal center (Ag1-N2 2.265(8), Ag1-N3 2.341(7), Ag1-O1A 2.472(8) and Ag1A-O2A 2.382(6) Å) compare well to those observed for **3.5** and for analogous Schiff base complexes.¹⁰⁹⁻¹¹²

As previously noted for the acetate oxygens in complex **3.5**, the oxygen atoms on the sulfonate groups engage the pyrrolic NH's of the macrocyclic ligand in hydrogen bonding interactions such that the two pyrrole rings on each bipyrrolic subunit are again tilted above and below the average plane of the macrocycle.

Figure 3.3 Top view of the *bis*-Ag(I) complex **3.6** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms and tosylate group carbon atoms (except for the carbon atom bound to sulfur) have been removed for clarity. The macrocycle lies on a crystallographic inversion center at (0,0,0). Dashed lines are indicative of hydrogen-bonding interactions.

No intermolecular argentophilic interactions were observed in the crystal packing of **3.6**. It appears probable that the bulky tosylate anions prevent the metal centers of two adjacent complexes from reaching the proximity conditions required for effective d^{10} - d^{10} contact.

3.3 SILVER(I) BINDING STUDIES

Several attempts to isolate a mononuclear silver(I) complex of macrocycle **2.2** proved unsuccessful. Unexpectedly, reaction of **2.2** and a silver salt in a 1:1 molar ratio did not afford a *mono*-Ag(I) species; rather, mass spectrometry data indicated the presence of both the free ligand and the *bis*-Ag(I) complex in the reaction mixture. This

apparent anomaly motivated a more detailed study of the silver(I) cation binding in the Schiff base oligopyrrolic ligand **2.2**.

3.3.1 UV-visible spectroscopy experiments

Since metal ion coordination produces a red shift in the UV absorption band at 370 nm (THF, 296 K) ascribed to the macrocycle, complexation of silver(I) could be followed by monitoring the spectral changes produced as a function of added cation. In particular, when increasing quantities of silver(I) trifluoroacetate[§] or silver(I) *p*-toluenesulfonate were added to solutions of **2.2** in THF, new bands at 405 or 409 nm, respectively, were seen to grow in at the expense of the original band at 370 nm. Typical spectral changes observed during these titrations are shown in Figure 3.4.

Figure 3.4 Typical UV-vis spectral changes observed during the Ag(I) binding titrations of macrocycle **2.2** in THF at 296 K. Left: $[\mathbf{2.2}] = 4.49 \mu\text{M}$, $[\text{AgO}_2\text{CCF}_3] = 0.19 - 24.29 \mu\text{M}$; right: $[\mathbf{2.2}] = 4.99 \mu\text{M}$, $[\text{AgO}_3\text{SC}_6\text{H}_4\text{CH}_3] = 0.52 - 34.05 \mu\text{M}$.

[§] Due to the poor solubility of silver(I) acetate in THF, silver(I) trifluoroacetate was used in the UV titration experiments for the formation of an analogue of the *bis*-Ag(I) complex **3.5**.

The normalized binding isotherms derived from the titration data are reported in Figure 3.5. In the case of the trifluoroacetate salt, the curve showed a linear response to increasing silver(I) concentration and saturated at precisely 2 equiv. of Ag(I) ions. Because of this strong response, which is indicative of a high binding affinity, no quantitative information could be derived on this system.

Figure 3.5 *Left:* binding isotherms obtained from the UV-vis titration spectra shown in Figure 3.4 (Δ : Ag(O₂CCF₃), ■ : Ag(p-toluenesulfonate). *Right:* Hill plot derived from the binding data for the formation of the tosylate complex **3.6**.

On the other hand, the binding of silver(I) tosylate appears to be considerably weaker as judged from the fact that more than two equivalents had to be added to achieve saturation (Figure 3.5). In this case, the binding isotherm reflects the typical sigmoidal behavior characteristic of homotropic allosteric systems. In order to assess the allosteric effects in this system, the binding data were analyzed using the Hill equation: $\log(Y/(Y-1)) = n_H \log[Ag+] + \log K$, where Y is the fractional saturation of the host, n_H is the Hill coefficient and K is the association constant. The intercept and slope obtained from the linear plot (Figure 3.5) were $\log K = (10.2 \pm 0.5)$ and $n_H = (2.0 \pm 0.1)$, respectively, with a correlation coefficient of 0.99. The Hill coefficient obtained in this way corresponds to the mathematical limit for a positive allosteric system involving two binding sites;⁹² it

thus serves to confirm the proposal that Ag(I) is bound to macrocycle **2.2** via a strongly cooperative process.

3.3.2 ^1H NMR spectroscopy experiments

Further support for the conclusion that the silver(I) binding in **2.2** is regulated by a positive allosteric effect came from ^1H NMR spectroscopic analyses. In particular, the spectrum of a mixture of 1 equiv. of **2.2** and ~ 1.3 equiv. of $\text{Ag}(\text{O}_2\text{CCH}_3)$ in $\text{THF-}d_8$ revealed the presence of two species (only) whose broad peaks overlapped. When this sample was cooled to -80°C the two sets of peaks were cleanly resolved and could be assigned to the free-base macrocycle **2.2** and the corresponding *bis*-silver(I) complex **3.5** (Figure 3.6).[‡]

Figure 3.6 Down-field regions of the ^1H NMR spectra (600 MHz, $\text{THF-}d_8$, 193 K) of **2.2** (top), a mixture of **2.2** and ~ 1.3 equiv. of $\text{Ag}(\text{O}_2\text{CCH}_3)$ (center) and **3.5** (bottom). The spectrum of the mixture features two separate sets of resonances for (from left to right) pyrrolic, iminic, and aromatic protons, which were assigned to species **2.2** and **3.5**.

[‡] An analogous experiment, conducted with silver tosylate, gave similar results; however, because of the overlap between the aromatic resonances of the tosylate anions and of the macrocycle, the visual comparison between the spectra appeared less straightforward.

Thus, even under conditions of intermediate binding site saturation, the coordination of a first Ag(I) cation appears to activate the system towards further coordination. In fact, as expected for a strongly cooperative ditopic receptor, no signals ascribable to a *mono*-Ag(I) complex were observed.

3.4 ORIGIN OF THE POSITIVE HOMOTROPIC ALLOSTERISM

Both in enzymatic and artificial systems, allostery has been related to a structural modification whereby a first binding event induces a non-linear response to subsequent guests.^{89,93,94} Generally, this modification involves a conformational change that affects the entropic penalty for ensuing binding events. As noted in Section 3.1 of this Chapter, in the case of synthetic systems, this has been accomplished most successfully via rotation about a symmetry axis of the host.^{94,95}

In the present case, coordination of a first silver(I) cation, along with concurrent hydrogen-bonding interactions involving the anionic counterion, is expected to change the orientation of the pyrrolic units to the “up-down” conformation seen in the solid state structure of complexes **3.5** and **3.6**. This change in orientation, in turn, allows for the coordination of a second ion pair within a less hindered and better pre-organized coordination site. As such, the allosteric silver(I) binding in **2.2** could be the result of an unprecedented mechanism of cooperativity in artificial systems.

The behavior observed with Ag(I) differs from what was seen with the previously reported Ni(II), Cu(II), and Zn(II) complexes (**2.17**, **2.18**, and **2.19**, respectively, Section 2.3), wherein no evidence of cooperative binding was seen. This apparent dichotomy can be rationalized in terms of steric effects. In the case of these divalent cations, the first coordinated metal center is expected to retain its two counteranions. As inferred from the

structure of the *bis*-Ni(II) complex **2.17** (Figure 2.9, Section 2.3), these counter anions are expected to occupy both sides of the mean macrocycle plane and participate in multiple hydrogen bonding interactions. Thus, in contrast to what is expected for the binding of Ag(I), coordination of a single divalent cation is not likely to produce a preorganized, unhindered site that would favor a subsequent binding event.

In order to understand better the factors affecting the cooperative binding of Ag(I) in **2.2**, the role of the anionic counterions, and specifically their hydrogen-bonding interactions with the macrocycle NH's, were investigated through a series of UV-vis titration experiments.

3.4.1 Role of the Anionic Counterions in the Absence of a Coordinating Cation

The putative effects of anions in regulating the binding behavior of macrocycle **2.2** were first analyzed in the absence of coordinating metal cations. Here, our goal was to explore whether the observed allostereism were caused exclusively by anion-driven effects. Towards this end, the binding of the carboxylate and sulfonate groups in **2.2** was investigated by carrying out UV-visible titrations using tetrabutylammonium (TBA) benzoate and TBA tosylate, respectively.

Since no previously reported data were available on the binding behavior of **2.2** as an anion receptor, the first experiments were aimed at determining the binding stoichiometry. This was done by constructing Job plots according to the *method of continuous variations* (i.e., by increasing the guest concentration while maintaining approximately constant the total concentration of all species in solution).^{118,119} The resulting data are shown in Figure 3.7. Interestingly, as inferred from the observation of maxima at 0.5 in the Job plots, both benzoate and tosylate anions bind to macrocycle **2.2** with a 1:1 host:guest stoichiometry.

Figure 3.7 Job plots used to infer the binding stoichiometry of anions interacting with macrocycle **2.2** (THF, 296 K, [anion]+[ligand **2.2**] $\sim$ 14.8 μ M). *Left*: tetrabutylammonium (TBA) benzoate, *right*: TBA tosylate.

While the coordinating Ag(I) cations direct the two counter-anions towards specific hydrogen-bonding orientations in complexes **3.5** and **3.6**, the macrocycle acts as a 1:1 anion binding receptor in the presence of benzoate and tosylate TBA salts. As such, the anion binding behavior of **2.2** did not provide new clues on the allosteric effects observed for silver binding.

3.4.2 Role of Hydrogen-Bonding Interactions in Regulating the Orientation of the Pyrrolic Subunits

In the hypothesis put forward to explain the observed allostereism in the present system (*vide supra*), hydrogen-bonding interactions between the anionic counterions and the pyrrolic NH's are proposed to play a key role. This is because these interactions are proposed to preorganize the second coordination site for optimal binding after the first equivalent of the silver(I) salt is bound. To the extent such rationalizations are correct, the

use of a silver source containing an anion with a poor hydrogen-bonding ability would be expected to lead to a lower level of cooperativity.

The tetraarylborates were identified as a family of appropriate anions for these experiments because of their stability and commercial availability as sodium or potassium salts. Silver(I) tetraphenylborate, tetrathienylborate, and tetrakis(*p*-chlorophenyl)borate salts (Figure 3.8) were prepared according to the literature procedure for the synthesis of AgPh_4B .¹²⁰ However, both the tetraphenylborate and tetrathienylborate salts proved poorly soluble in THF and therefore could not be used as silver sources for the desired UV-vis titration experiments. On the other hand, the moderately light-sensitive silver(I) tetrakis(*p*-chlorophenyl)borate salt proved soluble and was thus used for a UV-vis binding study.

Figure 3.8 From the left, schematic representations of the tetraphenylborate, tetrathienylborate, and tetrakis(*p*-chlorophenyl)borate anions.

The UV-vis titration experiments were carried out according to the experimental conditions previously used to study the binding of silver(I) trifluoroacetate and silver(I) tosylate in macrocycle **2.2** (see Section 3.3.1 of this Chapter). A normalized binding isotherm derived from the titration data with silver (I) tetrakis(*p*-chlorophenyl)borate is shown in Figure 3.9.

A Hill plot analysis of the binding data gave a Hill coefficient of (1.55 ± 0.05) and a $\log K$ of (8.3 ± 0.3) with a correlation coefficient of 0.99 (Figure 3.9).

Figure 3.9 Binding isotherm (left) and Hill plot (right) of the UV-vis titration of macrocycle **2.2** with silver(I) tetrakis(*p*-chlorophenyl)borate (THF, 296 K, $[2.2] = 5.7 \mu\text{M}$, $[\text{Ag}(p\text{-Cl-Ph})_4\text{B}] = 0.5 - 22.5 \mu\text{M}$).

Compared to the Hill coefficient of 2.0 obtained for the binding of silver tosylate, the significantly reduced n_H obtained in the tetrakis(*p*-chlorophenyl)borate case provides support for the notion that the anionic counterions, and particularly their ability to engage in hydrogen-binding interactions with the pyrrolic subunits, have a role to play in regulating the dynamics of cooperative binding in this particular cation coordinating system.

3.5 FUTURE DIRECTIONS

The binding studies described in the previous section examined the influence of the anionic counterions on the allostereism of silver binding in **2.2**. Such findings set the stage for the design of alternative systems where the regulating effects are further fine-tuned so as to enhance or diminish the cooperative effects.

For instance, the influence of the up-down conformation of the bipyrrrolic subunits on the allosteric behavior could be assessed through the preparation and study of appropriately modified macrocycles. Two potential candidates for these experiments are shown in Figure 3.10.

Figure 3.10 Proposed modifications of the macrocycle scaffold of **2.2** are expected to affect its conformational freedom and hence its allosteric behavior.

In the chiral cyclohexane-based system **3.7**, the coordination sites cannot be tilted above or below the average plane of the macrocycle; on the contrary, because of the *trans* substitution on the cyclohexane rings, the metal cations would be likely forced inside the macrocycle cavity. As the anionic counterions would probably assume a different and less favorable hydrogen-bonding geometry, the cooperativity of the system is expected to be substantially reduced.

In the benzobipyrrole-based system **3.8**, the two pyrrolic rings on each side of the macrocycle are tied together and thus the conformation of the bipyrrrolic subunits is locked. As proposed for the previous system, **3.7**, the geometric restriction imposed by the macrocyclic components is expected to inhibit, at least in part, the conformational flexibility that is considered necessary to observe an allosteric effect. As such, a decreased cooperativity is expected for silver(I) complexation in **3.8**.

