

# Transition-Metal Complexes of Expanded Porphyrins

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## ABSTRACT

Over the last 2 decades, the rapid development of new synthetic routes for the preparation of expanded porphyrin macrocycles has allowed for the exploration of a new frontier consisting of “porphyrin-like” coordination chemistry. In this Account, we summarize our exploratory forays into the still relatively poorly explored area of oligopyrrolic macrocycle metalation chemistry. Specifically, we describe our successful formation of both mono- and binuclear complexes and, in doing so, highlight the diversity of coordination modes available to expanded porphyrin-type ligands. The nature of the inserted cation, the emerging role of tautomeric equilibria, and the importance of hydrogen-bonding interactions in regulating this chemistry are also discussed.

## 1. Introduction

Living systems routinely synthesize tetrapyrrolic macrocycles, in either their metal-free forms (e.g., pheophorbide) or, more commonly, the corresponding metal complexes (e.g., chlorophyll, heme, coenzyme B<sub>12</sub>, 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.<sup>1</sup>

While the extraordinary chemistry of these tetrapyrrolic compounds continues to fascinate chemists, biologists, and materials scientists, the last few decades have witnessed the development of a new class of ligands termed “expanded porphyrins”.<sup>2,3</sup> 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 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 3 decades, the chemistry of expanded porphyrins has brought about remarkable synthetic advances and provided new insights into the fundamental features of aromaticity.<sup>4</sup> More recently, the scope of

expanded porphyrin chemistry has grown to encompass the field of anion binding and transport.<sup>5</sup> However, one of the main motivating forces behind the synthesis of expanded porphyrins is that they might extend the frontiers of “porphyrin-like” coordination chemistry.

To date, some of this latter promise has been realized. For instance, expanded porphyrins have been used to stabilize complexes containing typically large cations, including those of the lanthanide and actinide series. They have also allowed for the generation of complexes containing multiple cations. These synthetic findings, combined with a range of spectroscopic and physical properties, have prompted the study of expanded porphyrin metal complexes as photosensitizers in photodynamic therapy,<sup>6</sup> contrast agents in magnetic resonance imaging,<sup>7</sup> building blocks in nonlinear optical materials,<sup>8</sup> and enzyme models in bioinorganic chemistry.<sup>9</sup>

While we have previously reviewed the stabilization of actinides in oligopyrrolic macrocycles,<sup>10</sup> in this Account, we present our contribution to the coordination of transition metals in expanded porphyrins. With the intent to provide a critical overview of the reported metalation studies, we highlight the key factors influencing the metal coordination modes and the “degrees of freedom” of the macrocyclic cavities. As befits an Account of this type, the focus is almost entirely on the work from our laboratory. However, other contributions, particularly from the Chandrashekar,<sup>11</sup> Osuka,<sup>12</sup> and Furuta<sup>13</sup> groups, have played a key role in developing this area of chemistry. For instance, work with N-confused and inverted porphyrins<sup>14</sup> and expanded porphyrins<sup>13</sup> has provided a novel mode of metal binding in porphyrin-like chemistry, namely, coordination to the  $\beta$ -carbon atoms of the pyrrolic rings. These exciting developments are extending the range of expanded porphyrin coordination chemistry into the field of organometallic chemistry.

## 2. Carbon-Bridged Systems

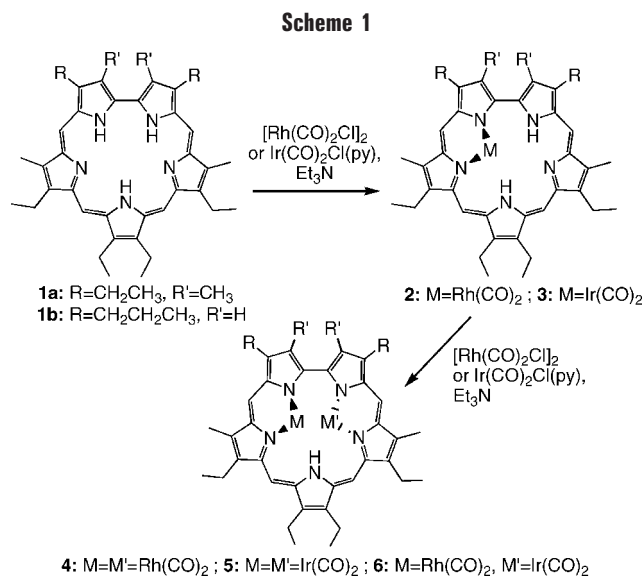
The expanded porphyrins that display the greatest resemblance to natural porphyrins are those that contain either *meso*-like bridging carbon atoms or direct links between the heterocyclic subunits. According to the nomenclature put forward by Franck and Nonn,<sup>15</sup> the name of these systems consists of three parts: (1) the number of  $\pi$  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, etc.), and (3) the number of bridging carbon atoms between each pyrrole subunit (in round brackets and separated by dots). For instance, according to this nomenclature, porphyrin would be named [18]tetraphyrin(1.1.1.1).

**2.1. [22]Pentaphyrin(1.1.1.1.0) (Sapphyrin).** The aromatic pentapyrrolic macrocycle **1** represents the first reported example of an expanded porphyrin and was

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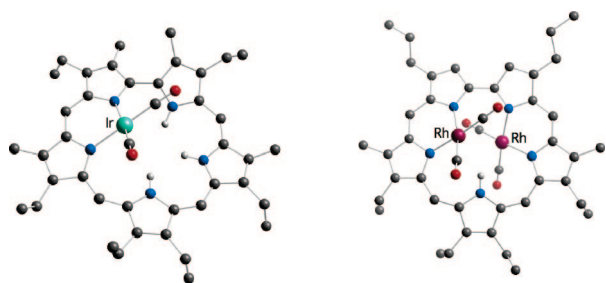


discovered serendipitously by Woodward and coworkers in the early 1960s.<sup>16</sup> Because this compound crystallizes as a dark blue solid, Woodward assigned it the name “saphyrin” and thus began a trivial nomenclature for these macrocycles whose names end with the suffix “phyrin” or “rin” taken from *porphyrin*. Although limited to widely recognized systems, this unorthodox nomenclature will generally be used in this Account.

