Benziporphyrins: Exploring Arene Chemistry in a Macrocyclic Environment

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ABSTRACT
Benziporphyrins are synthetic porphyrin analogues, in which one of the pyrroles is replaced with a benzenoid ring. The arene can be incorporated into the macrocycle in several ways leading to molecules with distinct physical and chemical properties. By appropriately changing the structure of benziporphyrins, it is possible to affect their aromaticity, tautomeric equilibria, and reactivity. Benziporphyrins are versatile ligands, which offer a means to study the metal−arene couple in a macrocyclic environment. The coordination brings the metal ion into the vicinity of the arene fragment leading to activation of C−H bonds or weak interactions, which can be observed spectroscopically.

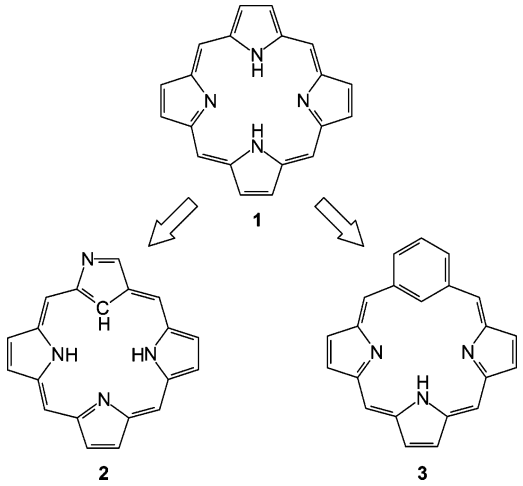
Introduction

The porphyrin ring (**1**) is a relatively simple organic structure consisting of four pyrrole rings linked by single-carbon methine bridges. The porphyrins are uniquely capable ligands, and their coordination chemistry has been intensely investigated, often with an intent to mimic their diverse biological functions.

Nature's original idea to construct a macrocycle from pyrrolic fragments has been creatively employed to generate a plethora of molecules, some of which have displayed remarkable coordinating properties. The large families of expanded, contracted, and isomeric porphyrins were created by changing the number and sequence of the constituent pyrrole rings and carbon linkages.[1] A group of modifications that we have found particularly interesting involves the introduction of C−H moieties into the coordination core of the porphyrin, to replace one or more of the pyrrolic nitrogens. Such molecules, known as carbaporphyrinoids, offer a possibility to stabilize rare types of metal−carbon bonds in a macrocyclic setting.[2]

The inner C−H fragment of a carbaporphyrinoid may belong to a heterocyclic or carbocyclic moiety. The first case is epitomized by N-confused (inverted) porphyrin (**2**),[3,4] which is a porphyrin isomer with a "typo"; one of the pyrrolic nitrogens is placed on the periphery of the macrocycle rather than in the core (Scheme 1). In this way, the electronic structure of **2** is profoundly altered leading to reactivity patterns unknown for the parent porphyrin.[5] Furthermore, this pyrrole confusion increases the number of potential donor atoms because both the inner carbon and the outer nitrogen can participate in binding metal ions.[2,6]

Scheme 1



In the other group of carbaporphyrinoids, the inner C−H bond belongs to a carbocyclic fragment. Various compounds of this type are known that incorporate in their structures different mono- and bicyclic moieties.[7] The choice of the carbocycle affects the degree of π conjugation in the system, and consequently, the macrocyclic aromaticity in some carbaporphyrinoids is attenuated (as in the case of azuliporphyrin[8]) or totally absent. These effects are conveniently observed using ^{1}H NMR spectroscopy, which will be the principal aromaticity criterion in this Account.

An exemplary system based on a carbocyclic unit is *meta*-benziporphyrin (**3**), wherein *m*-phenylene replaces one of the porphyrinic pyrroles. Compound **3** and related molecules containing benzenoid rings offer a possibility to study the behavior of an arene ring placed in the vicinity of a metal ion. The ensuing chemistry can be controlled by making appropriate modifications to the macrocycle, often similar to those used in the research on regular porphyrins.

The present Account summarizes published work on benziporphyrins. We will begin by reviewing the macrocycles synthesized to date and follow with a description of their reactivity. In the remaining part of the text, we will discuss the coordinating properties of benziporphyrins.

meta-Benziporphyrins

The *meta*-benziporphyrin of Berlin and Breitmaier (**6**), reported in 1994, was the first carbaporphyrin synthesized

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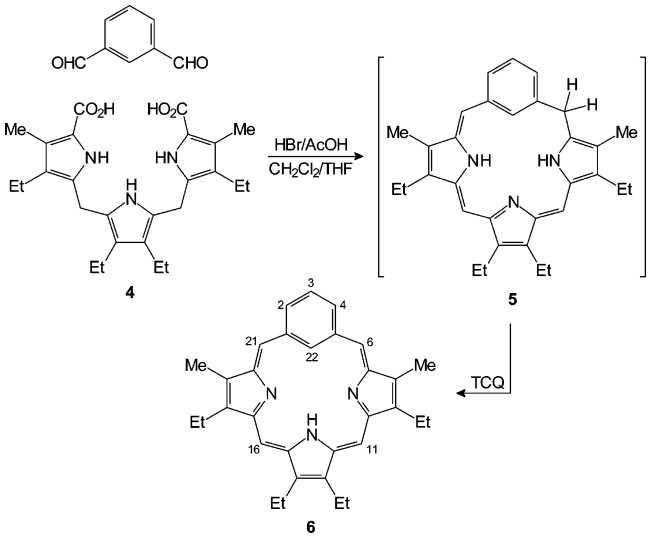
Scheme 2