Additionally, support for the proposed anion-driven cooperative effect could be obtained by excluding the anionic counterions from the primary coordination sphere of the metal cations. For example, the use of a metal center featuring non-labile neutral ligands (e.g., $[\text{Rh}(\text{CO})_2]^+$) would likely coordinate to the iminic donors of the macrocycle while leaving the anionic counterions in the outer coordination sphere. These experiments would examine the effect that steric hindrance within the metal primary coordination sphere would have on the allosteric behavior of the system.

Finally, a theoretical study aimed at calculating the individual geometries and stability constants for both the *mono*- and the *bis*-silver complexes is recommended. It would have the important effect of corroborating the available experimental data and of providing new clues and ideas for further experiments.

Although a complete elucidation of the cooperative behavior of **2.2** will require further theoretical and experimental analyses, this receptor represents the first example of what could emerge as a new (and potentially large) class of hosts for allosteric binding, namely multidentate oligopyrrolic macrocycles.

Chapter 4

Oxovanadium complexes of expanded porphyrins

4.1 BACKGROUND AND SIGNIFICANCE

The manifold role of vanadium in chemistry, biology and physiology^{121,122} continues to fuel interest in its coordination chemistry.¹²³ In fact, numerous high-valent vanadium compounds have been studied for their promising insulin-mimetic effects,¹²⁴ anticancer activity^{125,126} and antiviral properties.¹²⁷ On a very different level, a number of oxovanadium compounds have been employed in the area of synthetic organic chemistry, particularly to effect oxidative transformations.¹²⁸ Finally, in work that is perhaps more closely related to this Dissertation, the chemistry of vanadium porphyrins has proven to be quite rich.

The first vanadium porphyrin compound was described in 1934 by Treibs, who isolated a vanadyl porphyrinato species from crude petroleum.¹²⁹ Since then, vanadium petroporphyrins (i.e., metalloporphyrins found in fossil fuels) have continued to attract the attention of the geochemical community.¹³⁰ In fact, metals have detrimental consequences on the upgrading processes of raw petroleum and hence the physicochemical properties of vanadyl porphyrins have been investigated in the context of petroleum demetallization studies. However, the possibility to access and study a range of different metal-centered oxidation states, and in particular study the biologically relevant V(V)/V(IV) interplay, has promoted the study of vanadium porphyrin for their potential in biomedical applications. Indeed, several vanadium(IV) porphyrins are currently being studied for their anti-HIV properties.¹³¹

These rather disparate interests are providing an incentive to make and study new vanadium complexes of porphyrins and porphyrin analogues.

As described in the previous Chapters of the present Dissertation, a range of different expanded porphyrin metal complexes have been described to date. Core-expanded porphyrin analogues have been shown to coordinate both soft cations (e.g., Cu^+ and Ag^+) and hard cations (e.g., Gd^{3+} and UO_2^{2+}). However, the coordination chemistry of early transition metals in these types of macrocycles is all but unexplored.[¶] In fact, while the stabilization of actinide oxocations is well-documented in expanded porphyrin chemistry, as a class these species have not been established as being effective ligands for early transition metal oxocations.

The present Chapter describes the preparation and characterization of two novel oxovanadium(V) complexes of oligopyrrolic macrocycles (i.e., a tetrapyrrolic Schiff base system and a hexapyrrolic carbon-bridged macrocycle). The structural characterization of both complexes reveals a new supramolecular aspect of expanded porphyrin coordination chemistry, namely the bimodal (i.e., covalent and noncovalent) recognition of the nonspherical cationic guest VO_2^+ . Additionally, Section 4.4 describes initial evidence on vanadium coordination within other oligopyrrolic receptors. Taken in concert, the findings detailed in this Chapter indicate that expanded porphyrins constitute a promising class of ligands for the stabilization of vanadium and, by extension, other early transition metal cations.

[¶] Interesting vanadium complexes of non core-expanded artificial porphyrin derivatives, namely calixpyrrole and naphtho-fused tetraazachlorines, bacteriochlorines and isobacteriochlorines, have been reported. See: (a) Jubb, J., Scoles, L., Jenkins, H., Gambarotta, S. *Chem. Eur. J.*, **1996**, 2, 767-771; (b) Fukuda, T., Makarova, E. A., Luk'yanets, E. A., Kobayashi, N. *Chem. Eur. J.*, **2004**, 10, 117-133.

4.2 A TETRAPYRROLIC SCHIFF BASE MACROCYCLE

4.2.1 Preparation of the ligand

Macrocycle **4.1** (Scheme 4.1) is a tetrapyrrolic Schiff base expanded porphyrin with a 22 π -electron conjugated pathway. Interestingly, the ^1H NMR spectrum of this species did not display proton resonances that are characteristic of a 22 π -electron aromatic system, and the lack of ring current effects was attributed to the strong localized aromaticity of the phenyl ring and the steric effects of the pyrrolic β -substituents that served to enforce a lack of coplanarity for the full conjugated pathway).¹³²

The first example of this type of oligopyrrolic system was reported in 1996 by the Sessler group¹³³ and, since then, several analogues have been prepared.^{132,134,135} The substitution pattern on the periphery of the macrocycle has been varied (on the pyrrolic rings, as well as on the phenyl ring and on the *meso* bridge). Nonetheless, all the reported synthetic strategies require the preparation of a diformylated tetrapyrrolic subunit, which is then reacted with *ortho*-phenylenediamine to produce the desired macrocycle. Here, a new, efficient synthesis of this expanded porphyrin-type Schiff base macrocycle is described. It proceeds through a one-pot condensation/decarbonylation reaction and features diformylbipyrrole as the only pyrrolic precursor (Scheme 4.1).

Scheme 4.1 Preparation of macrocycle **4.1** using diformylbipyrrole.

The new synthesis of **4.1** relies on the reaction of 5,5'-diformyl-4,4'-diethyl-3,3'-dimethyl-2,2'-bipyrrole **4.2** with 1,2-phenylenediamine **4.3** in the presence of a catalytic amount of nitric acid. It should be noted that similar condensation conditions are known to yield the tetrapyrrolic octa-aza [2+2] Schiff base macrocycle **2.2**,⁸⁶ which was employed as a ligand for the coordination studies described in Chapters 2 and 3 of the present Dissertation. However, the use of a 2:1 diformylbipyrrole:1,2-phenylenediamine stoichiometry, along with a dropwise addition of the latter to the reaction mixture, directs the transformation towards the formation of the desired product **4.1** in 59% yield.

Since this novel preparation of macrocycle **4.1** differs significantly from the previously reported synthetic routes, detailed experimental and characterization data for **4.1** are included in Chapter 5 of the present dissertation. Additionally, a solid-state structural characterization of an acid salt of macrocycle **4.1** was obtained.

Probably owing to the rather small cavity size of macrocycle **4.1** (ca. 5×7 Å), the formation of a monoprotonated species in acidic media was proposed in previous work on this ligand.¹³⁵ However, as shown in Figure 4.1, macrocycle **4.1** was found to form a diprotonated nitrate salt, in which all the pyrrolic nitrogen atoms and one of the iminic nitrogens are protonated. The internal cavity of the resulting doubly charged species is characterized by an array of hydrogen-bonding donors (i.e., NH groups) and therefore it is not surprising that the nitrate anions in **4.1**·(HNO₃)₂ are engaged in multiple hydrogen-bonding interactions.

The torsion angles between alternate bonds along the conjugated pathway of **4.1**·(HNO₃)₂ range between 0° and $\pm 25^\circ$. Nonetheless, the macrocycle appears approximately planar, with the observed deviations being likely due to the presence β -substituents on the pyrrolic rings.

Figure 4.1 View of the acid salt **4.1**·(HNO₃)₂ showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity.

4.2.2 Preparation of an oxovanadium(V) complex

Macrocycle **4.1** has been shown to coordinate the high-valent actinide oxocations UO₂²⁺, NpO₂⁺ and PuO₂⁺.¹³⁵ As such, this oligopyrrolic receptor was selected for a study involving the coordination of vanadium oxocations, which can be considered as lighter congeners of the actinide oxocations within the first transition metal series.

A vanadium complex of expanded porphyrin **4.1** was obtained by treating the free base macrocycle with vanadyl acetylacetonate (VO(acac)₂) in THF at room temperature under aerobic conditions (yield: 61%). As illustrated by the UV-visible absorption spectra in Figure 4.2, the reaction was accompanied by a dramatic color change. This

meant that the conversion of the purple starting material **4.1** into the green vanadium complex **4.4** could be conveniently monitored by observing the changes in the UV-visible spectrum of the reaction mixture. After two days, the reaction was judged complete and the product was purified by preparative thin layer chromatography using alumina plates.

Figure 4.2 UV-visible absorption spectra of macrocycle **4.1** (dashed line) and of the dioxovanadium(V) complex **4.4** (solid line) in CH_2Cl_2 at room temperature.

Alternatively, complex **4.4** could be prepared using the vanadium(V) reagent $\text{VO}(\text{O}-i\text{Pr})_3$. This highly hygroscopic vanadium source was added dropwise to a THF solution of the free base macrocycle **4.1** under an argon atmosphere. After removal of the solvent, complex **4.4** was exposed to air and then isolated using the same purification procedure (chromatography on neutral alumina). However, when $\text{VO}(\text{acac})_2$ was used as a metal source and metal insertion was attempted under an inert atmosphere, no spectral evidence supporting the formation of a vanadium complex was observed. While features ascribable to trace amounts of product **4.4** were seen in the UV-visible spectrum of the

reaction mixture after a reaction time of four or five days, the formation of this complex was attributed to the presence of adventitious oxygen in the reaction vessel. In fact, while macrocycle **4.1** proved capable of stabilizing a dioxovanadium(V) complex, evidence for the formation of a vanadium(IV) complex could not be obtained.

The insertion of the dioxovanadium(V) cation was first inferred through electrospray ionization mass spectrometry. As often observed for metalation reactions using $\text{VO}(\text{acac})_2$ under aerobic conditions,¹³⁶ the resulting complex features a vanadium center in its highest oxidation state. However, with six nitrogen donors available for coordination, no inferences could be drawn regarding the geometry of the VO_2^+ cation in complex **4.4**.

An unambiguous description of the vanadium coordination geometry within the macrocycle cavity was obtained through X-ray diffraction analysis. Suitable single crystals grew as very dark lathes from a concentrated solution of **4.4** in CH_2Cl_2 and CH_3OH at -20°C . A top view of the refined crystal structure is shown in Figure 4.3. The monovalent VO_2^+ cation, in the expected cisoidal conformation, coordinates to three pyrrolic nitrogen atoms acting as a tridentate monoanionic ligand. The vanadium center lies in a highly distorted trigonal bipyramidal environment with a geometric parameter τ of 0.57 (where τ values of 0 and 1 indicate an ideal square pyramid and an ideal trigonal bipyramid, respectively).¹³⁷ The vanadium-oxygen distances (V1-O1, 1.618(3) Å and V1-O2, 1.635(3) Å), as well as the angle between the two oxo ligands (O1-V1-O2, $108.96(15)^\circ$), closely resemble those observed in other complexes of the VO_2^+ cation with a tridentate ligand.^{126,138-140} Similarly, the vanadium-nitrogen bond distances in **4.4**, with an average of 2.098 Å, compare well with those reported in the literature for complexes containing iminic nitrogen donors.¹³⁸⁻¹⁴⁰

Figure 4.3 View of the dioxovanadium complex **4.4** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. A primary carbon on one of the ethyl groups is disordered about two orientations as shown. Dashed lines are indicative of hydrogen-bonding interactions.

The structure of complex **4.4** can also be compared to those of vanadyl porphyrins, in which the V-N bond lengths typically range between 2.012 and 2.236 Å.¹⁴¹⁻
¹⁴⁴ However, it is important to appreciate that ligand **4.1** differs dramatically from porphyrins in that it supports the formation of a VO₂⁺ complex, rather than a VO²⁺ complex, as always found in high oxidation state vanadium porphyrins.

Complex **4.4** also differs from porphyrins in that the ligand does not fully complex the bound cation. In fact, three of the six nitrogen atoms of the macrocycle do not participate in the metal coordination. The pyrrolic nitrogen N5 is engaged in a hydrogen bonding interaction with one of the oxo ligands (N5-H...O2). Interestingly, the two remaining nitrogen atoms, bound to the phenyl ring, were found to be chemically

distinct. A hydrogen atom bound to nitrogen N3 was located in a difference Fourier map during the crystal structure refinement. This hydrogen is involved in a second hydrogen bonding interaction an oxo ligand atom, namely O2 (N3-H $\cdots$ O2). Thus, while nitrogen N4 is iminic (N4-C16, 1.293(5) Å and C16-C17, 1.434(6) Å), nitrogen N3 was found to be part of an unusual enamine involving the macrocyclic skeleton (N3-C9, 1.330(5) Å and C9-C8, 1.385(6) Å).

In fact, the formation of the enamine tautomer **4.1'** (Scheme 4.2) alters the conjugation pathway of the macrocycle, thus allowing it to act as a monoanionic tridentate ligand for the vanadium center in complex **4.4**.

Scheme 4.2 Formation of the oxovanadium complex **4.4** from the enaminic tautomer of macrocycle **4.1**.