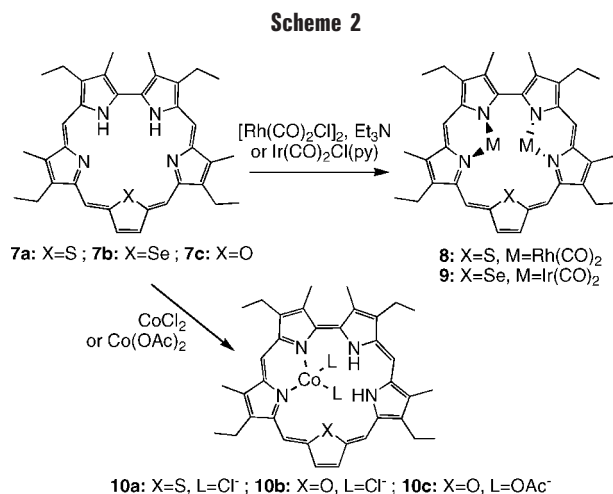
The size of the cavity (ca. 5.5 Å versus ca. 4.0 Å for porphyrins) and the presence of an additional nitrogen donor led Woodward and his group to envision the use of saphyrins for metal coordination. Their early investigations showed that Co<sup>II</sup> and Zn<sup>II</sup> complexes could be isolated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

When we re-examined this chemistry in the early 1990s, we proposed that the difficulty in the characterization of these complexes was due to the small size of the coordinating cations and thus to inherent kinetic instability. In fact, while our first metalation attempts using halides of larger cations (e.g., HgCl<sub>2</sub>, RhCl<sub>3</sub>, and IrCl<sub>3</sub>) led to the decomposition of the macrocycle, we were able to isolate the first fully characterized complexes of saphyrin using rhodium and iridium dicarbonyl chloride salts in the presence of triethylamine (Scheme 1).<sup>17,18</sup>

As shown in Figure 1,<sup>19</sup> in the resulting rhodium(I) and iridium(I) complexes, the metal carbonyl units are found above or below the average macrocycle plane and each metal center is bound to a dipyrinato moiety of the



**FIGURE 1.** Crystal structures of the mono-Ir(CO)<sub>2</sub> complex **3** and the bis-Rh(CO)<sub>2</sub> saphyrin complex **4**.



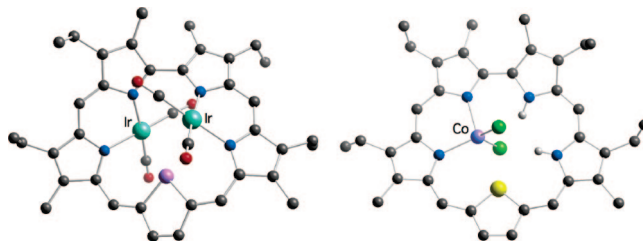
saphyrin scaffold. This coordination mode is reminiscent of the one reported for [Rh(CO)<sub>2</sub>]<sub>2</sub>(octaethylporphyrin) and was later observed in several stable Rh<sup>I</sup> complexes of expanded porphyrins, such as our amethyrin,<sup>20</sup> Chandrashekar’s core-modified smaragdyrin,<sup>21</sup> Furuta’s N-confused pentaphyrin,<sup>13</sup> and Osuka’s N-fused pentaphyrin.<sup>12</sup> Interestingly, the isolation of the mono-Rh(CO)<sub>2</sub> complex **2** and mono-Ir(CO)<sub>2</sub> saphyrin **3** allowed us to prepare the heterobimetallic species **6** by the simple addition of Ir(CO)<sub>2</sub>(py)Cl or Rh<sub>2</sub>(CO)<sub>4</sub>Cl<sub>2</sub>, respectively (Scheme 1).

Analogous complexes of Rh and Ir with heterosaphyrins have been reported (Scheme 2), including the structurally characterized monothiasaphyrin-bis[dicarbonylrhodium(I)]<sup>22</sup> **8** and monoselenasaphyrin-bis[dicarbonyliridium(I)]<sup>23</sup> **9** (Figure 2).

Our study of heterosaphyrins also led to the isolation of mono-cobalt(II) complexes<sup>22</sup> **10a–c** (Scheme 2). In contrast to what was seen in the case of Rh<sup>I</sup> and Ir<sup>I</sup>, the insertion of Co<sup>II</sup> cations was not accompanied by the deprotonation of the ligand. Rather, a tautomeric rearrangement of the pyrrolic protons takes place. This allows the metal center to retain its counterions (Cl<sup>-</sup> or OAc<sup>-</sup>) and coordinate two iminic nitrogens on neighboring pyrrolic subunits.

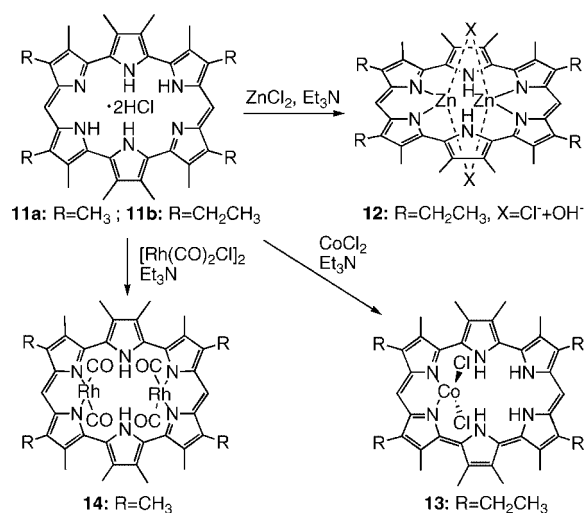
To date, the metalation chemistry of saphyrins has not displayed the diversity observed for other macrocycles (*vide infra*). However, the recent discovery of the biological activity of hydrophilic saphyrins<sup>24</sup> as potential cancer therapeutics is likely to fuel new studies of this most venerable expanded porphyrin.