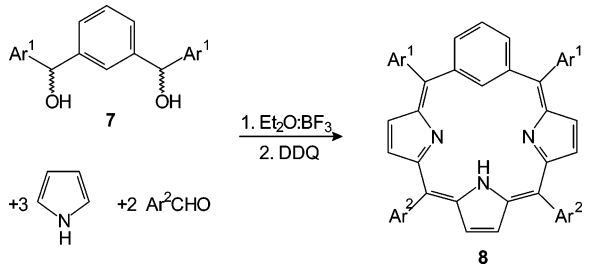


by design.[9] The condensation of isophthalaldehyde with the tripyrrane **4** followed by oxidation with chloranil (tetrachloro-*p*-benzoquinone, TCQ) yielded the benziporphyrin **6** in a 6% overall yield (Scheme 2). The synthesis was later refined in an independent study (28% yield).[10]

The β-substituted compound **6** is evidently an interesting object to study its coordinating properties. However, it was reported to be unstable in solution, requiring considerable perseverance to obtain a pure sample.[10] In addition, the synthesis of **6**, which requires the preparation of tripyrrane **4**,[11] is not a trivial task, judging by the variability of reported yields.

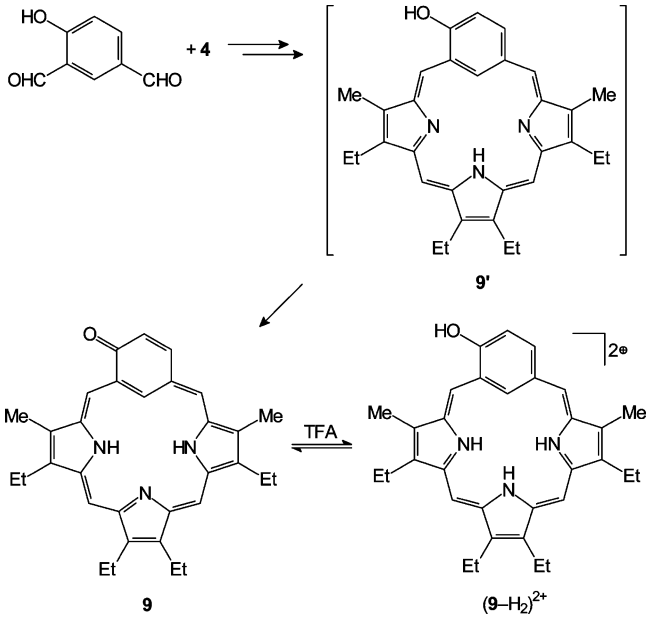
Looking for a viable synthetic and structural alternative for **6**, we decided to prepare its *meso*-substituted analogue.[12] The synthesis was accomplished by a mixed condensation of pyrrole, arylaldehyde, and precursor **7**, following the methodology of Lindsey[13] (Scheme 3). After oxidation with DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) and chromatographic workup, the *meso*-substituted compound **8** was obtained in 15% yield.[12] This is a satisfactory result, considering the simple synthesis of precursor **7** (see below).

Scheme 3



Precursor **7** had been found unreactive in an earlier report by Chandrashekar and co-workers.[14] Apparently, trifluoroacetic acid (TFA), used by those authors, is not the catalyst of choice for benziporphyrin syntheses. It is, however, very successful in effecting direct pyrrole–pyrrole coupling, and a variety of expanded porphyrinoids were isolated as main products.[14]

Scheme 4



Dicarbinols of type **7** were prepared conveniently in a reaction between isophthalaldehyde and an arylmagnesium bromide.[12] Alternatively, a substituted 1,3-dibromobenzene can be used as the substrate, which is lithiated and reacted with an arylaldehyde.[15]

meta-Benziporphyrins (**6** and **8**) display ^{1}H chemical-shift patterns characteristic of nonaromatic oligopyrroles. Their electronic spectra are porphyrin-like, but the intensity of the Soret band is reduced. The absence of macrocyclic aromaticity in *m*-benziporphyrins is a consequence of incompatibility between the porphyrinoid and benzenoid delocalization modes. The *m*-phenylene moiety retains an unperturbed benzenoid structure and remains isolated from the π-electron system of the tripyrrolic fragment. This isolation impacts the reactivity and coordination chemistry of benziporphyrins.

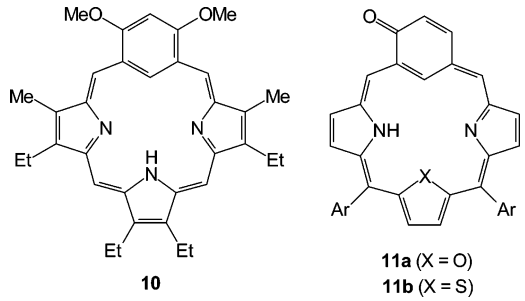
Oxybenziporphyrins

2-Oxybenziporphyrin (**9**) was obtained by Lash in a modified synthesis that used 5-formylsalicylaldehyde as the precursor (Scheme 4).[16] The phenolic tautomer **9′** is not observed and oxybenziporphyrin solely exists as the semiquinone form **9**, which, in contrast to **9′**, is a fully aromatic macrocycle. Oxybenziporphyrin undergoes two-step protonation, yielding an aromatic monocation and subsequently the dication $(\mathbf{9}-H_2)^{2+}$, in which the macrocyclic aromaticity is drastically reduced.