As an additional consequence of the tautomerism shown in Scheme 4.2, the macrocycle engages one of the oxo ligands in two hydrogen-bonding interactions. As such, complex **4.4** represents a new contribution to the area of nonspherical guest recognition, namely one that features a bimodal binding between a metal oxocation and a single molecular receptor. Indeed, the nonspherical guest VO_2^+ in **4.4** is stabilized through both covalent bonds and intramolecular hydrogen-bonding interactions.[‡]

The room-temperature ^1H NMR spectrum of complex **4.4** provides support for the notion that the solid-state structure shown in Figure 4.3 is retained in solution. As a result of the loss of symmetry in complex **4.4** compared to the free base macrocycle **4.1**, the protons on the four pyrrolic methyl groups resonate as four different singlets in the aliphatic region. Additionally, nine different protons were found to resonate in the down-field region between 7.5 and 11.5 ppm. Resonances in this region include: (a) a group of peaks in the 7.6-8.3 ppm range for the four expected aromatic protons and the proton on the *meso* bridge, (b) two doublets for the enaminic protons (a sharp CH peak at $\delta_{\text{H}} = 8.81$ ppm and a broad NH peak at $\delta_{\text{H}} = 9.80$ ppm), and (c) two singlets accounting for one iminic proton ($\delta_{\text{H}} = 9.61$ ppm) and one pyrrolic NH ($\delta_{\text{H}} = 11.43$ ppm).

In summary, the elucidation of the VO_2^+ coordination mode leads to the conclusion that the macrocycle undergoes an imine-enamine tautomerism so as to maximize the number of interactions (both covalent and non-covalent) with the singly charged nonspherical cationic guest. To the best of the author's knowledge, both the stabilization of an oxovanadium cation and the specific rearrangement observed in macrocycle **4.1** are unprecedented in the coordination chemistry of expanded porphyrins.

[‡] The field of multi-mode cation recognition was pioneered by Raymond and coworkers in the early 1990's. For early examples involving, respectively, the dioxouranium(VI) and the dioxoosmium(VI) cations, see: (a) Franczyk, T. S., Czerwinski, K. R., Raymond, K. N. *J. Am. Chem. Soc.*, **1992**, *114*, 8138-8146; (b) Borovik, A. S., Du Bois, J., Raymond, K. N. *Angew. Chem. Int. Ed.*, **1995**, *34*, 1358-1362.

4.2.3 Preparation of hydrophilic analogues

As already noted in Section 2.4 of the present dissertation, the evaluation of the potential of expanded porphyrins and their metal complexes in a number of biomedical applications often relies on the availability of hydrophilic analogues of the parent macrocyclic ligands.

In the case of Schiff base oligopyrrolic ligands such as texaphyrin and macrocycle **2.23** (cf. Section 2.4), the functionalization of the phenylenediamine precursor with polyethyleneglycol (PEG) chains proved to be a successful strategy for the preparation of ligands of higher hydrophilicity. As such, a PEG-containing phenylenediamine was selected here as a convenient starting material for the introduction of two PEG chains in the macrocyclic scaffold of **4.1**.

Reaction of 2,2'-diformyl-3,3',4,4'-tetramethyl-5,5'-bipyrrole **4.5** with 4,5-*bis*-(2-(2-methoxyethoxy)ethoxy)ethoxy)benzene-1,2-diamine **4.6** (Scheme 4.3) afforded the hydrophilic macrocycle **4.7** according to the experimental procedure previously employed for the preparation of **4.1**. Similarly, the PEG-containing vanadium complex **4.8** was obtained according to the metalation conditions described in the previous Section for the preparation of **4.4**.

Scheme 4.3 Preparation of a more hydrophilic analogue of macrocycle **4.1** and of the corresponding vanadium complex. The phenyl ring of the ligand has been functionalized with two polyethyleneglycol (PEG) chains.

Mass spectrometric and ^1H NMR spectroscopic data for **4.7** and **4.8** are consistent with the proposed structures depicted in Scheme 4.3. Additionally, the UV-visible absorption spectra of the PEG-containing species are practically identical to the ones of the original compounds **4.1** and **4.4** (Figure 4.2) and are characterized by a red shift of the absorption bands of the complex with respect to the ones of the free base macrocycle. In particular, the large absorption band of the ligand at ca. 590 nm is replaced by two sharp and intense bands at 667 nm and 726 nm in the spectrum of the complex.

Although compounds **4.7** and **4.8** are not fully water-soluble, they show good hydrophilicity and can be dissolved in a dimethylsulfoxide/water mixture (ca. 5% v/v DMSO). Thanks to the functionalization with polyethyleneglycol chains, these

tetrapyrrolic Schiff base macrocycles are now viable compounds for further experiments in hydrophilic media.

4.3 ISOAMETHYRIN

[24]Hexaphyrin(1.0.1.0.0.0) **4.9** (Scheme 4.4), commonly referred to as isoamethyrin, is a quaterpyrrole-containing isomer of [24]hexaphyrin(1.0.0.1.0.0), also known as amethyrin (cf. Section 1.2.2). Interestingly, macrocycle **4.9** is a 24 π -electron antiaromatic system, as judged by the strong downfield shifts of its inner NH protons (δ_{H} = 23.7, 23.9 and 24.2 ppm in CD_2Cl_2 at room temperature).¹⁴⁵

Early metalation studies showed that treatment of macrocycle **4.9** with the actinide oxocations UO_2^{2+} and NpO_2^{+} is accompanied by a dramatic color change and by oxidation of the ligand to a 22 π -electron aromatic system.¹⁴⁵ As a consequence, isoamethyrin is currently being evaluated for its potential use as a colorimetric actinide sensor.¹⁴⁶

Although the coordination chemistry of amethyrin is well established (cf. Section 1.2.2), the ability of isoamethyrin to coordinate transition metals was only recently examined. While exposure to most transition metal salts failed to provide evidence of complex formation (as inferred from UV-vis spectroscopic studies),¹⁴⁶ it was found that treatment of the free base **4.9** with copper(II) acetate readily afforded a binuclear Cu(II) complex.⁶³

Furthermore, as previously noted in the case of the Schiff base system **4.1**, the stabilization of the UO_2^{2+} and NpO_2^{+} cations¹⁴⁵ in macrocycle **4.9** provided an incentive

for the study of this oligopyrrolic receptor for the stabilization of lighter congeners of the heavy metal oxocations and particularly for high-valent vanadium species.

The oxovanadium adduct **4.10** was prepared by treating macrocycle **4.9** with $\text{VO}(\text{O-iPr})_3$ at 0°C under an argon atmosphere for 3 hours (Scheme 4.4). While longer reaction times and a higher temperature resulted in a decreased yield and in the appearance of numerous decomposition products, complex **4.10** proved to be air-stable and was separated from residual starting material and minor side products via chromatographic purification over neutral alumina.

Scheme 4.4 Preparation of an oxovanadium(V) derivative of isoamethyrin **4.9**.

The room-temperature ^1H and ^{13}C NMR spectra of **4.10** indicated that cation coordination results in the formation of a highly asymmetric species. For example, all of the aliphatic groups were found to be non-equivalent, with the six pyrrolic methyl group protons resonating as six separate singlets in the ^1H NMR spectrum. Additionally, and in accordance with previous metalation studies of **4.9** with the uranyl cation,¹⁴⁵ the non-aliphatic protons of complex **4.10** were found to resonate in the (4 – 11) ppm range, a finding that is consistent with antiaromatic character of the macrocycle being lost upon metal insertion.

The specific coordination mode of the vanadium oxocation in hexaphyrin **4.10** was inferred from an X-ray diffraction analysis (Figure 4.4). The vanadium center resides in a distorted square pyramidal environment with a geometric parameter τ of 0.35 (where τ values of 0 and 1 indicate an ideal square pyramid and an ideal trigonal bipyramid, respectively).¹³⁷ The observed connectivity and the bond distances in the first coordination sphere of the metal cation in **4.10** closely resemble those seen in the oxovanadium complex **4.4** described in the previous Section. It is noteworthy that in both cases, the macrocyclic scaffold acts as a monoanionic tridentate ligand.

Figure 4.4 View of the oxovanadium complex **4.10** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. A primary carbon on one of the ethyl groups is disordered about two orientations as shown. Dashed lines are indicative of hydrogen-bonding interactions.

Interestingly, the X-ray structure reveals that a hydroxo group has undergone insertion into the α carbon of a pyrrole ring, a finding that leads us to conclude that the oligopyrrolic skeleton undergoes nucleophilic attack by hydroxide anion during the course of metal coordination. This type of reactivity, while unusual, has been observed previously during the formation of a uranyl sapphyrin complex,¹⁴⁷ and several *bis*-Cu(II) complexes of *meso*-aryl-substituted hexaphyrins.¹⁴⁸ In one extreme case reported by Osuka and coworkers, metal insertion was found to occur concurrent with hydrolytic cleavage of a pyrrole ring.¹⁴⁹

Both the O3H group and the pyrrolic N3H group contribute to the stabilization of the VO_2^+ cation through two hydrogen-bonding interactions to the O1 and O2 oxo ligands, respectively. This type of stabilization differs from that seen in the previous Schiff base system **4.4** and defines a new type of bimodal oxocation recognition within a macrocyclic cavity.

The stability in solution of this solid-state structure, as well as the presence of a bound OH group, were confirmed by high-resolution mass spectrometry and by NMR spectroscopy (the hydrogen-bound hydroxylic proton resonates as a deshielded singlet at $\delta_{\text{H}} = 11.00$ ppm).

The formation of the vanadium complex **4.10** can be monitored by following the changes in the UV-visible absorbance spectral characteristics of the reaction mixture. Specifically, over the course of the reaction, the yellow free base **4.9** is converted into a dark brown product (Figure 4.5). In fact, while the complexation of UO_2^{2+} and Cu^{2+} was reported to yield in both cases a pink aromatic species, the formation of the non-conjugated system **4.10** is characterized by completely different spectral changes.

Figure 4.5 UV-visible absorption spectra of macrocycle **4.9** (dashed line) and of the dioxovanadium(V) derivative **4.10** (solid line) in CH_2Cl_2 at room temperature.

In summary, the present work, in combination with other studies reporting the stabilization of uranyl, neptunyl, and copper complexes, underscores the versatility of isoamethyrin as a ligand, specifically its ability to stabilize very different kinds of transition metal cation complexes, to undergo oxidation upon metal coordination, and to achieve bimodal recognition of nonspherical guests.

4.4 OTHER SYSTEMS

The new complexes **4.4** and **4.10** described in the present Chapter indicate that expanded porphyrins show promise as a new class of macrocyclic ligands for the stabilization of biologically-relevant vanadium cations. As such, they provide an incentive for the investigation of vanadium coordination in other oligopyrrolic systems.

4.4.1 A dipyrromethane-based macrocycle

Owing to its rather simple synthesis,⁶⁵ macrocycle **2.1** is one of the most studied oligopyrrolic receptors. Only four years since the first reported syntheses in 2003, ligand **2.1** has already displayed a rich and diverse coordination chemistry. This was reviewed in Chapter 2 of the present Dissertation (Section 2.2). In order to probe further the coordinating ability of macrocycle **2.1b**, this system was investigated in the context of the present vanadium insertion study.

As judged by high-resolution mass spectrometric data, treatment of free base **2.1b** with VO(acac)₂ under aerobic condition afforded an oxovanadium complex.

NMR spectroscopic data indicated the formation of a diamagnetic vanadium(V) species of significantly lower symmetry with respect to the starting material. For instance, both ¹H and ¹³C NMR spectra featured two non-equivalent methoxy group resonances and two non-equivalent iminic resonances. In general, the NMR spectra of the isolated solid featured two separate sets of peaks ascribable to the presence of two tetradentate pockets, each defined by one dipyrromethane unit and two iminic nitrogens from each of the two diimine units. As such, the loss of symmetry of the macrocycle skeleton was found to be consistent with the structure proposed in Scheme 4.5. The vanadium(V) oxocation is expected to coordinate to one of the tetradentate pockets of the ligand in a way that is reminiscent of the uranyl complex of **2.1** reported by Arnold and coworkers (cf. complex **2.6**, Section 2.2).⁶⁸

Scheme 4.5 Proposed preparation of an oxovanadium complex of the dipyrromethane-based macrocycle **2.1**.

Further, consistent with the proposed connectivity for **4.11** (Scheme 4.5), the ^1H NMR spectrum of the isolated product revealed a singlet peak resonating at $\delta_{\text{H}} = 14.89$ ppm. This signal integrated for two protons and was attributed to two deshielded pyrrolic NH's. Indeed, the pyrrolic NH's of the non-coordinating dipyrromethane moiety are expected to engage in hydrogen-bonding interactions with the oxo ligand of the cationic guest.

Although the collected characterization data supports the formation of a novel oxovanadium(V) complex, it should be noted that the exact molecular identity of the product has not been fully elucidated. For instance, a proton signal corresponding to the putative hydroxyl group in **4.11** was not observed in the ^1H NMR spectrum of the isolated species. Unfortunately, in spite of numerous crystallization attempts, a single crystal of this new vanadium complex was not obtained and thus a definitive description of its structure cannot be provided.

4.4.2 Texaphyrin

In the dioxovanadium(V) complexes described in Sections 4.2 and 4.3, the oligopyrrolic receptors were found to act as monoanionic tridentate ligands. This

consideration led to the evaluation of texaphyrin, a well-known monoanionic oligopyrrolic ligand, as a potential receptor for oxovanadium coordination. In fact, as reviewed in Section 1.3.1, multiple coordination studies have shown that texaphyrin can act as a monoanionic ligand in both a tridentate and a pentadentate fashion.

Several metalation reactions were attempted using different vanadium sources (i.e., $\text{VO}(\text{acac})_2$, $\text{VO}(\text{Oi-Pr})_3$, and $\text{VOSO}_4 \cdot 5\text{H}_2\text{O}$). However, treatment of texaphyrin **4.12** with vanadium reagents in methanol or tetrahydrofuran, both at room temperature or under reflux conditions, failed to provide any identifiable vanadium complex, with long reaction times merely leading to decomposition of the macrocycle.

Scheme 4.6 Proposed preparation of a vanadium texaphyrin complex.

Conversely, treatment of **4.12** with $\text{VOSO}_4 \cdot 5\text{H}_2\text{O}$ in N,N-dimethylformamide at 180°C (Scheme 4.6) led to the formation of a green new product, which was found to be compatible with a vanadium texaphyrin complex. Indeed, as previously observed for all the metal complexes of texaphyrin,^{50,51} the UV-visible absorption spectrum of the reaction product featured a rather intense band at approximately 740 nm. Additionally, the

presence of a bound oxovanadium cation was confirmed by high-resolution mass spectrometry.