**2.2. [24]Hexaphyrin (1.0.0.1.0.0) (Amethyrin).** Amethyrin **11**, a 24 π-electron hexapyrrolic macrocycle, owes



**FIGURE 2.** Crystal structures of the bis-Ir(CO)<sub>2</sub> selenasaphyrin complex **9** and the mono-CoCl<sub>2</sub> thiasaphyrin complex **10a**.

Scheme 3



its name to the purple color (from the Greek word *amethus*) displayed by its protonated form in organic solution. This system is of considerable importance from a historical perspective because it was the first expanded porphyrin in which multiple modes of cation complexation were demonstrated and the first with which the in-plane coordination of two cations was established unequivocally.<sup>25</sup> For instance, in an early metalation study, it was found that the reaction of the dichloride acid salt of amethyrin with ZnCl<sub>2</sub> in the presence of Et<sub>3</sub>N afforded the bis-zinc complex **12** after purification by column chromatography (Scheme 3). X-ray diffraction analysis of the isolated product (Figure 3) showed that each zinc center coordinates a dipyrinato moiety and two bridging counterions, namely, a chloride and a hydroxyl anion (with the latter presumably exchanged for chloride during chromatographic purification).

In a parallel metalation study, it was found that the reaction of amethyrin with CoCl<sub>2</sub> produced a complex wherein only a single metal cation is coordinated (**13**, Scheme 3). In analogy to what was observed for the cobalt complexes **10a–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 Co<sup>II</sup> center appears to fill its coordination sphere with two iminic nitrogen atoms from neighboring pyrrolic units (Figure 3).

Amethyrin also forms a mono- and a bis-[Rh(CO)<sub>2</sub>] adduct (**14**, Scheme 3);<sup>20</sup> however, in contrast to what is seen for the bis-[Rh(CO)<sub>2</sub>] complexes of octaethylporphyrin, sapphyrin, and various heterosapphyrins, in the case of amethyrin, the two rhodium centers 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 macrocycle free base with Ni(acetylacetonate)<sub>2</sub>; however, this complex was not structurally characterized, and thus, the coordination mode of the metal centers could not be deduced.<sup>26</sup> Conversely, the treatment of amethyrin with CuCl and subsequent exposure to air afforded a bis-Cu<sup>II</sup> complex in which the divalent oxidation state for the copper centers was confirmed by electron paramagnetic resonance (EPR) and superconducting quantum interference device (SQUID) magnetometry. In the crystal structure of complex **15**, the slightly bowl-shaped macrocycle hosts two copper centers held at the unusually short CuCu distance of 2.761(1) Å. Each metal cation is bound to three nitrogen donors, so that all of the pyrrolic nitrogen atoms are engaged in metal coordination (Figure 3).<sup>27</sup> The required charge balance for the overall complex led to two possible hypotheses regarding the conjugation pathway of the macrocycle: (i) metal insertion is accompanied by oxidation of the ligand from a 24  $\pi$ -electron to a 22  $\pi$ -electron system, thereby giving rise to a hexadentate dianionic ligand; (ii) alternatively, the bis-[( $\mu$ -chloro)copper(II)](amethyrin) could be a dianionic species with two counterions, presumably protons, being present in the crystal structure (but not observed experimentally). While this issue is still not resolved, a comparison with what has been observed recently in the case of a bis-[Cu<sup>II</sup>( $\mu$ -Cl)] complex of amethyrin isomer **16** (see below; Scheme 4) leads us to favor the first of these hypotheses.

**2.3. [24]Hexaphyrin(1.0.1.0.0.0) (Isoamethyrin).** This quaterpyrrole-containing isomer of amethyrin (**16**, Scheme 4) is a 24  $\pi$ -electron antiaromatic system, as judged by the strong downfield shifts of its inner NH protons ( $\delta$  = 23.7, 23.9, and 24.2 ppm in CD<sub>2</sub>Cl<sub>2</sub> at room temperature).<sup>28</sup> Treatment of this macrocycle with the actinide oxocations UO<sub>2</sub><sup>2+</sup> and NpO<sub>2</sub><sup>+</sup> is accompanied by a dramatic color change and oxidation of the ligand to a 22

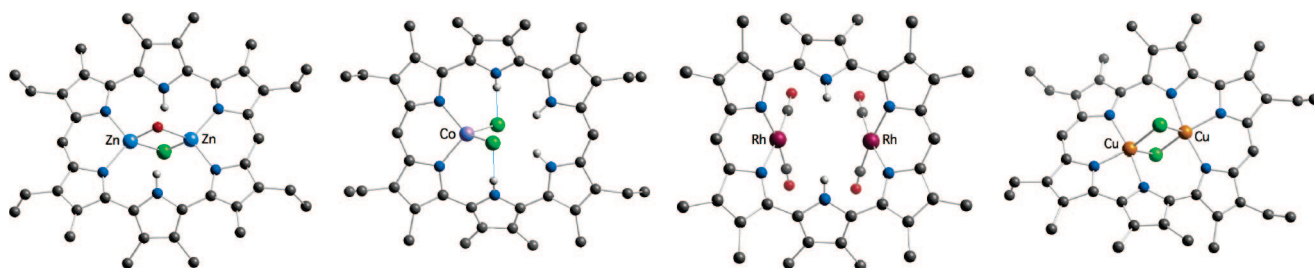
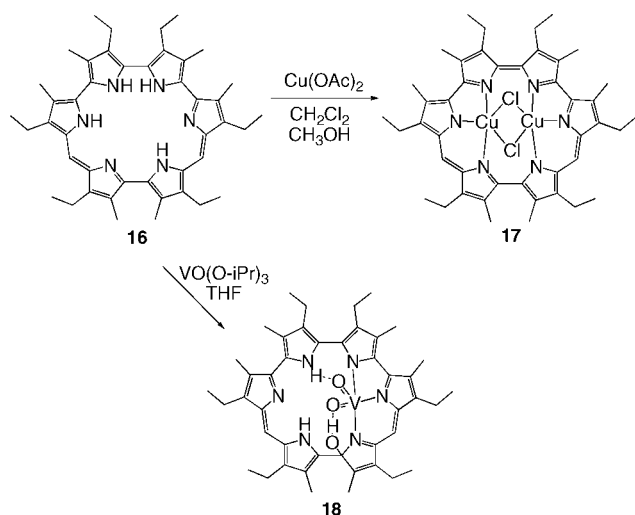