The use of appropriately substituted precursors allowed the preparation of nonaromatic 2,4-dimethoxybenziporphyrins, such as **10** (Scheme 5).[15,17] The macrocyclic aromaticity of their dications was explained by sizable contributions of oxonium resonance forms. **10** could be converted into aromatic systems by cleaving one or two methoxy functions on the phenylene. Some of the latter compounds were later accessed in an alternative synthesis starting from resorcinol.[18]

Heteroanalogues of oxybenziporphyrin partly substituted in *meso* positions were obtained by Chandrashekar

Scheme 5



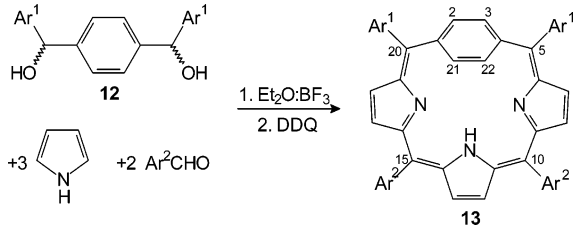
and co-workers.[19] Condensation of 5-formylsalicylaldehyde with appropriate tripyrranes yielded 24-oxa- and 24-thia-2-oxybenziporphyrins (**11a** and **11b**). Their β-substituted variants were later reported by Lash and co-workers.[20] The same group recently described the synthesis of oxynaphthiporphyrin, a modification of **9** with a benzene ring fused to the C(3)−C(4) bond.[21]

para-Benziporphyrin

As discussed earlier, the structure of *meta*-benziporphyrin rules out macrocyclic delocalization. In oxybenziporphyrin, the tautomeric preferences of the molecule were employed to restore aromaticity in the macrocycle. The following example shows how the aromaticity is affected by the way the phenylene is incorporated into the structure.

Tetraaryl-*para*-benziporphyrin (**13**) was obtained in a simple modification of the synthesis described for the *meta* form (**8**). Precursor **7** was replaced with its *para* isomer **12** to yield the desired macrocycle in a 1−3% yield (Scheme 6).[22,23] The procedure is significantly less efficient for the *para* isomer, most probably for steric reasons. A 6% yield was recently reported by Hung et al. for 24-thia-*p*-benziporphyrin obtained by condensing **12** with 16-thiatripyrrane.[24]

Scheme 6



para-Benziporphyrin **13** was characterized by X-ray crystallography (Figure 1). The *p*-phenylene moiety is significantly tilted (ca. 45° from the plane of the three N atoms). The C−C bond lengths within the phenylene deviate slightly from the ideal benzene geometry, indicating weak conjugation with the rest of the macrocycle.[22]

This observation was substantiated by ^{1}H NMR data. At 168 K, the phenylene protons 2,3-H and 21,22-H, located respectively outside and inside the macrocycle, have strongly divergent chemical shifts of 7.68 ppm (outer) and 2.32 ppm (inner). This difference, caused by the diatropicity of the macrocycle, is quite unusual for protons

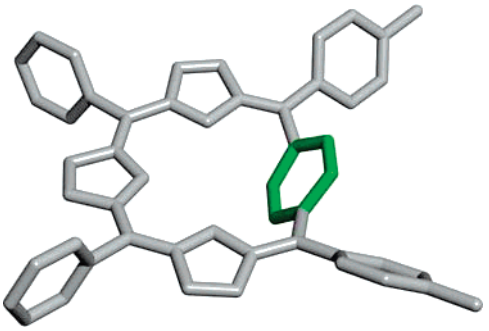


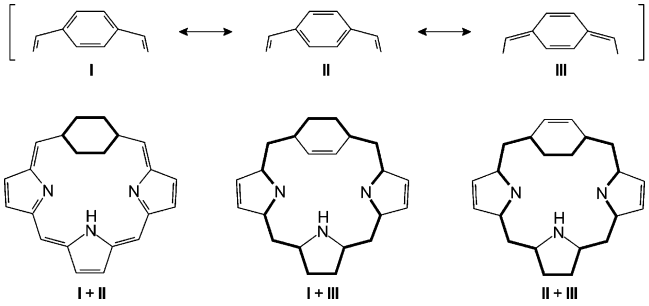
FIGURE 1. Molecular model of **13**. Crystal structure coordinates were taken from ref 22.

FIGURE 2. Flexibility of the *p*-benziporphyrin molecule.

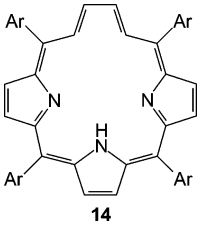
attached to the same benzene ring. At higher temperatures, the two signals were broadened by a dynamic process and finally coalesced into a singlet. This behavior results from a conformational change involving a seesaw motion of the *p*-phenylene. Protons 2,3-H and 21,22-H are swapped between the inner and outer positions as shown in Figure 2.

The structural and spectroscopic features of **13** can be rationalized in terms of resonance between three canonical structures **I**−**III** (Scheme 7). The Kekulé structures **I** and **II** describe the [6]annulene aromaticity of the phenylene fragment. However, each of them may also define a macrocyclic delocalization pathway when supplemented with the quinoid structure **III**. These macrocyclic pathways contain 18 π electrons, similarly as in the classical annulene model of porphyrin.[25] The two pathways are topologically equivalent, with each of them reminiscent of the recently synthesized vacataporphyrin (**14**, Scheme 8).[26] The simultaneous accessibility of local and macro-