The employed experimental procedure has been reported as an effective method for the preparation of vanadyl porphyrins;¹⁵⁰ however, in the case of texaphyrin, the harsh metal insertion conditions (i.e., $\text{VOSO}_4 \cdot 5\text{H}_2\text{O}$, DMF, 180°C) led to the formation of numerous side products. Unfortunately, in spite of several chromatographic purifications, the target molecule could not be completely separated from the unwanted co-products.

While the present initial investigation has provided support for the notion that texaphyrin can be used as a platform for vanadium coordination, further studies are required for the identification of a convenient reaction route that would optimize the formation of the desired vanadium complex over other the numerous side products observed so far.

4.5 FUTURE DIRECTIONS

The coordination chemistry of early transition metals in oligopyrrolic receptors is still in its infancy. Nonetheless, the findings reported in the present Chapter allow one to envision several directions for further investigations.

The pyrrolic nitrogen atoms in macrocycles **4.1** and **4.9** have been shown to effectively coordinate to the VO_2^+ cation both as neutral iminic donors and as anionic amidic donors. As such, the use of small pyrrolic fragments as ligands for vanadium coordination could provide intriguing opportunities for the preparation of new simple complexes of this biologically relevant element. For instance, prodigiosins **4.14** (Scheme 4.7) are a class of naturally occurring tripyrrolic compounds that fully reproduce the coordinating fragment in complexes **4.4** and **4.10**; they thus appear as promising

candidates for vanadium coordination studies. Moreover, the metalation behavior of prodigiosins towards high-valent vanadium species could be compared to those of simple dipyrromethenes such as **4.15**. These latter compounds that are known to act as bidentate chelators in the homoleptic and heteroleptic complexation of transition metals. Thus, this comparison could be potentially quite informative.

Scheme 4.7 Pyrrole-based skeleton of prodigiosins (left) and dipyrromethenes (right).

The bimodal recognition of vanadium oxocations in macrocycles **4.1** and **4.4** has allowed us to identify a new aspect of the coordination chemistry expanded porphyrin ligands. Given the number of oligopyrrolic macrocycles prepared to date, the study of such supramolecular aspect of oxovanadium coordination can be pursued further using a wide variety of appealing ligands. Additionally, it should be noted that the parallelism proposed in Section 4.1, between the binding of oxoactinide and oxovanadium cations, has led to the evaluation of uranyl-binding macrocycles **4.1** and **4.4** as oxovanadium receptors. Similarly, other known uranyl-binding macrocycles, such as sapphyrin,¹⁴⁷ oxasapphyrin,¹⁵¹ and alaskaphyrin,¹⁵² could be investigated as potential receptors for early transition metal cations.

An appropriate hydrophilic functionalization of the oligopyrrolic ligands will then allow the evaluation of the potential biological activity of pyrrole-based vanadium complexes. Furthermore, electrochemical studies will reveal the influence of the

oligopyrrolic ligands on the redox chemistry of the vanadium centers, and specifically on the biologically relevant V(V)/V(IV) and V(IV)/V(III) redox pairs.

While the study of vanadium biochemistry continues to reveal new roles of this transition element in biology (e.g., in the newly discovered vanadium-binding proteins called *vanabins*),¹²² numerous investigations on synthetic vanadium compounds aim at identifying new candidates for biomimetic studies or for drug discovery. As illustrated by the vanadium complexes reported in this Chapter, expanded porphyrin macrocycles may have a role to play in the search for stable bio-compatible vanadium species.

Chapter 5

Experimental Procedures

5.1 GENERAL PROCEDURES

Prior to use, all glassware was soaked in KOH-saturated isopropyl alcohol for ca. 12 h and then rinsed with water and acetone before being thoroughly dried. Tetrahydrofuran (THF) was dried by passage through two columns of activated alumina. Acetonitrile, methanol and dimethylformamide were dried by passage through two columns of molecular sieves. Toluene was dried by passage through one column of Q-5 reactant and one column of neutral alumina. When used as reaction medium, dichloromethane was freshly distilled from CaH_2 . Dichloromethane used for chromatographic purifications was purchased from Fisher Scientific and used as received. *n*-Pentane was stirred over concentrated H_2SO_4 for more than 24 h, neutralized with K_2CO_3 , and distilled from CaH_2 . Triethylamine was distilled over barium oxide. Hexanes were purchased from Fisher Scientific and used as received.

Unless otherwise stated, reagents and metal salts were purchased commercially (Aldrich, Acros or Strem) and used as received. Precursors and reagents that could not be obtained from commercial sources were prepared according to previously published procedures, with the references for the preparation being cited in the main text.

Solutions were stirred magnetically.

Column chromatography purifications were carried out using Sorbent Technologies standard grade silica gel (60 Å, 40-63 µm) or neutral alumina (standard activity I, 50-200 µm). Silica gel and neutral alumina plates for analytical thin layer chromatography were purchased from Sorbent Technologies, Inc. or from Mallinckrodt

Baker, Inc. Neutral alumina plates for preparative thin layer chromatography (20×20 cm) were purchased from Analtech, Inc.

As specified in the individual synthetic procedures below, reactions and manipulations of air-sensitive compounds were carried out under an atmosphere of dry, oxygen-free argon by means of standard Schlenk techniques or in a Vacuum Atmospheres drybox.

Air-sensitive filtrations were performed using positive argon pressure to force solutions through a specially constructed filtration cannula. The port of the cannula was made by welding a stainless steel filter support to one end of a cannula purchased from Popper & Sons Inc. The filter was then constructed by fitting the port end of the stainless steel cannula with a piece of hardened filter paper (Whatman's No. 5) and then securing it with Teflon tape.

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Mercury 400 MHz, a Varian Inova 500 MHz, or a Bruker AC 250 MHz spectrometer. Chemical shifts (δ) are reported in ppm and referenced to the solvent. CD_2Cl_2 (Cambridge Isotope Labs) used for the characterization of air-sensitive Cu(I) complexes was dried through three freeze-pump-thaw cycles, before being transferred to a dry box where the NMR samples were prepared. All other deuterated NMR solvents were purchased from Cambridge Isotope Labs and used as received.

UV-visible spectra were recorded at room temperature on a Beckman DU-640 spectrophotometer.

Low- and high-resolution mass spectra were obtained at the Mass Spectrometry Facility of the Department of Chemistry and Biochemistry, University of Texas at Austin.

Elemental combustion analyses were performed by Atlantic Microlabs Inc., Norcross, GA or by Midwest Microlabs Inc., Indianapolis, IN.

5.2 SYNTHETIC DETAILS AND CHARACTERIZATION DATA

Bis-Cu(II) complex 2.10, [(C₃₈H₃₂N₈)Cu₂]: One equivalent of the free base macrocycle **2.1a** (13.9 mg, 0.0230 mmol) was dried overnight in a Schlenk flask under vacuum. The flask was charged with approximately one equivalent of Cu₅Mes₅ (16.0 mg, 0.0222 mmol) and 20 mL of THF. Within 20 minutes, the light yellow slurry became a dark brown solution. The reaction mixture was stirred overnight at ambient temperature before the solvent was removed under vacuum. The dark brown-green powder was re-dissolved in CH₂Cl₂, filtered, and exposed to air. Slow vapor diffusion of hexanes into CH₂Cl₂ produced 7.1 mg of **2.10** in the form of dark green crystals (45% yield). CI-HRMS M⁺ *m/z* 727.14317 (calc. for C₃₈H₃₃N₈Cu₂ 727.14147). Anal. calcd. for C₃₈H₃₂N₈Cu₂ · 1/2CH₂Cl₂: C, 60.03; H, 4.32; N, 14.55. Found: C, 60.09; H, 4.41; N, 14.31. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Bis-Cu(I) complex 2.13, [(C₃₈H₃₆N₈)Cu₂Cl₂]: One equivalent of the free base macrocycle **2.1a** (90 mg, 0.149 mmol) was dissolved in 10 mL of CH₂Cl₂ and treated with 0.30 mL of 1M HCl in diethylether and stirred for 10 minutes at room temperature. After the solvent was removed, the red-orange powder was dried overnight under vacuum. Then, the flask was charged with approximately one equivalent of Cu₅Mes₅ (100.0 mg, 0.1385 mmol) and 20 mL of THF. Within 30 minutes, the red-orange slurry became a orange-brown solution. The solution was stirred overnight at ambient temperature and the solvent removed under vacuum. The brown-orange powder was re-dissolved in THF, filtered under argon, and layered with *n*-pentanes to yield 36.7 mg of **2.13** as dark orange crystals (31% yield). ¹H NMR (400 MHz, CD₂Cl₂) δ 11.110 (br s, 4H, NH), 8.16 (s, 4H,

CHN), 7.27 (br d, 8H, ArH), 6.83 (m, 4H, pyrrolic CH), 6.20 (m, 4H, pyrrolic CH), 2.22 (s, 6H, CH₃), 1.83 (s, 6H, CH₃). ¹³C NMR (100 MHz, CD₂Cl₂) δ 148.8, 147.0, 145.0, 128.0, 127.4, 123.8, 117.7, 108.2, 36.8, 29.0, 27.0. Anal. calcd. for C₄₂H₄₀N₈O₄Cu₂·1.5THF: C, 58.02; H, 5.31; N, 12.30. Found: C, 58.64; H, 5.19; N, 12.37. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Bis-Cu(I) complex 2.14, [(C₄₆H₅₂N₈)Cu₂Cl₂]: One equivalent of the free base macrocycle **2.1c** (41.2 mg, 0.0575 mmol) was dissolved in 10 mL of CH₂Cl₂, treated with 0.15 mL of 1M HCl in diethylether, and stirred for 20 minutes at room temperature. After removal of the solvent under reduced pressure, the red-orange powder was dried overnight. Next, the flask was charged with approximately one equivalent of Cu₅Mes₅ (45.0 mg, 0.0623 mmol) and 20 mL of THF. The orange-brown solution was stirred overnight at ambient temperature before the solvent was removed under vacuum. The dark brown powder was re-dissolved in THF, filtered under argon, and layered with *n*-pentanes to yield 29 mg of **2.14** as orange crystal (55% yield). ¹H NMR (400 MHz, 296 K, CD₂Cl₂) δ 10.99 (br s, 4H, NH), 8.23 (s, 4H, CHN), 7.24 (m, 8H, ArH), 4.12 (s, 2H, CH₂), 4.08 (s, 2H, CH₂), 2.46 (q, 8H, CH₂CH₃), 2.23 (s, 12H, CH₃), 1.00 (t, 12H, CH₂CH₃). ¹³C NMR (62 MHz, 296 K, CD₂Cl₂) δ 146.0, 145.0, 134.5, 132.0, 127.0, 125.5, 125.0, 118.0, 17.5, 15.5, 9.5. Anal. calcd. for C₄₆H₅₂N₈Cu₂Cl₂·4CH₂Cl₂: C, 47.86; H, 4.82; N, 8.93. Found: C, 47.96; H, 4.91; N, 9.01. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Bis-Zn(II) complex 2.16, [(C₃₈H₃₆N₈)Zn₂F₂(BF₄)₂]: Free base macrocycle **2.1a** (81.0 mg, 0.134 mmol) was suspended in dry THF (30 mL) under an argon atmosphere. Upon addition of Zn(BF₄)₂·5H₂O (70.4 mg, 0.295 mmol), the yellow slurry became a

bright orange solution. The reaction mixture was stirred under argon for 3 hours and then concentrated to precipitate a pale orange solid. After filtration, the obtained crude powder was dissolved in a minimal amount of acetone and then placed in a freezer (-20°C) overnight to yield 71 mg of **2.16** as yellow crystals (56% yield). ¹H NMR (400 MHz, 296 K, DMSO-*d*₆): δ 11.96 (s, 2H, NH), 11.56 (s, 2H, NH), 8.80 (s, 4H, CHN), 7.65 (br s, 4H, ArH), 7.37 (br s, 4H, ArH), 7.22 (br s, 4H, pyrrolic CH), 6.49 (br s, 4H, pyrrolic CH), 1.89 (s, 12H, CH₃). ¹³C NMR (100 MHz, 296 K, DMSO-*d*₆): δ 178.70, 148.00, 147.50, 142.97, 132.98, 132.72, 127.81, 125.05, 120.70, 118.18, 113.29, 111.75, 107.72, 36.56, 36.07, 27.86, 27.60, 27.26, 26.81. CI-MS: M⁺ *m/z* 735; HR CI-MS: M⁺ *m/z* 735.148048 (calc. for C₃₈H₃₅N₈⁶⁶Zn₂: 735.150539). Anal. calcd. [C₃₈H₃₆B₂F₁₀N₈Zn₂]·2/5(THF): C, 51.14; H, 5.01; N, 9.94. Found: C, 51.33; H, 4.87; N, 9.48. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Bis-Cu(I) complex 2.20, [(C₄₈H₅₆N₈O₄)Cu₂(NO₃)₂]: A flame-dried Schlenk flask was charged with the macrocycle acid salt **2.2**·(HNO₃)₂ (40.6 mg, 0.0435 mmol) and allowed to stand overnight under vacuum before being transferred into a Vacuum Atmospheres drybox containing an argon atmosphere, where it was charged with Cu₅Mes₅ (36.2 mg, 0.0501 mmol). The flask was transferred from the drybox to a Schlenk line and THF (20 mL) was added under argon. After 4 h, the solvent was removed under reduced pressure. A dark red powder was obtained and washed with *n*-pentane. It was then dissolved in about 2 mL of CH₂Cl₂ and layered with *n*-pentane. Collection of the resulting crystalline solid gave 18.4 mg of **2.20** (34% yield). ¹H NMR (400 MHz, CD₂Cl₂): δ 11.00 (s, 4H, NH), 8.27 (s, 4H, CHN), 6.79 (s, 4H, ArH), 3.93 (s, 12H, OCH₃), 2.77 (q, 8H, CH₂CH₃), 2.07 (s, 12H, CH₃), 1.29 (t, 12H, CH₂CH₃). ¹³C NMR (125 MHz, CD₂Cl₂): δ 149.47, 144.84, 139.38, 138.60, 129.31, 126.04, 121.07, 102.52,

56.75, 18.22, 16.43, 10.28. Anal. calcd. $[(C_{48}H_{56}Cu_2N_8O_4)(NO_3)_2] \cdot 3CH_2Cl_2$: C 46.58; H, 4.75; N, 10.65. Found: C, 46.85; H, 4.96; N, 10.00. This compound was also characterized through X-ray diffraction analysis (see Appendix A).