FIGURE 3. Crystal structures of amethyrin complexes (from left to right: bis-Zn<sup>II</sup> complex **12**, mono-Co<sup>II</sup> complex **13**, bis-Rh(CO)<sub>2</sub> complex **14**, and bis-Cu<sup>II</sup> complex **15**).

Scheme 4



$\pi$ -electron aromatic system.<sup>28</sup> As a consequence, isoamethyrin is currently being evaluated for its potential use as a colorimetric actinide sensor.<sup>29</sup>

The ability of isoamethyrin to coordinate transition metals was recently examined. While exposure to most transition-metal salts failed to provide evidence of complex formation,<sup>29</sup> using appropriate metal precursors, two novel complexes could be obtained (Scheme 4).<sup>30</sup> In particular, it was found that treatment of the free base **16** with copper(II) acetate afforded the corresponding bis- $\text{Cu}^{\text{II}}$  complex **17**, which bears a remarkable resemblance to the amethyrin complex **15**. In complex **17** (Figure 4), each copper center coordinates three pyrrolic nitrogen donors and two bridging chloride anions and the two Cu atoms are separated by an unusually short distance [2.744(2) Å]. As observed in the case of actinyl cations, metal coordination is accompanied by ligand oxidation.

Interestingly, an analogue of complex **17** without the bridging chloride anions has not been isolated to date; rather, exposure of such putative species to any chlorinated solvent was found to give a chloro-bridged complex. However, the specific origin of the chloride anions in this complex is still under investigation.

Another structurally characterized transition-metal complex of isoamethyrin, an oxovanadium(V) derivative, was prepared by the addition of  $\text{VO(O-}i\text{-Pr)}_3$  to the free base macrocycle at 0 °C in tetrahydrofuran (THF). The resulting product, **18**, contains a single coordinated  $\text{VO}_2^+$  cation that is ligated to three (only) of the potential six pyrrolic donor atoms. The cationic species is also hydrogen-bonded to one of the pyrrolic NH protons through one of the oxo ligands (Figure 4). The result is a bimodal stabilization analogous to that seen in a different kind of oxovanadium expanded porphyrin complex (cf. complex **38**, Section 3.3). Separate from this, both the crystallographic and nuclear magnetic resonance (NMR) spectroscopic data are consistent with the macrocyclic scaffold undergoing nucleophilic attack by a hydroxide anion at the  $\alpha$  carbon of a pyrrole ring during the course of metal insertion. This type of reactivity, while unusual, has been observed previously during the formation of our uranyl sapphyrin complex<sup>31</sup>

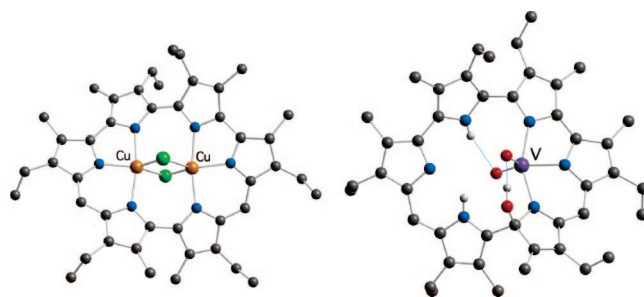
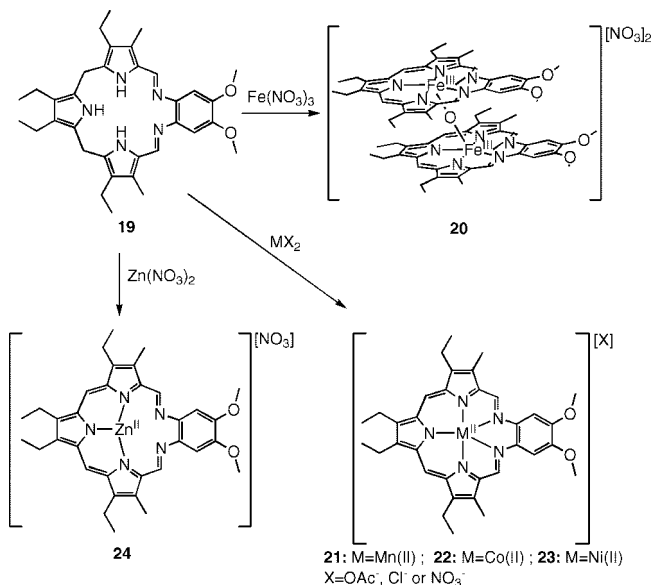


FIGURE 4. Crystal structures of bis- $\text{Cu}^{\text{II}}$  isoamethyrin **17** and oxovanadium(V) isoamethyrin derivative **18**.