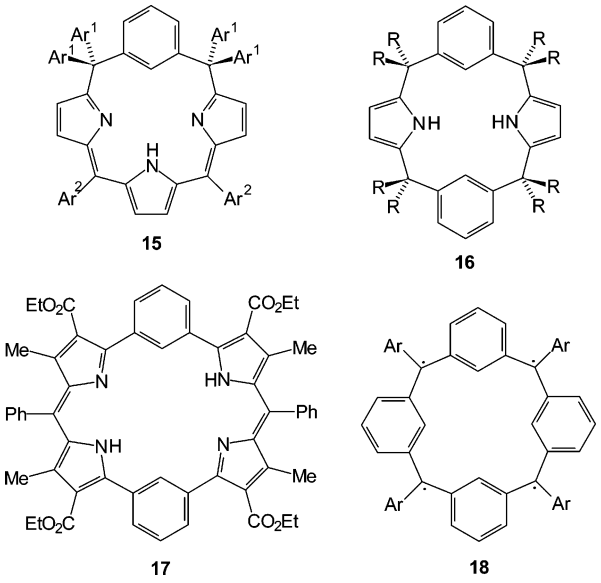
Scheme 7



Scheme 8



Scheme 9



cyclic aromaticity distinguishes **13** from the *meta*-benziporphyrins with an isolated [6]annulene subsystem and from oxybenziporphyrin, where macrocyclic aromaticity is achieved by transforming the benzene moiety into a semiquinone.

Beyond Benziporphyrins

The basic structural motif in benziporphyrins may be modified in ways that are similar to the modification of regular porphyrins. For instance, molecule **15** is a modified *m*-benziporphyrin with two tetrahedral *meso* bridges at positions 6 and 21 (Scheme 9).[23] This recently synthesized compound, named *m*-benziporphodimethene, is closely related to calixphyrins synthesized by Sessler and co-workers.[27] A few more examples of hybrid pyrrole−benzene macrocycles are known in the literature. Compound **16**, *trans*-calix[2]benzene[2]pyrrole, was also reported by Sessler's group along with other hybrid systems and described as "missing-link macrocycles" uniting the classes of calixarenes and calixpyrroles.[28]

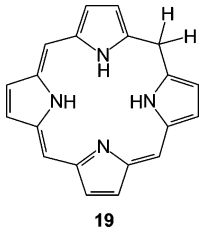
An interesting analogue of benziporphyrin is compound **17**, synthesized by Carré et al., in which the *m*-phenylene rings are directly attached to pyrroles.[29] **17**, crafted in a multistep procedure, has a coordinating potential, and dinuclear Ni^{II}, Pd^{II}, and Rh^{I} complexes were obtained.

A different sort of analogy may be sought among macrocycles composed entirely of phenylene fragments linked by sp^2 bridges, i.e., preserving the mode of attachment found in benziporphyrins. This condition is met by Rajca's macrocyclic polyradicals, formally derived from calixarenes, which have the general structure **18** (Ar is a dendritic polyradical fragment).[30]

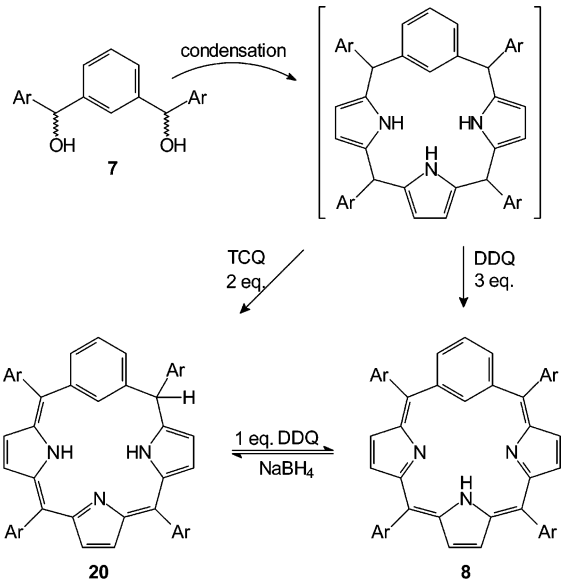
Benziphlorins and Substituted Benziporphodimethenes

The generic phlorin **19** is a reduced form of porphyrin containing a single tetrahedral meso bridge (Scheme 10).

Scheme 10



Scheme 11



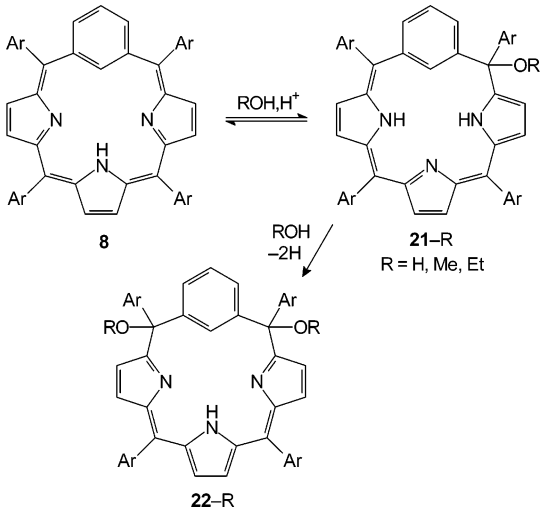
Concomitantly, the number of inner hydrogens is increased to three. The phlorins are nonaromatic and readily oxidizable to porphyrins unless the sp^3 bridge is protected by two aryl or alkyl substitutents.[31]

m-Benziporphyrins are not stabilized by macrocyclic aromaticity, and consequently, the respective phlorin-like derivatives should be less prone to oxidation. However, no attempt was made to isolate the β-substituted benziphlorin **5** (originally termed "porphyrinogen," Scheme 2), which was postulated as the immediate product of the condensation.[9] The enhanced stability of *m*-benziphlorin was only revealed for the *meso*-substituted systems (Scheme 11).[12]

As discussed earlier, in the synthesis of tetraaryl-*m*-benziporpyrin (**8**), the use of 3 equiv of DDQ for oxidizing the reaction mixture leads directly to **8** and no benziphlorin is formed. However, oxidation with 2 equiv of chloranil (a milder oxidant) yields the blue *m*-benziphlorin **20**, which, similarly to **19**, has a saturated meso bridge. Compound **20** can be oxidized to **8** with an additional equivalent of DDQ. This reaction is fully reversible.