Bis-Cu(II) complex 2.21, $[(C_{48}H_{54}N_8O_4)Cu_2(NO_3)_2]$: Crystals of **2.20** (10.0 mg) were exposed to air and dissolved in about 3 mL of CH_2Cl_2 . Slow vapor diffusion of *n*-pentane into the dichloromethane solution gave **2.21** as a crystalline solid. FAB-MS: M^+ m/z 932; HR FAB-MS: M^+ m/z 932.283378 (calc. for $C_{48}H_{54}Cu_2N_8O_4$: 932.286001). Anal. calcd. $[(C_{48}H_{54}Cu_2N_8O_4)(NO_3)_2] \cdot 1CH_2Cl_2 \cdot 2H_2O$: C 49.83; H, 5.29; N, 11.86. Found: C, 49.77; H, 5.14; N, 11.09. This compound was also characterized through X-ray diffraction analysis (see Appendix A).

Bis-Cu(II) complex 2.24, $[(C_{66}H_{88}N_8O_{16})Cu_2]$: A flame-dried Schlenk flask was charged with macrocycle acid salt **2.23** (40.0 mg, 0.0319 mmol) and allowed to stand overnight under vacuum before being transferred into a drybox containing an argon atmosphere, where it was charged with Cu_5Mes_5 (15 mg, 0.016 mmol). The flask was transferred from the drybox to a Schlenk line and THF (30 mL) was added under argon. After 12 hours, the reaction mixture was exposed to air and the solvent was removed under reduced pressure. The obtained brown powder was washed with *n*-pentane. It was then dissolved in about 2 mL of CH_2Cl_2 and layered with *n*-pentane. Collection of the resulting brown solid gave 23 mg of **2.20** (53% yield). CI-MS: $(M+1)^+$ m/z 1376. HR CI-MS: $(M+1)^+$ m/z 1375.4985 (calc. for $C_{66}H_{89}N_8O_{16}Cu_2$: 1375.4989). Anal. calcd. $[C_{66}H_{88}Cu_2N_8O_{16}] \cdot 1/2(n\text{-pentane})$: C, 58.24; H, 6.71; N, 7.93. Found: C, 58.55; H, 6.36; N, 8.56).

Bis-Zn(II) complex 2.25, [(C₆₆H₈₈N₈O₁₆)Zn₂Cl₄]: Free base macrocycle **2.23** (56.6 mg, 0.0452 mmol) was dissolved in dry THF (30 mL) under an argon atmosphere. Upon addition of ZnCl₂ (18.4 mg, 0.135 mmol), the brown solution became a fine suspension. The reaction mixture was stirred for 3 hours and then the solvent was removed under reduced pressure. The crude powder obtained in this way was dissolved in a 50/50 v/v mixture of CH₂Cl₂ and CH₃OH and then layered with *n*-pentane to yield a fine hygroscopic powder, which was dried under vacuum (40°C, 4 hours) to give 38 mg of **2.25** (55% yield). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 10.90 (s, 4H, NH), 8.29 (s, 4H, CHN), 7.05 (s, 4H, ArH), 7.00 (s, 4H, pyrrolic CH), 6.31 (s, 4H, pyrrolic CH), 4.24-3.31 (m, 60H, PEG OCH₂), 2.26 (s, 6H, CH₃), 1.83 (s, 6H, CH₃). ¹³C NMR (100 MHz, 296 K, CD₂Cl₂): δ 151.70, 149.55, 149.39, 134.85, 134.76, 128.42, 126.98, 110.38, 102.79, 72.27, 71.15, 70.92, 70.78, 69.94, 69.48, 59.00, 37.59, 29.78, 28.38, 26.60. CI-MS: M⁺ *m/z* 1377. HR CI-MS: M⁺ *m/z* 1377.500317 (calc. for C₆₆H₈₉N₈O₁₆Zn₂: 1377.497946). Anal. calcd. [C₆₆H₉₂Cl₄N₈O₁₆Zn₂]·2(CH₂Cl₂): C, 48.16; H, 5.71; N, 6.61. Found: C, 47.87; H, 5.43; N, 6.95.

Macrocycle 2.27, [C₇₆H₁₂₀N₈O₄Si₄]: 5,5'-Diformyl-3,3',4,4'-dimethyl-2,2'-bipyrrole (90.2 mg, 0.370 mmol) and 4,5-*bis*(triisopropylsiloxy)benzene-1,2-diamine were combined in a three-neck round-bottom flask under argon and suspended in dry CH₃OH (50 mL). After addition of a catalytic amount of concentrated HNO₃ (3 drops), the red reaction mixture was stirred for one hour under reflux condition. The resulting suspension was cooled to room temperature and filtered to collect 156 mg of **2.27**·(HNO₃)₂ as a brick-red powder (58% yield). The yellow free base **2.27** was then obtained by washing a dichloromethane suspension of the acid salt with a saturated aqueous solution of NaHCO₃. Acid salt **2.27**·(HNO₃)₂: ¹H NMR (400 MHz, CD₂Cl₂): δ

12.20 (br s, 6H, NH and CHNH⁺), 7.97 (br s, 4H, CHN), 6.75 (s, 4H, ArH), 2.28 (s, 12H, CH₃), 2.02 (s, 12H, CH₃), 1.38 (sep, 12H, CH(CH₃)₂), 1.16 (d, 72H, CH(CH₃)₂). Free base **2.27**: ¹H NMR (400 MHz, CDCl₃): δ 8.19 (s, 4H, CHN), 6.60 (s, 4H, ArH), 2.20 (s, 12H, CH₃), 1.97 (s, 12H, CH₃), 1.35-1.25 (m, 12H, CH(CH₃)₂), 1.14 (d, 72H, CH(CH₃)₂), pyrrolic NH protons not observed. ¹³C NMR (125 MHz, CDCl₃): 145.91, 145.47, 139.69, 128.14, 126.83, 125.71, 119.85, 109.63, 18.04, 14.11, 13.13, 10.22, 9.02. CI-MS: M⁺ *m/z* 1321; HR CI-MS: M⁺ *m/z* 1320.847197 (calc. for C₇₆H₁₂₀N₈O₄Si₄: 1320.850969).

Bis-Ag(I) complex 3.5, [(C₄₈H₅₆N₈O₄)Ag₂(CH₃CO₂)₂]: Macrocycle acid salt **2.2**·(HNO₃)₂ (51.0 mg, 0.0546 mmol) was suspended in CH₂Cl₂ and washed three times with a saturated aqueous solution of NaHCO₃ to obtain the free base **2.2**. The bright orange organic phase was dried over anhydrous Na₂SO₄ and the solvent was removed *in vacuo*. The solid was dissolved in THF (30 mL) under argon and Ag(O₂CCH₃) (20.0 mg, 0.120 mmol) was added. The dark red solution was stirred overnight under argon at room temperature. The reaction mixture was then exposed to air and filtered through Celite before the solvent was removed under reduced pressure. The brick-red solid was dissolved in CH₂Cl₂ (2 mL), layered with *n*-pentane and placed in a freezer at -20°C. After 24 h, the supernatant solution was decanted off to provide 58.1 mg of **3.5** as a microcrystalline brick-red powder (92%). UV-vis (THF): λ_{max}, nm (log ε) 404 (4.98). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 11.55 (s, 4H, NH), 8.37 (s, 4H, CHN), 6.74 (s, 4H, ArH), 3.90 (s, 12H, OCH₃), 2.74 (q, 8H, CH₂CH₃), 2.07 (s, 12H, CH₃), 1.62 (s, 6H, CH₃COO), 1.23 (t, 12H, CH₂CH₃). ¹³C NMR (100 MHz, 296 K, CD₂Cl₂): δ 178.83, 149.01, 146.68, 138.17, 137.96, 129.41, 126.79, 120.07, 102.90, 56.62, 22.64, 18.04, 16.53, 10.47. FAB-MS: (M+1)⁺ *m/z* 1023; HR FAB-MS: (M+1)⁺ *m/z* 1023.2573 (calc. for C₄₈H₅₇N₈O₄Ag₂: 1023.2604). Anal. calcd. [(C₄₈H₅₆N₈O₄Ag₂)(CH₃CO₂)₂]·(H₂O): C 53.80;

H, 5.56; N, 9.65. Found: C, 53.43; H, 5.39; N, 9.48. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Bis-Ag(I) complex 3.6, [(C₄₈H₅₆N₈O₄)Ag₂(C₇H₇SO₃)₂]: Macrocycle **2.2** (20.2 mg, 0.0247 mmol) was treated with silver(I) *p*-toluenesulfonate (70.9 mg, 0.519 mmol) according to the procedure described above for the preparation of **3.5**. Complex **3.6** (38.2 mg) was isolated as a microcrystalline powder (81%). UV-vis (THF): λ_{max} , nm (log ϵ) 409 (4.98). ¹H NMR (400 MHz, 296 K, THF-*d*₈): δ 11.23 (s, 4H, NH), 8.41 (d, 4H, CHN), 7.31 (d, 4H, tosylate ArH), 6.85 (d, 4H, tosylate ArH), 6.82 (s, 4H, ArH), 3.85 (s, 12H, OCH₃), 2.79 (q, 8H, CH₂CH₃), 2.14 (s, 6H, tosylate CH₃), 2.01 (s, 12H, CH₃), 1.27 (t, 12H, CH₂CH₃). ESI-MS: (M+1)⁺ *m/z* 1023. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Macrocycle 4.1, [C₃₇H₄₄N₆]: 5,5'-Diformyl-4,4'-diethyl-3,3'-dimethyl-2,2'-bipyrrole (100mg, 0.37 mmol) was dissolved in CH₃OH (50 mL) and concentrated HNO₃ (3 drops) was added. A solution of benzene-1,2-diamine (20 mg, 0.18 mmol) in CH₃OH (20 mL) was added dropwise (within 20 minutes) to the stirring dialdehyde solution. The reaction mixture was heated to reflux for 5 h in an argon atmosphere, allowed to cool to room temperature and filtered through a fritted funnel to remove a red solid (2+2 condensation side product). After concentrating the emerald green mother liquors to a volume of about 20 mL, triethylamine (3 drops) and water (2 mL) were added under vigorous stirring. The obtained purple suspension was placed in a refrigerator (4°C) for several hours and then filtered to collect a purple solid. The powder obtained in this way was recrystallized from CH₂Cl₂/CH₃OH. This gave 61 mg of macrocycle **4.1** (59% yield). UV-vis (CH₂Cl₂): λ_{max} , nm (log ϵ), 385 (4.87), 580 (4.39). ¹H NMR (400 MHz, 296 K,

CD₂Cl₂): δ 8.65 (s, 2H, iminic CHN), 7.57-7.55 (m, 2H, ArH), 7.41-7.39 (m, 2H, ArH), 7.15 (s, 1H, meso), 2.82-2.75 (m, 8H, CH₂CH₃), 2.30 (s, 6H, CH₃), 2.24 (s, 6H, CH₃), 1.29 (t, 6H, CH₂CH₃), 1.23 (t, 6H, CH₂CH₃), (pyrrolic NH not observed). ¹³C NMR (100 MHz, 296 K, CD₂Cl₂): δ 147.42, 145.71, 144.39, 143.01, 138.48, 134.05, 129.28, 126.17, 124.53, 119.35, 117.33, 115.70, 18.62, 17.80, 16.71, 16.35, 11.78, 11.46. CI-MS: (M+1)⁺ m/z 571; HR CI-MS: (M+1)⁺ m/z 571.35650 (calc. for C₃₇H₄₃N₆: 571.35437). Anal. calcd. [C₃₇H₄₂N₆](H₂O): C, 75.48; H, 7.53; N, 14.27. Found: C, 75.88; H, 7.68; N, 14.05. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Oxovanadium(V) complex 4.4, [(C₃₇H₄₁N₆)VO₂]: Free base macrocycle **4.1** (50 mg, 0.09 mmol) was stirred with VO(acac)₂ (70 mg, 0.27 mmol) in THF (20 mL). After 2 days, no residual starting material was observed in the UV-visible absorption spectrum of the reaction mixture. The olive green mixture was filtered through Celite and the solvent was evaporated under reduced pressure. The resulting green solid was purified through preparative thin layer chromatography (alumina, 2% hexanes/CH₂Cl₂). The top green fraction was collected and the product was recrystallized from CH₂Cl₂/*n*-pentane to yield 35 mg of complex **4.4** (61% yield). UV-vis (CH₂Cl₂): $\lambda_{\max}$, nm (log ϵ), 368 (4.83), 450 (4.87), 665 (4.19), 727 (4.58). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 11.43 (s, 1H, pyrrolic NH), 9.80 (br d, 1H, ArNH), 9.61 (s, 1H, iminic CHN), 8.82 (d, 1H, CHNH), 8.24 (d, 1H, ArH), 8.22 (d, 1H, ArH), 7.92 (s, 1H, meso), 7.69-7.61 (m, 2H, ArH), 3.12-2.92 (m, 8H, CH₂CH₃), 2.77 (s, 3H, CH₃), 2.70 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.31 (s, 3H, CH₃), 1.51-1.27 (m, 12H, CH₂CH₃). ¹³C NMR (100 MHz, 296 K, CD₂Cl₂): δ 153.00, 149.95, 149.46, 149.05, 146.21, 139.55, 138.67, 138.17, 136.71, 132.34, 131.80, 130.33, 129.84, 129.42, 126.35, 125.37, 123.73, 121.32, 118.77, 117.23, 114.14, 95.19, 19.54, 19.02, 18.89, 18.34, 17.20, 16.97, 16.77, 16.49, 13.52, 12.71. ESI-MS: (M+1)⁺ m/z 653;