Scheme 5



and Osuka's bis- $\text{Cu}^{\text{II}}$  complexes of *meso*-aryl-substituted hexaphyrins.<sup>32</sup> In one extreme case reported by Osuka and coworkers, metal insertion was found to occur concurrently with hydrolytic cleavage of a pyrrole ring.<sup>33</sup>

### 3. Nitrogen-Bridged Systems

Imine-containing pyrrolic macrocycles or Schiff-base expanded porphyrins<sup>34</sup> are systems wherein a *meso* carbon is formally substituted by a nitrogen atom. In many cases, the metal complexes of such systems have proven 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 appreciated by workers in the area since the first seminal studies of Schiff-base pyrrolic macrocycles by Fenton and coworkers.<sup>35</sup> As a consequence, the coordination chemistry of nitrogen-bridged expanded porphyrins has generally evolved in parallel with their synthetic development.

**3.1. Texaphyrin.** Arguably, the best studied of the Schiff-base oligopyrrolic macrocycles is texaphyrin (**19**, Scheme 5). This system 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.

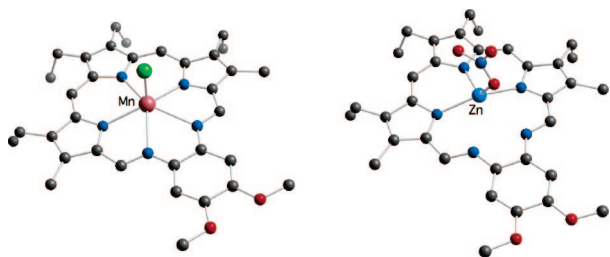


FIGURE 5. Crystal structures of texaphyrin complexes **21** and **24**.

The lutetium(III) and gadolinium(III) complexes of a water-soluble texaphyrin have been the subject of clinical studies as potential photosensitizers and radiation enhancers for arteriosclerotic disease and cancer, respectively. The chemistry involved in these medical applications lies outside the scope of this Account and has been reviewed elsewhere.<sup>6</sup>

The penta-aza 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 nonradioactive lanthanide(III) cations;<sup>36</sup> however, it was not until 2002 that a series of first-row transition-metal complexes ( $\text{Mn}^{\text{II}}$ ,  $\text{Fe}^{\text{III}}$ ,  $\text{Co}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$ , and  $\text{Zn}^{\text{II}}$ ) of texaphyrin were reported.<sup>37</sup> In the case of these latter cations, it was found that the metal insertion proceeds through a simultaneous oxidation/metalation process analogous to the one previously observed in the preparation of lanthanide complexes. Specifically, the nonaromatic texaphyrin macrocycle **19**, termed “sp<sup>3</sup> texaphyrin” because of the hybridization state of the meso-like carbon bridges, undergoes oxidation to the aromatic form upon complexation of the metal cation (Scheme 5).

The  $\text{Fe}^{\text{III}}$  complex **20** of texaphyrin was isolated as a  $\mu$ -oxo dimer, a common product in iron porphyrin chemistry.<sup>38</sup> Conversely, the corresponding manganese and cobalt texaphyrin complexes, **21** and **22**, feature  $\text{Mn}^{\text{II}}$  and  $\text{Co}^{\text{II}}$  centers, respectively, even though these cations are

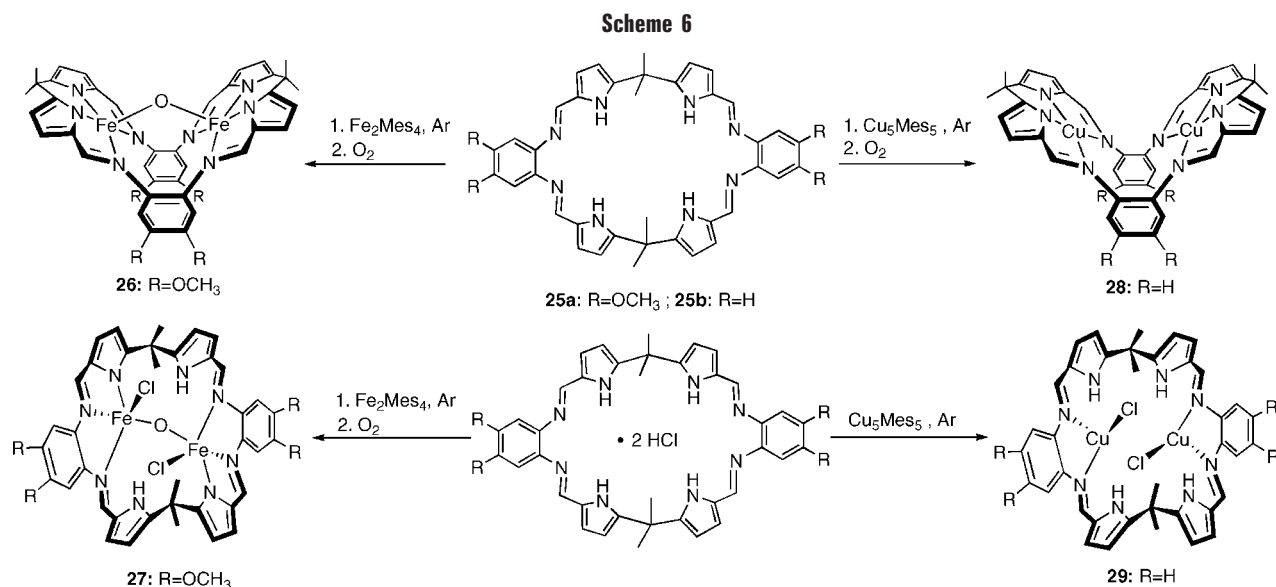
typically stabilized in the +3 oxidation state in porphyrins. Presumably, the increased cavity size, as well as the decreased ligand charge, favors the stabilization of lower oxidation states, which are found in rather uncommon six- or seven-coordinate geometries (cf., e.g., the crystal structure of **21** in Figure 5).