Compounds structurally related to **20** were generated by addition of a molecule of water or alcohol to *m*-benziporphyrin **8** (Scheme 12). This acid-catalyzed reaction leads selectively to 6-hydroxy- and 6-alkoxy-*m*-benziphlorins (**21**−R). These species are formed reversibly, and the position of equilibrium can be controlled by the concentration of the nucleophile. Benziphlorins **21**−R undergo further modification in the presence of oxidants

Scheme 12



leading to red-colored compounds **22**−R,[32] which are hydroxy- or alkoxy-substituted analogues of the benziporphodimethene **15**.[23]

Oxidative Substitutions at the Internal Carbon

In the presence of Ag^{I} or Cu^{II} salts, *m*-benziporphyrins undergo oxidative substitutions at the internal carbon, C(22). Examples of this reactivity reported so far include acetoxylation,[12,33] pyridination,[34] and chlorination.[35] These reactions, which are formally aromatic substitutions, take place under surprisingly mild conditions and are highly regioselective.

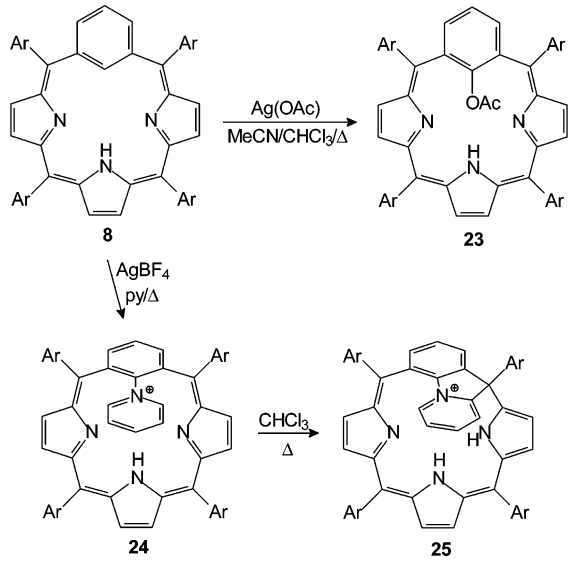
Reaction of tetraaryl-*m*-benziporphyrin **8** with 2 equiv of silver(I) acetate produced 22-acetoxy-*m*-benziporphyrin (**23**) in 66% yield (Scheme 13).[12] Its structure, as characterized by X-ray crystallography, is shown in Figure 3.

In the above reaction, silver(I) plays the role of an oxidant and elemental silver is obtained as a byproduct. It was hypothesized that, whatever the mechanism of oxidation, it might be possible to effect other substitutions with the help of silver(I) salts. Indeed, pyridination of the internal carbon was achieved by refluxing **8** in pyridine with a large excess of $AgBF_4$ (Scheme 13).[34] The product, 22-pyridiniumyl-*m*-benziporphyrin (**24**), is a cationic species containing a pyridinium substituent attached to the internal carbon.

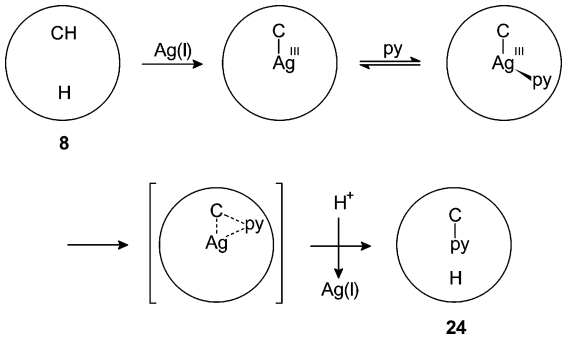
The reaction with pyridine resembles the substitutions observed for π-radical cations of regular porphyrins and metalloporphyrins.[36] In the case of porphyrin radicals, however, only peripheral substitution is observed, which contrasts with the behavior of **8**, which is exclusively pyridinated on the internal 22-C. This selectivity is unlikely for a radical intermediate.

An alternative mechanism was proposed wherein the substitution proceeds through a highly oxidized silver species (Scheme 14),[34] such as the stable Ag^{III} complexes known for regular porphyrins and carbaporphyrinoids.[21,37] This species undergoes reversible axial coordination of pyridine followed by a reductive elimination step yielding,

Scheme 13



Scheme 14



after extrusion of Ag^{I}, the pyridiniumyl compound **24**. 22-Acetoxy-*m*-benziporphyrin (**23**) would form on a similar route.

When the pyridinium derivative **24** was refluxed in a chloroform solution, it slowly isomerized to the benziphlorin **25**.[34] In this species, a new bond was formed between the macrocycle and pyridinium moiety, resulting in the closure of a five-membered ring (Scheme 13). The overall reaction is an intramolecular redox process, but the mechanistic details are not known.