HR CI-MS: (M+1)⁺ *m/z* 653.2803 (calc. for C₃₇H₄₂N₆O₂V: 653.2809). Anal. calc. [C₃₇H₄₁N₆O₂V] ·(CH₂Cl₂): C, 61.87; H, 5.88; N, 11.39. Found: C, 61.77; H, 5.60; N, 11.11. This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Macrocycle 4.7, [C₄₇H₆₂N₆O₈]: 5,5'-Diformyl-3,3',4,4'-tetramethyl-2,2'-bipyrrole (50mg, 0.20 mmol) was suspended in CH₃OH (30 mL) and concentrated HNO₃ (2 drops) was added. A solution of 4,5-bis(2-[2-(2-methoxyethoxy)ethoxy]ethoxy)benzene-1,2-diamine (43 mg, 0.10 mmol) in CH₃OH (10 mL) was added to the stirring dialdehyde solution. The reaction mixture was heated to reflux for 3 h in an argon atmosphere, allowed to cool to room temperature and then concentrated to precipitate an emerald green solid. The precipitate was collected on a fritted filter, dissolved in CH₂Cl₂ and washed three times with a saturated aqueous solution of NaHCO₃ to liberate the free base macrocycle. The dark purple organic phase was dried over anhydrous Na₂SO₄ and the solvent was removed *in vacuo*. The resulting solid was recrystallized from CH₂Cl₂/*n*-pentane to give macrocycle **4.7** as a dark purple powder (33.5 mg, 40%). UV-vis (CH₂Cl₂): λ_{max}, nm (logε), 407 (4.86), 587 (4.38). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 8.79 (s, 2H, iminic CHN), 7.32 (s, 3H, 2 ArH and 1 meso CH), 4.34-3.33 (m, 30H, PEG chains), 2.41/2.36/2.35/2.27 (s × 4, 24H, CH₃), (pyrrolic NH not observed). ESI-MS: (M+1)⁺ *m/z* 840. HR ESI-MS: (M+1)⁺ *m/z* 839.4704 (calc. for C₄₇H₆₃N₆O₈: 839.4707).

Oxovanadium(V) complex 4.8, [(C₄₇H₆₁N₆O₈)VO₂]: Free base macrocycle **4.8** (10 mg, 0.01 mmol) was stirred with VO(acac)₂ (13 mg, 0.03 mmol) in THF (15 mL). After 2 days, the olive green mixture was filtered through Celite and the solvent was evaporated under reduced pressure. The green solid obtained in this way was purified by

means of column chromatography (alumina, 0-5% CH₃OH/CH₂Cl₂). The top green fraction was collected and the product was recrystallized from CH₂Cl₂/*n*-pentane to yield 5 mg of complex **4.8** (54% yield). UV-vis (CH₂Cl₂): λ_{max} , nm (log ϵ), 372 (4.83), 463 (4.87), 667 (4.19), 726 (4.58). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 10.51 (s, 1H, pyrrolic NH), 9.84 (s, 1H, iminic CHN), 9.78 (d, 1H, ArNH), 8.54 (br d, 1H, CHNH), 8.20 (s, 1H, ArH), 7.95 (s, 1H, meso), 7.63 (s, 1H, ArH), 4.51-3.30 (m, 30H, PEG chains), 2.86/2.76/2.75/2.73/2.62/2.60/2.40/2.38 (s $\times$ 8, 24H, CH₃). ESI-MS: (M+1)⁺ m/z 921. HR ESI-MS: (M+1)⁺ m/z 921.3964 (calc. for C₄₇H₆₂N₆O₁₀V: 921.3967).

Oxovanadium(V) complex 4.10, [(C₄₄H₅₃N₆O)VO₂]: Free base macrocycle **4.9** (48 mg, 0.072 mmol) was dissolved in THF (50 mL) under an argon atmosphere and the solution was cooled to 0°C. VO(O-*i*Pr)₃ (0.03 mL, 0.12 mmol) was added dropwise using a syringe. The reaction mixture was stirred for 2h at 0°C, then it was exposed to air and warmed to room temperature before the solvent was evaporated under reduced pressure. The obtained purple/brown solid was dried in vacuo for 1 h and then purified through column chromatography (alumina, 0-1% MeOH/CH₂Cl₂, slow gradient). After the top light pink fraction was discarded, a dark brown fraction was collected and the brown solid that resulted was recrystallized from CH₂Cl₂/pentane to yield 11 mg of complex **4.10** (21% yield). UV-vis (CH₂Cl₂): λ_{max} , nm (log ϵ), 517 (4.62), 597 (2.82), 655 (2.82), 820 (3.95). ¹H NMR (400 MHz, 300 K, CDCl₃): δ 11.00 (s, 1H, OH), 9.54 (s, 1H, NH), 7.61 (s, 1H, meso), 6.41 (s, 1H, meso), 4.15 (s, 1H, NH), 2.92-2.55 (m, 12H, CH₂CH₃), 2.67 (s, 3H, CH₃), 2.62 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.47 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 1.87 (s, 3H, CH₃), 1.38-1.21 (m, 15H, CH₂CH₃), 1.09 (t, 3H, CH₂CH₃). ¹³C NMR (100 MHz, 300 K, CDCl₃): δ 172.8, 157.0, 156.8, 156.2, 152.4, 149.2, 146.2, 145.4, 141.6, 140.5, 139.4, 139.2, 139.1, 138.3, 136.4, 134.3, 133.5, 129.9, 128.7, 124.5, 123.3,

122.0, 120.6, 118.7, 99.6, 91.0, 20.3, 19.3, 18.6, 18.4, 18.3, 17.9, 16.7, 16.2, 15.2, 15.0, 14.9, 14.7, 14.3, 13.0, 12.6, 11.5, 11.2. ESI-MS: (M+1)⁺ *m/z* 765. HR ESI-MS: (M+1)⁺ *m/z* 765.3691 (calc. for C₄₄H₅₄N₆O₃V : 765.3680). This compound was also characterized by X-ray diffraction analysis (see Appendix A).

Oxovanadium(V) complex 4.11, [(C₄₂H₄₂N₈O₄)VO(OH)]: Free base macrocycle **2.1b** (50.0 mg, 0.0627 mmol) was stirred with VO(acac)₂ (35.0 mg, 0.1316 mmol) in THF (15 mL). After 2 days, the bright red mixture was filtered through Celite and the solvent was evaporated under reduced pressure. The resulting red solid was purified by means of column chromatography (alumina, 0-2% CH₃OH/CH₂Cl₂). The second orange/red fraction was collected and the product was recrystallized from CH₂Cl₂/*n*-pentane to yield 15.1 mg of complex **4.11** (30% yield). ¹H NMR (400 MHz, 296 K, CD₂Cl₂): δ 14.87 (s, 2H, pyrrolic NH), 8.29 (s, 2H, CHN), 8.06 (s, 2H, CHN), 6.94 (d, 2H, pyrrolic β-CH), 6.81 (m, 4H, 2 pyrrolic β-CH and 2 ArH), 6.60 (s, 2H, ArH), 6.55 (d, 2H, pyrrolic β-CH), 5.86 (m, 2H, pyrrolic β-CH), 3.86 (s, 6H, OCH₃), 3.80 (s, 6H, OCH₃), 3.13 (s, 6H, CH₃), 1.77 ((s, 6H, CH₃). ¹³C NMR (100 MHz, 296 K, CD₂Cl₂): 162.82, 156.20, 148.64, 148.46, 148.27, 147.52, 140.08, 136.75, 133.86, 130.53, 125.05, 121.97, 113.89, 111.25, 98.80, 96.88, 56.30, 56.18, 38.96, 32.57, 24.82. ESI-MS: (M-OH)⁺ *m/z* 789, M⁺ *m/z* 807. HR ESI-MS: (M-OH)⁺ *m/z* 789.2714 (calc. for C₄₂H₄₂N₈O₅V: 789.2718).

Appendix A

Crystallographic experimental methods

A.1 GENERAL PROCEDURES

The X-ray data refinements for all the crystal structures reported in the present dissertation were performed by Dr. Vincent M. Lynch of the X-ray Diffraction Laboratory, Department of Chemistry and Biochemistry, University of Texas at Austin. This Appendix describes the experimental methods used by Dr. Lynch in obtaining each of these structures. Relevant data tables for all the refinements are included.

The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoK α radiation ($\lambda = 0.71073$ Å). Data collections were conducted at 153 K using an Oxford Cryostream low temperature device.

Data reductions were performed using DENZO-SMN.¹⁵³ The structures were solved by direct methods using SIR97¹⁵⁴ and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.¹⁵⁵ The following definitions apply to all the refinements:

$$R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o| \text{ for reflections with } F_o > 4(\Sigma(F_o)),$$

$$R_w = \{\Sigma w(|F_o|^2 - |F_c|^2)^2/\Sigma w|F_o|^4\}^{1/2}, \text{ where } w \text{ is the weight given each reflection,}$$

$$\text{Goodness of fit, } S = [\Sigma w(|F_o|^2 - |F_c|^2)^2/(n - p)]^{1/2},$$

where n is the number of reflections and p is the number of refined parameters.

Unless otherwise specified, hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to $1.2 \times U_{eq}$ of the attached atom ($1.5 \times U_{eq}$ for methyl hydrogen atoms). Neutral atom scattering factors and values used to calculate

the linear absorption coefficients are from the International Tables for X-ray Crystallography.¹⁵⁶

A.2 EXPERIMENTAL DETAILS

Bis-Cu(II) complex 2.10, [(C₃₈H₃₂N₈)Cu₂](CH₂Cl₂)_{1.5}: Crystals grew as dark green, almost black needles by vapor diffusion of hexanes into a methylene chloride solution of the copper complex. A total of 335 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 203 seconds per frame. Details of crystal, data collection and structure refinement are listed in Table A.1.

The data were corrected for absorption using the Gaussian integration method. The transmission factors ranged from 0.656 – 0.887.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.047*P)^2 + (11.7915*P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.114, with $R(F)$ equal to 0.0544 and a goodness of fit, S , of 1.12. The data were checked for secondary extinction effects but no correction was necessary.

Bis-Cu(I) complex 2.13, [(C₃₈H₃₆N₈)Cu₂Cl₂](C₄H₈O)₂: Crystals grew as orange-brown prisms by diffusion of *n*-pentane into a THF solution of the complex. A total of 461 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 111 seconds per frame. Details of crystal, data collection and structure refinement are listed in Table A.1.

Two large peaks persisted in the electron density map after all the expected atoms were accounted for. The largest peak was near to Cu2 and within bonding distance of the imine nitrogen atoms, N6 and N7 and the chloride ion, Cl2. It was assumed that this peak was due to an occupational disorder of Cu2, which had a slightly higher U_{eq} than did

Cu1. The site occupancy factor for this pair of atoms was refined by assigning the variable, x , to the site occupancy for Cu2 and $(1-x)$ to the site occupancy for Cu2a. At the same time as the site occupancy factor was refined, a common isotropic displacement factor was refined for both Cu2 and Cu2a. In this way, the site occupancy for Cu2 refined to 92(2)%. In addition, a smaller peak persisted in the difference electron density map and was found to be 1.87 Å from pyrrole nitrogen atom, N5. This peak could not be explained in a chemically reasonable way and was not accounted for in the final refinement model. Both the peak near Cu2 and the unexplained peak near N5 persisted in two data collections on two different batches of crystals.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.0493 \cdot P)^2 + (2.5494 \cdot P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.122, with $R(F)$ equal to 0.0456 and a goodness of fit, S , of 1.14. The data were checked for secondary extinction effects but no correction was necessary.

Bis-Cu(I) complex 2.14, $[(C_{46}H_{52}N_8)Cu_2Cl] \cdot (C_4H_4O)_3$: Crystals grew as orange-brown needles by diffusion of *n*-pentane into a THF solution of the macrocyclic complex. A total of 342 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 170 seconds per frame. Details of crystal data, data collection and structure refinement are listed in Table A.1.

The copper complex resides on a crystallographic two-fold rotation axis at 0, y , 3/4. The chloride ions lie on the two-fold rotation axis, which bisects the macrocycle. In addition to the Cu complex, there are two regions of disordered solvent. The solvent appears to be THF. One of the solvate molecules lies near the two-fold rotation axis while the other lies on a general position. The contribution to the scattering due to the disordered solvent was removed by use of the utility SQUEEZE in PLATON98¹⁵⁷ as

incorporated in WinGX.¹⁵⁸ The methyl carbon bound to C18 was found to be disordered about two orientations. The site occupancy of the two orientations was refined while refining a common isotropic displacement parameter for the two atoms, C19 and C19a. The site occupancy factor refined to a value very close to 1/2 and was subsequently fixed at 1/2.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.114, with $R(F)$ equal to 0.0567 and a goodness of fit, S , of 1.42.

Bis-Zn(II) complex 2.16, $[(C_{38}H_{36}N_8)Zn_2F_2(BF_4)_2] \cdot (C_3H_6O)_3$: Crystals grew as orange plates by slow evaporation from acetone. A total of 333 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 238 seconds per frame. Details of crystal, data collection and structure refinement are listed in Table A.2.