Finally, the solid-state structure of the  $\text{Zn}^{\text{II}}$  complex **24** provided the first example of texaphyrin acting as a tridentate ligand (Figure 5). In fact, the relatively small  $\text{Zn}^{\text{II}}$  cation is seen to coordinate only the tripyrrolyldimethene fragment. This stands in contrast to what is observed in the case of the largest lanthanide cations (e.g.,  $\text{La}^{\text{III}}$ ), 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”.

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  $\text{Mn}^{\text{II}}$  texaphyrin complex was prepared; it was found to act *in vitro* as a catalyst for the decomposition of peroxyxynitrite,<sup>39</sup> a reactive oxygen species whose cytotoxic effects have been implicated in numerous disorders, including cancer, amyotrophic lateral sclerosis, and atherosclerosis.

**3.2. Dipyrromethane-Based Macrocycles.** 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 co-workers, 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.<sup>40</sup> Later, a bis- $\text{Mn}^{\text{II}}$  accordion porphyrin complex was found to act as a functional mimic for binuclear enzymes, such as mono-oxygenases<sup>9</sup> and catalases.<sup>41</sup>

More recently, we reported the preparation of the dipyrromethane-based macrocycle **25**, which proved to



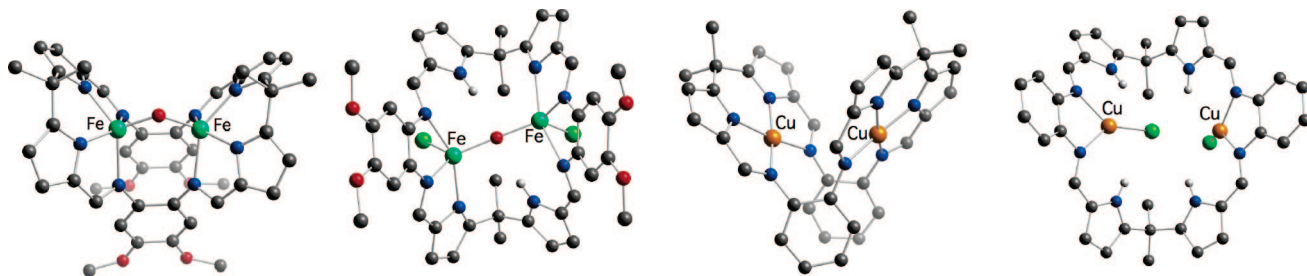


FIGURE 6. Crystal structures of bis-Fe<sup>III</sup> complexes **26** and **27**, bis-Cu<sup>II</sup> complex **28**, and bis-Cu<sup>I</sup> complex **29**.

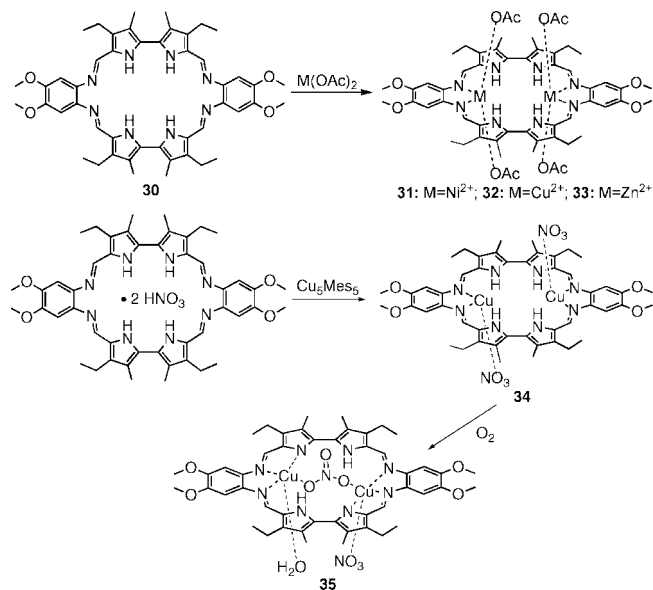
be an efficient receptor for the chloride anion.<sup>42</sup> However, the wide nitrogen-rich cavity of this ligand prompted us to investigate its potential as a binucleating cation receptor. While our first metalation attempts using simple iron salts (e.g., FeCl<sub>3</sub>, Fe(acetylacetonate)<sub>3</sub>, and [Fe(CH<sub>3</sub>CN)<sub>6</sub>]-[AlCl<sub>4</sub>]<sub>2</sub>) failed to afford identifiable metal complexes, the organometallic Fe<sub>2</sub>Mes<sub>6</sub> reagent proved to be an excellent iron source.<sup>43</sup> This organometallic species is a convenient deprotonating agent and, further, does not introduce any anionic counterion into the reaction mixture. The reactions of **25** (both as the free base and as the dihydrochloride salt) with iron and copper mesityl reagents are summarized in Scheme 6; the structures of the resulting complexes are depicted in Figure 6.

The  $\mu$ -oxo bis-Fe<sup>III</sup> complexes **26** and **27** were the first examples of iron complexes in which a Fe<sup>III</sup>-O-Fe<sup>III</sup> bridge is stabilized within a single macrocyclic framework. Interestingly, however, the structures of the complexes obtained during the metal insertion reaction depended upon the protonation state of the starting macrocycle. In complex **26**, obtained from the free base **25**, the macrocycle behaves as a bis-tetradentate ligand. On the other hand, when the same reaction conditions are applied to the corresponding acid salt, **25**·2HCl, the resulting complex **27** features a bis-tridentate ligand and retains two chloride anions.