It was recently reported that *m*-benziporphyrin **8** undergoes selective chlorination at the internal carbon

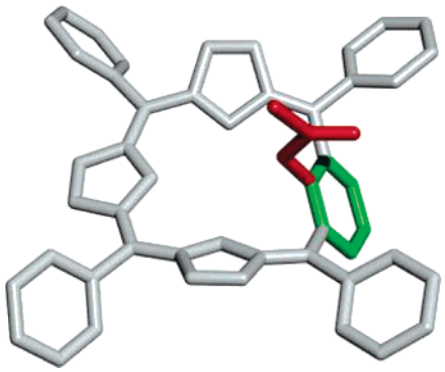
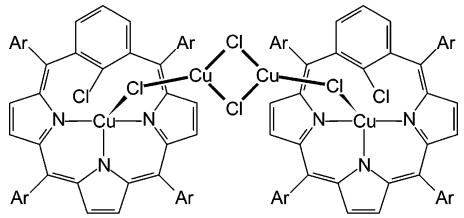


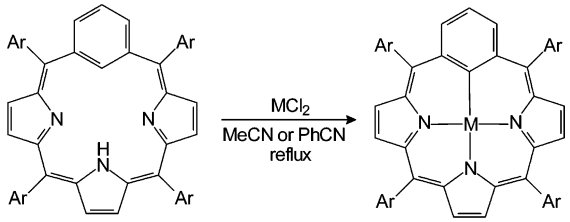
FIGURE 3. Molecular model of 22-acetoxybenziporphyrin **23**. Crystal structure coordinates were taken from ref 12.

Scheme 15



26

Scheme 16



8

27–Ni (M = Ni)
27–Pd (M = Pd)
27–Pt (M = Pt)

when refluxed with $CuCl_2$ in tetrahydrofuran.[35] The 22-chlorinated product was isolated as a tetranuclear mixed-valence copper complex **26** (Scheme 15). Copper(II) is the oxidant in this reaction, and the mechanism may resemble that proposed above for silver salts.

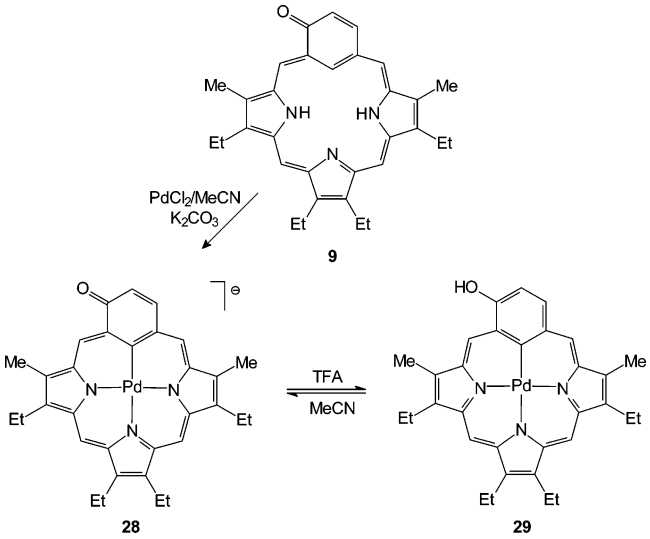
Complexes with a Metal−Carbon Bond

m-Benziporphyrin (**8**) was found to react with Ni^{II},[23] Pd^{II},[12] and Pt^{II} [12] salts and yield tetracoordinate complexes containing a M−C bond (**27**−M, Scheme 16). No X-ray structures were reported, but the coordinating environment of the metal ion is expected to be square-planar, in analogy to the regular porphyrin complexes with d^8 ions. The complexes are stable to moisture and oxygen, but the Ni−C bond in **27**−Ni is easily cleaved by acid (see below). The coordinated metal ion strongly interacts with the chromophore inducing remarkable changes in the electronic spectra. The Ni^{II} species is olive-brown in solution, whereas the colors of Pd^{II} and Pt^{II} complexes are deep orange and green, respectively.

Palladium(II) was also successfully inserted into 2-oxybenziporphyrin (**9**) providing new insight into the electronic structure of this ligand.[38] When **9** was reacted with $PdCl_2$ in refluxing acetonitrile, an anionic complex **28** was formed in a nearly quantitative yield (Scheme 17). The keys to successful metalation were the addition of anhydrous K_2CO_3, which provided the counterion for **28**, and close adherence to stoichiometry.

Complex **28** is conspicuous for its ambident reactivity toward electrophiles.[38] When **28** was titrated with TFA, it underwent reversible protonation on the external oxygen and the phenolic species **29** was formed (Scheme 17). Compound **29** is actually a complex of the