The complex lies around a crystallographic two-fold rotation axis at $\frac{1}{2}, y, \frac{1}{2}$. Z' equals $\frac{1}{2}$. Each of the two Zn-tetrafluoroborate ion pairs is disordered about two orientations of equal weight. The site occupancy factor for the pair of Zn ions were determined by setting the site occupancy of one ion, Zn1, to equal the variable x and the site occupancy factor for the other orientation designated as Zn1a, equal to $1-x$. Both ions were allowed to refine isotropically. The isotropic displacement parameter for the two ions was constrained to be equal. The site occupancy factors refined to a value very close to $\frac{1}{2}$. In subsequent refinements, a site occupancy of $\frac{1}{2}$ was used for both ions. The geometry of the tetrafluoroborate anions were restrained to be equivalent throughout the refinement. The site occupancy factors for the atoms of the anion were set to $\frac{1}{2}$ to match that of the Zn ions to which they are bound. Ultimately, the Zn ions and the atoms of the

anion were refined anisotropically. Their anisotropic displacement parameters were restrained to be approximately isotropic in the final stages of the refinement.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02*P)^2 + (27.8554 * P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.157, with $R(F)$ equal to 0.0705 and a goodness of fit, S , of 1.22.

The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_c/[1 + (1.2(2) \times 10^{-6}) * F_c^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor.

Bis-Cu(I) complex 2.20, $[(C_{48}H_{56}N_8O_4)Cu_2(NO_3)_2] \cdot (CH_2Cl_2)_2$: Crystals grew as small, red, well-formed prisms by slow diffusion of pentane into a methylene chloride solution of the copper complex. Details of crystal, data collection and structure refinement are listed in Table A.3.

There are two crystallographically unique copper complexes in the crystal. Each complex resides around a crystallographic inversion center. Complex 1, containing the copper ion Cu1, lies around the inversion center at 0,0,0. Complex 2, containing copper ion Cu2, lies around an inversion center at 1, 1/2, 1/2. The crystal has a pseudo-A center relating complex 1 to complex 2. The conformations of the different complexes are very similar, differing in the orientation of a methyl group on an ethyl group and in the orientation of the solvent molecules.

The pseudo A center is such that of the 11,327 reflections with $k+l = 2n + 1$, only 1785 have $I > 3(\sigma)I$. The structure was refined assuming there was a true A centering. An A centered triclinic cell was reduced to a primitive triclinic cell of half the volume. The dimensions of this new, smaller, triclinic cell are $a = 9.4950(3)$, $b = 10.9765(3)$, $c = 14.3738(5)\text{\AA}$, $\alpha = 72.633(1)$, $\beta = 85.426(1)$, $\gamma = 76.235(1)^\circ$, $V = 1388.6(1)\text{\AA}^3$. The

resulting refined structure was, as expected, much like the averaged structure in the larger cell, with reasonable agreement factors, R , for the averaged structure of 0.0651, with a $R_w = 0.143$ and a goodness of fit, S , = 1.00. The differences in orientation of the methyl group on one ethyl group resulted in a disordering of that methyl carbon in the averaged structure. If not for the observation of the many reflections with hkl , $k+l = 2n+1$, the smaller cell would yield a reasonable structure.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.110, with $R(F)$ equal to 0.0722 and a goodness of fit, S , of 1.52.

The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_c/[1 + (1.2(2) \times 10^{-6}) \cdot F_c^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor.

Bis-Cu(II) complex 2.21, [(C₄₈H₅₄N₈O₄)Cu₂(NO₃)₂](H₂O)₂(CH₃OH)(CH₂Cl₂):

Crystals grew as dark brown, almost black lathes by slow vapor diffusion of *n*-pentane in a dichloromethane solution. A total of 439 frames of data were collected using ω -scans with a scan range of 0.5° and a counting time of 140 seconds per frame. Details of crystal, data collection and structure refinement are listed in Table A.3.

The hydrogen atom on the pyrrolic nitrogen atom, N1, was located in a ΔF map. The position of this atom, H1N, was allowed to ride on the position of N1 with an isotropic displacement parameter set to 1.2xUeq of N1.

The complex lies around a crystallographic two-fold rotation axis at x , 3/4, 3/4. The two-fold rotation axis bisects one of the nitrate ions of the complex. This nitrate ion composed of atoms, N1a, O1a, O2a and its symmetry relative, bridges the Cu(II) ions. Atoms O1a and N1a lie on the rotation axis. Atom O2a and its symmetry relative bind to

the Cu ions (Figure S4). The second nitrate ion composed of atoms N1b, O1b, O2b and O3b, resides in a general position. O1b is bound to the Cu(II) ion. The crystallographic symmetry imposes an occupational disorder such that in a given macrocyclic complex, one Cu ion is bound to two nitrate ions while the other Cu ion is bound to only one nitrate ion (Figure 3). The final coordination site of this second ion is filled with a water molecule. As a result, the refinement model has atoms N1b, O2b and O3b with an occupancy factor of 1/2. Atom O1b has an occupancy factor of 1 as a result of the water coordination. The electron densities at these positions support this model.

Bis-Ag(I) complex 3.5, [(C₄₈H₅₆N₈O₄)Ag₂(CH₃COO)₂](C₅H₁₂)(C₄H₈O):
Crystals grew as red orange needles by vapor diffusion of *n*-pentane into a THF solution of the Ag macrocycle complex. A total of 521 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 116 seconds per frame. Details of crystal, data collection and structure refinement are listed in Table A.4.

The data were corrected for absorption by the Gaussian integration method. The transmission factors ranged from 0.736 – 0.953. The hydrogen atoms on the water molecules could not be located in the ΔF maps generated at the end of the refinement. These hydrogen atoms were not included in the final refinement model.

The asymmetric unit contains two silver complexes. Each complex lies around a different crystallographic inversion center. There are three regions in the asymmetric unit that contain solvent molecules. One region, near 0,0,0, is occupied by a molecule of *n*-pentane. Two other regions nearer to the macrocycle appear to contain THF molecules of unknown occupancy. The solvent lies in a columnar shaped channel along $\frac{1}{2}$, $\frac{1}{2}$, *c*. The disorder could not be reasonably modeled. The contribution to the scattering by the

two molecules were removed by use of the utility SQUEEZE in PLATON98¹⁵⁷ as found in the program WinGX.¹⁵⁸

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.122, with $R(F)$ equal to 0.0563 and a goodness of fit, S , of 1.46. The data were checked for secondary extinction effects but no correction was necessary.

Bis-Ag(I) complex 3.6, $[(C_{48}H_{56}N_8O_4)Ag(C_7H_7SO_3)_2] \cdot (C_4H_8O)_2$: Crystals grew as orange-brown needles by slow diffusion of *n*-pentane in a THF solution of the silver complex. A total of 280 frames of data were collected using ω -scans with a scan range of 1.1° and a counting time of 199 seconds per frame. Details of crystal data, data collection and structure refinement are listed in Table A.4.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.043 \cdot P)^2 + (3.0414 \cdot P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.187, with $R(F)$ equal to 0.0889 and a goodness of fit, S , of 1.05. The data were checked for secondary extinction effects but no correction was necessary.

Dinitrate salt of macrocycle 4.1, $[(C_{37}H_{44}N_6)(NO_3)_2] \cdot (CHCl_3)_2(CH_2Cl_2)_{0.5}$: Crystals grew as dark, nearly black plates by vapor diffusion of hexanes into a chloroform/methylenechloride solution of the complex. A total of 453 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 155 seconds per frame. Details of crystal data, data collection and structure refinement are listed in Table A.5.

In order to locate the hydrogen atom bound to one of the iminic nitrogen atoms, hydrogen atom positions were calculated for both N3 and N4. These hydrogen atoms

were allowed to refine without constraints to see which nitrogen atom, if any, was truly protonated. The hydrogen atom on N4 refined with a very high Uiso and a position impossibly close to N4 and was therefore excluded from the model. The hydrogen atom on N3, H3N, refined to a reasonable position with a reasonable Uiso value. Therefore, it was concluded that N3 was protonated.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.176, with $R(F)$ equal to 0.0997 and a goodness of fit, S, of 1.40. The data were checked for secondary extinction effects but no correction was necessary.

Oxovanadium(V) complex 4.4, [(C₃₇H₄₁N₆)VO₂](CH₂Cl₂)₃: Crystals grew as very dark, almost black lathes by slow evaporation from a dichloromethane solution of the complex. A total of 511 frames of data were collected using ω -scans with a scan range of 1° and a counting time of 115 seconds per frame. Details of crystal data, data collection and structure refinement are listed in Table A.5.

The hydrogen atoms on nitrogen were observed in a ΔF map and refined with isotropic displacement parameters. One methyl carbon, C37, on an ethyl group was found to be disordered. The disorder was modeled by assigning the variable x to the site occupancy for C37 and (1-x) to the site occupancy for the alternate orientation represented by atom, C37a. An isotropic displacement parameter was constrained to be equal for C37 and C37a while the variable x was refined. The bond length to C36 was restrained to be equal for C37 and C37a. The site occupancy factor refined to 85(2)% for C37. C37 was refined anisotropically while C37a was refined isotropically.

A chlorine atom on one of the methylene chloride molecules was also disordered. The solvent disorder was modeled in a similar manner to that described above. The

major component of the disorder, Cl2c, had a site occupancy factor of 81(2)%, while the minor component, Cl3c, had a site occupancy factor of 19(2)%. Both atoms were refined anisotropically.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.136, with $R(F)$ equal to 0.0703 and a goodness of fit, S , of 1.16. The data were checked for secondary extinction affects but no correction was applied.

Oxovanadium(V) complex 4.10, [C₄₄H₅₃N₆O₃V]: Crystals grew as small, dark plates by slow evaporation from dichloromethane/methanol solution of the complex. A total of 140 frames of data were collected using ω -scans with a scan range of 2° and a counting time of 480 seconds per frame. Details of crystal data, data collection and structure refinement are listed in Table A.6.

One of the methyl groups on an ethyl group was found to be disordered. The disorder was modeled by assigning the variable x to the site occupancy factor for one methyl position defined by C32 and $(1-x)$ for the site occupancy factor for the alternate position defined by C32A. A common isotropic displacement parameter was refined for both C32 and C32A. In this way, the site occupancy factor for C32 was estimated to be 68(2)%.

The function, $\sum w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.02 \cdot P)^2]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_w(F^2)$ refined to 0.128, with $R(F)$ equal to 0.0714 and a goodness of fit, S , of 1.12. The data were checked for secondary extinction effects but no correction was necessary.

A.3 CRYSTALLOGRAPHIC DATA TABLES

Table A.1 Crystal data and structure refinement parameters for the copper complexes of macrocycle **2.1**.

	2.10	2.13	2.14
empirical formula	C _{39.5} H ₃₅ Cl ₃ Cu ₂ N ₈	C ₄₆ H ₅₂ Cl ₂ Cu ₂ N ₈ O ₂	C ₅₈ H ₆₄ Cl ₂ Cu ₂ N ₈ O ₃
	2.10 ·(CH ₂ Cl ₂) _{3/2}	2.13 ·(C ₄ H ₈ O) ₃	2.14 ·(C ₄ H ₈ O) ₃
formula weight	855.18	946.94	1119.18
crystal system	orthorhombic	monoclinic	monoclinic
space group	<i>Pbca</i>	P21/n	C2/c
<i>a</i> , Å	14.7258(2)	16.9594(1)	24.2390(6)
<i>b</i> , Å	20.3270(2)	15.0893(1)	15.9732(4)
<i>c</i> , Å	25.0991(3)	18.9670(2)	14.2036(4)
α , °	90	90	90
β , °	90	114.5110(5)	98.937(1)
γ , °	90	90	90
<i>V</i> , Å ³	7512.9(1)	4416.34(6)	5432.5(2)
<i>Z</i>	8	4	4
<i>D</i> (Calc'd), mg/m ³	1.512	1.424	1.381
abs. coeff., mm ⁻¹	1.387	1.132	0.934
<i>F</i> (000)	3496	1968	2376
crystal size	0.37 × 0.12 × 0.09	0.30 × 0.26 × 0.25	0.61 × 0.08 × 0.06
θ for data collection	2.93 – 27.48	2.95 – 27.49	2.93 – 27.43
limiting indices	–15 ≤ <i>h</i> ≤ 19 –26 ≤ <i>k</i> ≤ 26 –32 ≤ <i>l</i> ≤ 32	–21 ≤ <i>h</i> ≤ 22 –19 ≤ <i>k</i> ≤ 19 –24 ≤ <i>l</i> ≤ 24	–29 ≤ <i>h</i> ≤ 30 –20 ≤ <i>k</i> ≤ 20 –18 ≤ <i>l</i> ≤ 18
reflections collected	70825	19669	11259
independent reflections	8594	10107	6112
completeness to θ_{max}	99.9 %	99.8 %	98.5 %
absorption correction	gaussian	none	none
data/restraints/parameters	8594 / 18 / 487	10107 / 12 / 568	6112 / 2 / 272
goodness-of-fit on <i>F</i> ²	1.068	1.142	1.415
<i>R</i> , <i>R</i> _w	0.0544, 0.1337	0.0456, 0.1222	0.0567, 0.1220

Table A.2 Crystal data and structure refinement parameters for the zinc complex **2.16** of macrocycle **2.1**.