The dramatic effect of the starting form of the ligand on the coordination modes within the macrocycle cavity was further established by a related study involving the formation of copper complexes from **25**.<sup>44</sup> The reaction of Cu<sub>5</sub>Mes<sub>5</sub> with **25**·2HCl gave the bis-Cu<sup>I</sup> complex **29**, which retains two chloride anions of the starting material and does not involve the pyrrolic nitrogen atoms in metal coordination. Conversely, the treatment of the free base **25** with Cu<sub>5</sub>Mes<sub>5</sub> at room temperature and subsequent air oxidation of the resulting putative Cu<sup>I</sup> species afforded the bimetallic Cu<sup>II</sup> complex **28**, wherein the macrocycle behaves as a bis-tetradentate ligand for two copper centers constrained within what is essentially a square-planar geometry. The coordination mode of the copper atoms in this binuclear complex is reminiscent of the bis-Cu<sup>II</sup> accordion porphyrin reported by Mertes et al. (*vide supra*)<sup>9</sup> and other copper complexes of oligopyrrolic Schiff-base macrocycles as described by Brooker et al.<sup>45</sup>

The versatility of this oligopyrrolic Schiff-base macrocycle was further highlighted by the work of Love and Arnold, who reported the preparation of a bis-Pd<sup>II</sup> complex<sup>46</sup> and a mono-UO<sub>2</sub><sup>2+</sup> adduct<sup>47</sup> of **25** as well as an

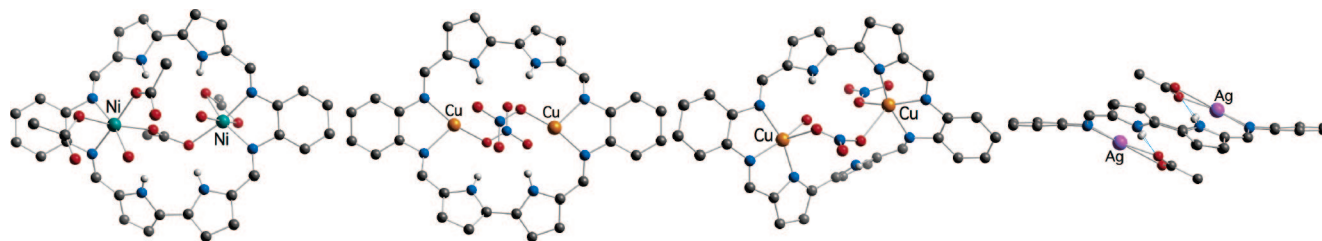
Scheme 7



unusual metal-directed expansion of the macrocycle scaffold.<sup>48</sup> Interestingly, the monouranyl complex could be used as a substrate for the further coordination of Mn<sup>II</sup>, Fe<sup>II</sup>, and Co<sup>II</sup> cations to afford three different heterobimetallic complexes.<sup>49</sup>

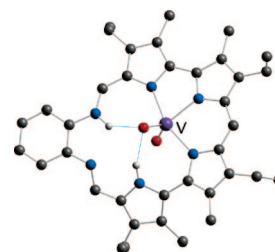
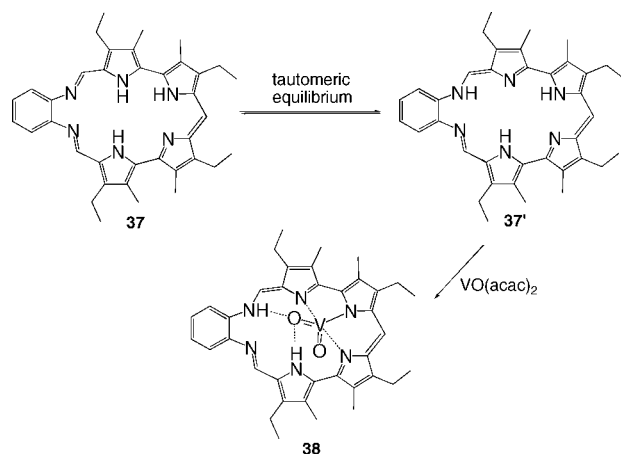
**3.3. Bipyrrrole-Based Macrocycles.** The appearance of the bipyrrrole subunit in a Schiff-base expanded porphyrin dates back to the early 1990s, namely, to the synthesis of the tetrapyrrolic octa-aza macrocycle **30** (Scheme 7). Our first investigations revealed that **30** binds methanol within its cavity, thus providing the first example of neutral substrate complexation by an expanded porphyrin.<sup>50</sup> Early metalation studies revealed that macrocycle **30** reacts readily with simple metal salts to give binuclear Ni<sup>II</sup>, Cu<sup>II</sup>, and Zn<sup>II</sup> complexes (Scheme 7). The crystal structure of the bis-Ni<sup>II</sup> complex **31** showed that the two metal centers coordinate the macrocycle via the iminic nitrogen atoms, whereas the pyrrolic NH protons are engaged in hydrogen-bonding interactions with the acetate counterions (Figure 7).<sup>51</sup>

A recent re-examination of this chemistry indicated that **30** can also be used for the coordination of monovalent cations, such as Cu<sup>I</sup> and Ag<sup>I</sup>.<sup>51,52</sup> As previously observed for the bis-Ni<sup>II</sup> complex **31**, the X-ray crystal structures of the copper(I) and silver(I) complexes, **34** and **36**, respectively, revealed that the monovalent metal cations coordinate **30** through the iminic nitrogens and not the pyrrolic nitrogen atoms.



**FIGURE 7.** Crystal structures of complexes **31**, **34**, **35**, and **36** (side view) derived from macrocycle **30**. The methoxy groups on the phenyl rings and the alkyl substituents on the pyrrole rings have been removed for clarity.

**Scheme 8**



**FIGURE 8.** Crystal structure of the oxovanadium(V) complex **38** showing two hydrogen-bonding interactions with one of the oxo ligands.

A new Cu<sup>II</sup> complex (**35**, Scheme 7) was obtained through air-oxidation of the bis-Cu<sup>I</sup> complex **34**.<sup>51</sup> An X-ray structural analysis (Figure 7) revealed that the macrocycle adjusts to the increased metal charges through a dramatic conformational change that allows for the coordination of an anionic pyrrolic nitrogen donor to each metal center. Presumably, this rearrangement reflects the fact that, in the absence of other available anionic counterions, the coordination mode is driven by the change in the oxidation state of the metal centers.