Scheme 17

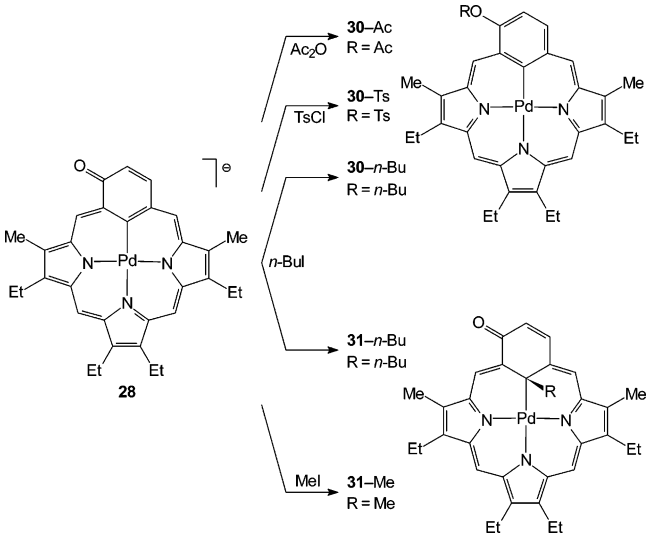


9

28

29

Scheme 18

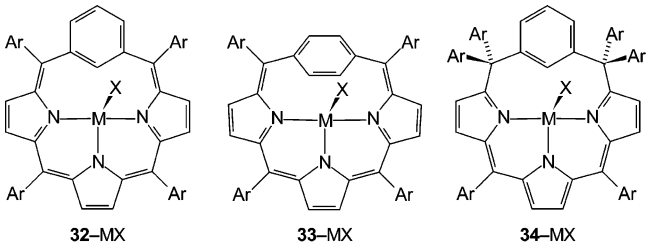


2-hydroxybenziporphyrin tautomer **9′**, unseen for the free base oxybenziporphyrin. Compound **29** is a fairly weak acid and is not deprotonated in pyridine solutions. Reactions of **28** with acetic anhydride or *p*-toluenesulfonyl chloride yielded analogous O-substituted products (**30**−Ac and **30**−Ts, Scheme 18). As could be expected, the macrocyclic aromaticity was significantly reduced in all O-substituted systems, relative to their precursor **28**.

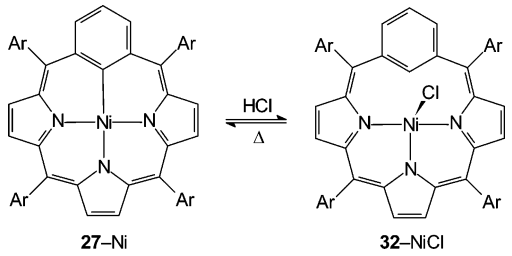
Compound **28** reacted differently in the reaction with methyl iodide. The substitution took place selectively at the internal carbon to form the 22-methylated product **31**−Me (Scheme 18). Interestingly, when *n*-butyl iodide was used for the reaction, an approximately equimolar mixture of O- and C-substituted products was obtained (**30**−*n*-Bu and **31**−*n*-Bu, respectively). These examples show that the site of attack depends on the electrophile, and in some cases, no regioselectivity is observed.

The observed reactivity of the palladium complex **28** led to the conclusion that the energetic preference of the free base **9** to exist as the semiquinone tautomer is not

Scheme 19



Scheme 20



very strong and may be overcome by metal complexation. This was further confirmed by a density-functional theory (DFT) study, which showed that the energy difference between the phenolic tautomer **9′** and the semiquinone **9** is less than 13 kcal/mol.[38]

Several more benziporphyrin complexes with a metal−carbon bond are known. The Ni^{II} complex of the *meso*-substituted variant of **10** was recently prepared.[15] Palladium(II) was inserted to 24-oxa-2-oxybenziporphyrin (**11a**) giving an uncharged complex. Silver complexes of oxybenziporphyrin and oxynaphthiporphyrin[21] provided additional examples of the Ag^{III} oxidation state, which is stabilized by porphyrinoids with trianionic coordination cores.[37]

Complexes with a Weak Metal−Arene Interaction

In the preceding section, the role played by the macrocyclic environment was to facilitate the formation of a M−C bond and then to improve its thermodynamic stability. However, the macrocyclic effect may not always suffice to enforce the metalation of the arene. In such a case, we are left with a phenylene ring that is held proximate to the metal ion without actually forming a covalent bond.

Complexes of this type, depicted in Scheme 19, were obtained for *meta*- and *para*-benziporphyrins (**8** and **13**) and for the benziporphodimethene **15**.[22,23] With one exception, they were simply prepared by reacting the free base with a metal salt. The formation of the M−C bond was usually prevented by at least one of the following circumstances.

First, when coordinated in the tripyrrolic brace, the Zn^{II}, Cd^{II}, and Hg^{II} ions are not electrophilic enough to attack the internal C−H bond. This is particularly evident with the **32**−$Hg(CF_3CO_2)$ complex, obtained from mercury(II)

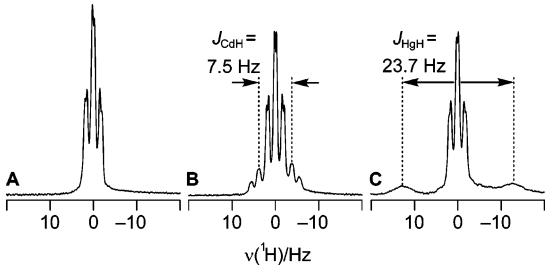


FIGURE 4. Hyperfine structure of the 22-H signals in complexes (A) **32**−ZnCl, (B) **32**−CdCl, and (C) **32**−HgCl ($CDCl_3$, 298 K).

trifluoroacetate, which is known to efficiently mercurate porphyrins.[39] However, during the insertion of nickel(II) to *m*-benziporphyrin, the initially forming **32**−NiCl was subsequently transformed into the organometallic **27**−Ni species. It was therefore expedient to bring the reaction to completion and then convert the isolated **27**−Ni into **32**−NiCl by addition of gaseous HCl (Scheme 20).

Second, in the *p*-benziporphyrin molecule, the orientation of the phenylene with respect to the metal center does not facilitate the formation of a σ bond. A different steric effect is observed in *m*-benziporphodimethene **15**. Molecular modeling and spectral data indicate that the phenylene fragment is removed from the center of the ring farther than in *m*-benziporphyrin. Consequently, the formation of the M−C bond may induce greater strain in the macrocycle of **15**. Indeed, of the three species **32**−NiCl, **33**−NiCl, and **34**−NiCl, only the *m*-benziporphyrin complex underwent internal metalation when refluxed in chloroform/acetonitrile.