2.16	
empirical formula	C ₄₇ H ₅₄ B ₂ F ₁₀ N ₈ O ₃ Zn ₂
	2.16 ·(CH ₃ COCH ₃) ₃
formula weight	1121.34
crystal system	monoclinic
space group	C2/c
<i>a</i> , Å	27.6016(3)
<i>b</i> , Å	10.8804(2)
<i>c</i> , Å	20.1887(3)
α , °	90
β , °	126.536(1)
γ , °	90
<i>V</i> , Å ³	4871.51(13)
<i>Z</i>	4
<i>D</i> (Calc'd), mg/m ³	1.529
abs. coeff., mm ⁻¹	1.074
<i>F</i> (000)	2304
crystal size, mm	0.27 × 0.25 × 0.12
θ for data collection, °	2.92 – 27.47
limiting indices	–35 ≤ <i>h</i> ≤ 35
	–14 ≤ <i>k</i> ≤ 12
	–26 ≤ <i>l</i> ≤ 26
reflections collected	9640
independent reflections	5574
completeness to $\theta = 27.47^\circ$	99.8 %
absorption correction	none
data/restraints/parameters	5574 / 166 / 385
goodness-of-fit on <i>F</i> ²	1.184
<i>R</i> , <i>R</i> _w	0.0705, 0.1481

Table A.3 Crystal data and structure refinement parameters for the copper complexes (**2.20** and **2.21**) of macrocycle **2.2**.

	2.20	2.21
empirical formula	C ₅₀ H ₆₀ Cl ₄ Cu ₂ N ₁₀ O ₁₀	C ₅₀ H ₆₄ Cl ₂ Cu ₂ N ₁₀ O ₁₃
	2.20 ·(CH ₂ Cl ₂) ₂	2.21 ·(H ₂ O) ₂ (CH ₃ OH)(CH ₂ Cl ₂)
formula weight	1229.96	1211.09
crystal system	triclinic	orthorhombic
space group	P-1	<i>Pnna</i>
<i>a</i> , Å	9.4951(2)	15.1527(3)
<i>b</i> , Å	15.2612(3)	17.0720(3)
<i>c</i> , Å	20.5254(5)	24.7324(5)
<i>α</i> , °	105.963(1)	90
<i>β</i> , °	100.546(1)	90
<i>γ</i> , °	95.513(1)	90
<i>V</i> , Å ³	2777.34(10)	6397.9(2)
<i>Z</i>	2	4
<i>D</i> (Calc'd), mg/m ³	1.471	1.257
abs. coeff., mm ⁻¹	1.023	0.810
<i>F</i> (000)	1272	2520
crystal size, mm	0.22 × 0.18 × 0.10	0.50 × 0.18 × 0.13
<i>θ</i> for data collection, °	2.97 – 25.00	2.94 – 25.00
limiting indices	–11 ≤ <i>h</i> ≤ 11	–17 ≤ <i>h</i> ≤ 17
	–18 ≤ <i>k</i> ≤ 18	–20 ≤ <i>k</i> ≤ 20
	–24 ≤ <i>l</i> ≤ 24	–29 ≤ <i>l</i> ≤ 29
reflections collected	18383	10603
independent reflections	9759	5623
completeness to <i>θ</i> = 25.00°	99.8%	99.7 %
absorption correction	none	none
data/restraints/parameters	9759 / 30 / 676	5623 / 235 / 345
goodness-of-fit on <i>F</i> ²	1.506	2.203
<i>R</i> , <i>R</i> _w	0.0722, 0.1100	0.0798, 0.1464

Table A.4 Crystal data and structure refinement parameters for the silver complexes (**3.5** and **3.6**) of macrocycle **2.2**.

	3.5	3.6
empirical formula	C ₆₁ H ₈₂ Ag ₂ N ₈ O ₉ 3.5 ·(C ₅ H ₁₂)(C ₄ H ₈ O)	C ₇₀ H ₈₆ Ag ₂ N ₈ O ₁₂ S ₂ 3.6 ·(C ₄ H ₈ O) ₂
formula weight	1287.09	1511.33
crystal system	triclinic	triclinic
space group	P-1	P-1
<i>a</i> , Å	14.0709(2)	14.3725(8)
<i>b</i> , Å	14.4030(2)	15.9097(11)
<i>c</i> , Å	16.1673(3)	16.4557(12)
<i>α</i> , °	103.526(1)	103.728(4)
<i>β</i> , °	104.757(1)	100.885(4)
<i>γ</i> , °	94.708(1)	98.759(3)
<i>V</i> , Å ³	3045.39(8)	3512.1(4)
<i>Z</i>	2	2
<i>D</i> (Calc'd), mg/m ³	1.404	1.429
abs. coeff., mm ⁻¹	0.704	0.683
<i>F</i> (000)	1340	1568
crystal size, mm	0.59 × 0.09 × 0.08	0.38 × 0.07 × 0.07
<i>θ</i> range for data collection, °	2.94 – 27.48	2.12 – 25.00
limiting indices	–18 ≤ <i>h</i> ≤ 17 –18 ≤ <i>k</i> ≤ 18 –20 ≤ <i>l</i> ≤ 20	–17 ≤ <i>h</i> ≤ 15 –17 ≤ <i>k</i> ≤ 18 –19 ≤ <i>l</i> ≤ 19
reflections collected	19969	18760
independent reflections	13844	12124
completeness to <i>θ</i> _{max}	99.2 %	97.9 %
absorption correction	gaussian	semi-empirical
data/restraints/parameters	13844 / 439 / 658	12124 / 102 / 861
goodness-of-fit on <i>F</i> ²	1.459	1.041
<i>R</i> , <i>R</i> _w	0.0563, 0.1131	0.0889, 0.1354

Table A.5 Crystal data and structure refinement parameters for macrocycle **4.1** and its oxovanadium complex **4.4**.

	4.1 ·(HNO ₃) ₂	4.4
empirical formula	C _{39.50} H ₄₇ Cl ₇ N ₈ O ₆	C ₄₀ H ₄₇ Cl ₆ N ₆ O ₂ V
	4.1 ·(HNO ₃) ₂ (CHCl ₃) ₂ (CH ₂ Cl ₂) _{0.5}	4.4 ·(CH ₂ Cl ₂) ₃
formula weight	978.00	907.48
crystal system	triclinic	triclinic
space group	P-1	P-1
<i>a</i> , Å	12.5610(9)	12.4914(2)
<i>b</i> , Å	12.5940(8)	13.0026(3)
<i>c</i> , Å	16.2560(14)	14.8379(5)
α , °	74.137(3)	89.426(1)
β , °	76.088(3)	88.093(1)
γ , °	89.165(2)	61.536(1)
<i>V</i> , Å ³	2397.5(3)	2117.44(9)
<i>Z</i>	2	2
<i>D</i> (Calc'd), mg/m ³	1.355	1.423
abs. coeff., mm ⁻¹	0.466	0.656
<i>F</i> (000)	1014	940
crystal size, mm	0.33 x 0.18 x 0.04	0.24 × 0.23 × 0.18
θ for data collection, °	3.18 to 25.00	3.13 to 27.50
limiting indices	-14 ≤ <i>h</i> ≤ 14	-15 ≤ <i>h</i> ≤ 16
	-14 ≤ <i>k</i> ≤ 14	-16 ≤ <i>k</i> ≤ 16
	-17 ≤ <i>l</i> ≤ 19	-19 ≤ <i>l</i> ≤ 19
reflections collected	14427	16243
independent reflections	8122	9540
completeness to θ_{max}	96.4 %	98.0 %
absorption correction	none	none
data/restraints/parameters	8122 / 378 / 571	9540 / 63 / 517
goodness-of-fit on <i>F</i> ²	1.325	1.122
<i>R</i> , <i>R</i> _w	0.0997, 0.1473	0.0703, 0.1106

Table A.6 Crystal data and structure refinement parameters for the oxovanadium complex (**4.10**) of macrocycle **4.9**.

4.10	
empirical formula	C ₄₄ H ₅₃ N ₆ O ₃ V
formula weight	764.86
crystal system	triclinic
space group	P-1
<i>a</i> , Å	12.6960(5)
<i>b</i> , Å	12.8190(5)
<i>c</i> , Å	13.9100(6)
α , °	74.891(2)
β , °	65.9560(19)
γ , °	81.4270(19)
<i>V</i> , Å ³	1993.60(14)
<i>Z</i>	2
<i>D</i> (Calc'd), mg/m ³	1.274
abs. coeff., mm ⁻¹	0.296
<i>F</i> (000)	812
crystal size, mm	0.12 × 0.05 × 0.03
θ for data collection, °	2.19 – 24.93
limiting indices	–15 ≤ <i>h</i> ≤ 15 –15 ≤ <i>k</i> ≤ 15 –16 ≤ <i>l</i> ≤ 15
reflections collected	10519
independent reflections	6900
completeness to θ_{max}	99.0 %
absorption correction	none
data/restraints/parameters	6900 / 0 / 508
goodness-of-fit on <i>F</i> ²	1.118
<i>R</i> , <i>R</i> _w	0.0714, 0.1040

Appendix B

Magnetic measurements

B.1 GENERAL PROCEDURES

Solution magnetic measurements were carried out using the Evans method.⁷⁵ Millimolar solutions of the metal complexes were prepared in CDCl_3 and placed in 5 mm diameter NMR tubes, while pure CDCl_3 was placed in a concentric capillary tube within the NMR tube containing the sample solution. NMR spectra were recorded using a Varian Mercury 400 MHz spectrometer. Calculations of the magnetic moments (μ_{eff}) were based on the difference in chemical shift ($\Delta\delta$) observed for the residual CHCl_3 signal in neat solvent and in the solution containing the paramagnetic species. The magnetic moments were derived using the formula reported by Grant,⁷⁷ as corrected for high-field superconducting NMR spectrometers according to the formula of Schubert.⁷⁶

Solid-state magnetic measurements were conducted using a Superconducting Quantum Interference Device (SQUID) magnetometer. All experiments and data analyses were conducted in collaboration with Dr. Utkur Mirsaidov and Prof. John T. Markert in the Department of Physics of the University of Texas at Austin.

The solid-state magnetic susceptibility of crystalline samples was measured between 4 and 300 K at a field of 1 kOe using a Quantum Design Model MPMS SQUID magnetometer. Each sample was placed in a gelatin capsule. The susceptibility of the capsule was measured separately and its contribution was subtracted from the overall susceptibility. A temperature-independent susceptibility parameter (χ_0) was included in the fitting procedures. This contribution was attributed to the combination of a negative

contribution from Langevin diamagnetism and a positive contribution from van Vleck paramagnetism.¹⁵⁹

B.2 EXPERIMENTAL DETAILS AND DATA ANALYSES

Bis-Cu(II) complex 2.10

Evans magnetic moment — μ_{eff} (CDCl₃, 296 K) = (2.0±0.1) μ_{B} . Calculated value for two independent Cu(II) centers (d⁹, S=1/2): 2.45 μ_{B} .

SQUID magnetic susceptibility — The molar magnetic susceptibility data for **2.10** (see Figure 2.5) were fitted to a modified Bleaney-Bowers equation:¹⁶⁰

$$\chi_{\text{molar}} = (1-p) \frac{2Ng^2\beta^2}{kT} \left(\frac{1}{3 + e^{\frac{-J}{kT}}} \right) + p \frac{2Ng^2\beta^2}{3kT} S(S+1) + \chi_0$$

Where,

p = molar fraction of paramagnetic impurity, N = Avogadro's Number, g = gyromagnetic factor, β = Bohr magneton, k = Boltzmann constant, J = exchange coupling constant, S = spin quantum number, χ_0 = temperature-independent susceptibility.

A reasonable fit ($R = \sum_i [(\chi^{\text{obs}})_i - (\chi^{\text{calc}})_i]^2 / \sum_i (\chi^{\text{obs}})^2 = 0.00037$) was obtained using the following parameters: $p = (0.0118 \pm 0.0007)$, $g = (1.9 \pm 0.1)$, $J = (-41.0 \pm 0.2) \text{ cm}^{-1}$, $S = 1/2$, $\chi_0 = (0.00065 \pm 0.00005) \text{ emu/mol}$.

Bis-Ni(II) complex 2.17 and bis-Cu(II) complexes 2.18 and 2.21

Evans magnetic moments — **2.17**: μ_{eff} (CDCl₃, 296 K) = (4.0 ± 0.1) μ_{B} . Calculated value for two independent octahedral Ni(II) centers (*high spin* d⁸, S=1): 4.00 μ_{B} .

2.18: μ_{eff} (CDCl₃, 296 K) = (2.5 ± 0.1) μ_{B} . **2.21**: μ_{eff} (CDCl₃, 296 K) = (2.5 ± 0.1) μ_{B} . Calculated value for two independent Cu(II) centers (d⁹, S=1/2): 2.45 μ_{B} .

SQUID measurements — The susceptibility data per mole formula unit (Figures B.1 – B.3) fit well to the Curie law plus a temperature-independent contribution χ_0 :

$$\chi = A \frac{2Ng^2\beta^2}{3kT} S(S+1) + \chi_0$$

where N is the Avogadro number, $g = 2.00$ is the spin-only Landé factor, β is the Bohr magneton, k is the Boltzmann constant, and T is the temperature. The spin S was set to 1 for the *bis*-Ni(II) complex **2.17**, and 1/2 for the *bis*-Cu(II) complexes **2.18** and **2.21**. The factor A is a fitting parameter and $A=1$ is expected for ideal Curie behavior. The obtained fit value for A was (1.0087 ± 0.0003) for **2.17**, (1.01 ± 0.01) for **2.18** and (1.105 ± 0.008) for **2.21**. Fit χ_0 values for complexes **2.17**, **2.18** and **2.21** were $(-0.9 \pm 1.0) \times 10^{-3}$ emu/mol, $(4.20 \pm 0.09) \times 10^{-3}$ emu/mol and $(0.0075 \pm 0.0003) \times 10^{-3}$ emu/mol, respectively.

Figure B.1 Experimental (triangles) and calculated (solid line) magnetic susceptibility of complex **2.17** in the temperature range (4 - 300 K).

Figure B.2 Experimental (triangles) and calculated (solid line) magnetic susceptibility of complex **2.18** in the temperature range (4 - 300 K).

Figure B.3 Experimental (triangles) and calculated (solid line) magnetic susceptibility of complex **2.21** in the temperature range (4 - 300 K).

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