More recent studies of the coordination chemistry of **30** revealed that the complexation of silver cations is subject to strong cooperative behavior.<sup>52</sup> This latter conclusion was supported by a combination of NMR and UV-vis spectroscopic experiments, which served to demonstrate that coordination of a first silver(I) cation activates the macrocycle strongly toward the complexation of a second silver ion. Such positive homotropic allosterism was unprecedented in expanded porphyrin chemistry, and hence, receptor **30** could be the first example of a new (and potentially large) class of hosts for cooperative metal coordination.

The bipyrrrolic subunit is also featured in the smaller Schiff-base macrocycle **37**, which was shown to bind the uranyl and neptunyl cations.<sup>53</sup> We recently found that this system acts as a receptor for a lighter congener of the actinide oxocations, namely, the VO<sub>2</sub><sup>+</sup> cation.<sup>54</sup> Interestingly, NMR spectroscopic data and X-ray diffraction analysis of the oxovanadium(V) adduct **38** revealed that the metal ion does not react with the free base macrocycle **37** but rather with enaminic tautomer **37'** (Scheme 8). As a consequence of this enamine-imine tautomeric re-

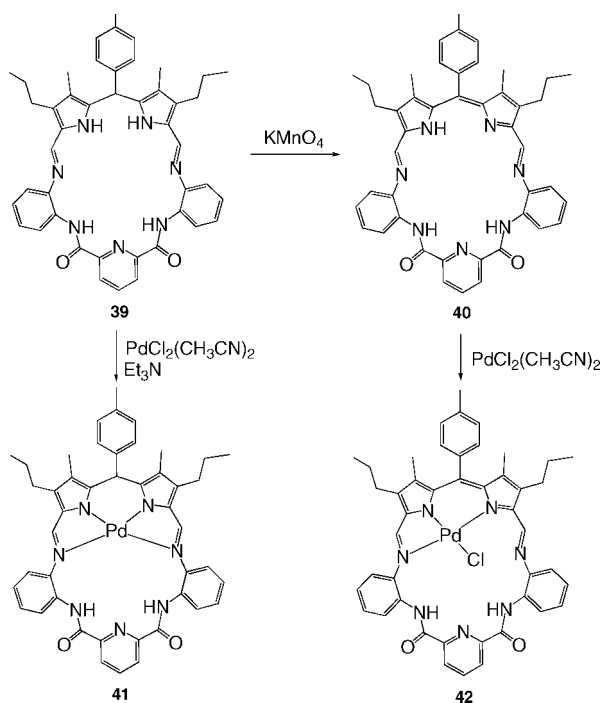
arrangement, the nonspherical cation VO<sub>2</sub><sup>+</sup> is accommodated through metal-ligand interactions involving three pyrrolic nitrogens, as well as via hydrogen-bonding interactions involving a pyrrolic NH and an enaminic NH (Figure 8). The coordination of the VO<sub>2</sub><sup>+</sup> cation by **37'** is important not only because it provides the first structurally characterized example of early transition-metal coordination in an expanded porphyrin but also because it represents an interesting case of bimodal (i.e., covalent and noncovalent) recognition of a nonspherical guest within an oligopyrrolic receptor.

**3.4. Other Systems.** A dipyrromethane subunit, combined with a diamidopyridine fragment, is featured in the Schiff-base hybrid macrocycle **39**. This ligand, which proved to be an effective anion-binding receptor,<sup>55</sup> can be selectively oxidized to the conjugated di-iminodipyrromethene system **40** (Scheme 9). A first metalation study of this macrocycle has shown that the Pd<sup>II</sup> cation binds preferentially to the pyrrolic moiety, both in the dipyrromethane system **41** and in the oxidized dipyrromethene analogue **42**.<sup>56</sup>

## 4. Concluding Remarks

A major thrust of modern coordination chemistry is the engineering of nano-scaled spaces for the stabilization, activation, and/or recognition of metal ions. In the expanded porphyrin field, this has inspired the preparation of a number of macrocyclic receptors and the subsequent exploration of their cavities as novel coordination environments. These initial investigations have begun to reveal what promises to be a very diverse coordination chemistry. For instance, the metalation chemistry of texaphyrin was found to run the gamut from the large lanthanide cations to the small zinc(II) ion. Moreover, the cobalt complexes of sapphyrin and amethyryn, as well as the vanadium complex of the Schiff-

Scheme 9



base macrocycle **37**, have served to showcase the role of tautomeric equilibria in the metalation of conjugated expanded porphyrins. Studies of congeners **25** and **30** have illustrated the importance of macrocycle protonation and counterion effects in terms of defining the final structure of a given metal-containing complex. Finally, the role played by hydrogen-bonding interactions in the cooperative binding of  $\text{Ag}^{\text{I}}$  cations in **30** and the bimodal recognition of the nonspherical  $\text{VO}_2^+$  cation in the Schiff-base system **38** and isoamethyrin **18** reveals a supramolecular aspect to the coordination chemistry of oligopyrrolic macrocycles that could provide a starting point for future investigations.

Given the large number of expanded porphyrin systems currently being reported in the literature, we expect that this area of research will grow rapidly in the near future. It has the potential to produce metal complexes with properties very different from those stabilized in more common tetrapyrrolic macrocycles, including porphyrins. The chemistry of bimetallic expanded porphyrin complexes is particularly promising, because it will likely provide new opportunities to investigate magnetic interactions and engineer binuclear catalytic centers wherein two metal ions act in a concerted way on a given reaction substrate. In any event, expanded porphyrin complexes have already demonstrated their potential utility in fields as diverse as drug discovery, bio-inspired catalysis, optical data storage, and nuclear-waste remediation, and it is likely that this will continue to be the case.

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