The seesaw motion of the phenylene ring observed for the free base *p*-benziporphyrin (**13**) is hindered by the coordination of a metal ion. As a consequence, the ^1H NMR spectra of diamagnetic complexes **33**−MX featured two well-resolved phenylene signals, at ca. 8 and 2 ppm, which corresponded to the outer and inner protons, respectively.

The metal−arene interaction in the benziporphyrin complexes was first observed spectroscopically for the Cd systems. The ^{111}Cd and ^{113}Cd isotopes, which constitute 25% of the naturally occurring cadmium, possess a $^1/_2$ nuclear spin. When the Cd^{II} ion is coordinated by a porphyrin, the ^1H spectrum of the resulting complex will usually show couplings between the peripheral protons of the ligand and the spin-active metal nuclei (on the order of several hertz). These couplings, which are readily recognized by characteristic satellite patterns, were also seen in the spectra of cadmium benziporphyrins. However, in the ^1H NMR spectrum of **32**−CdCl, a coupling was also found between the Cd center and the internal proton of the phenylene (22-H), with the J_{CdH} constant of 7.5 Hz (Figure 4B).

This coupling is transmitted directly between the Cd and 22-H nuclei rather than along the roundabout pathway of covalent bonds. Sufficient accumulation of electron density between the two nuclei is therefore implied because the observed interaction is of a scalar nature. Couplings of this type are often classified as "nonbonding"

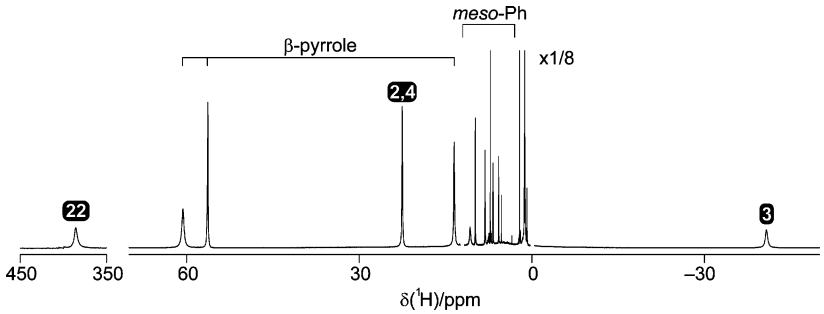


FIGURE 5. ^{1}H NMR spectrum of **32**−NiCl ($CDCl_3$, 298 K). White-on-black labels correspond to the *m*-phenylene signals.

or "through-space" because their magnitude cannot be rationalized in terms of formal bonds in the molecule.[40]

Direct couplings between phenylene protons (carbons) and the metal ion were likewise observed for the remaining Cd and Hg complexes (^{199}Hg also has $I = {}^1/_2$). Their magnitude varied with both the type of ligand and coordinated metal ion. Importantly, for complexes **32**−HgX, the couplings were also found to depend on the axial ligation. For X = Cl, the relevant J_{HgH} constant was 23.7 Hz, whereas for X = CF_3CO_2, it increased to 38.2 Hz.[23]

The crystal structure determined for compound **32**−CdCl revealed a close contact between the metal ion and the phenylene, with the Cd···H(22) and Cd···C(22) distances of 2.67 and 2.72 Å, respectively.[23] The corresponding separations in the *p*-benziporphyrin complex **33**−CdCl were larger (3.07 Å for Cd···H and 2.76 Å for Cd···C), a result of the different orientation of the phenylene. The values cited above are smaller than expected for a van der Waals contact, suggesting that the interaction between the cadmium and phenylene might have some bonding character.

The problem of the metal−arene interaction in the Cd systems was addressed with DFT calculations and AIM analysis.[23] It was found that the accumulation of electron density between the metal ion and arene is small and that the interaction is of a closed-shell type. The observation of Cd−H couplings would thus support the statement that scalar coupling can be transmitted through noncovalent interactions between electron pairs.[41] The couplings observed here for benziporphyrin complexes show only moderate dependence on the relative positioning of the arene with respect to the metal ion.

Complementary evidence for a metal−arene interaction was discovered in the paramagnetic nickel(II) complexes **32**−NiCl, **33**−NiCl, and **34**−NiCl.[23] As with other nickel systems with the $S = 1$ electronic spin state, they exhibited ^{1}H NMR spectra with paramagnetically shifted but still relatively narrow lines. The shifts of the peripheral protons of **32**−NiCl covered a range from −40 to 60 ppm (at 298 K, Figure 5). However, an exceptional shift of nearly 400 ppm was observed for the internal proton 22-H. A very large value (ca. 200 ppm) was found for the corresponding proton in compound **34**−NiCl.

It was found that these unusual shifts are predominantly of contact origin and that the dipolar contribution is small, i.e., there must be a substantial amount of spin density in the vicinity of 22-H. This situation was described as the result of electron donation from the C−H bond to the metal ion. This description corresponds to the definition of an agostic bond, and accordingly, the observed mechanism of spin transfer was dubbed "agostic" for brevity.

The difference between the chemical shifts of 22-H in **32**−NiCl and **34**−NiCl (400 versus 200 ppm) clearly shows that the agostic mechanism is strongly distance-dependent. Importantly, the alignment of the C−H bond with respect to the half-filled orbitals on Ni^{II} has a very strong influence on the observed shifts. A spectacular example was provided by the *p*-benziporphyrin complex **33**−NiCl, for which a shift of 0.0 ppm (298 K) was measured for the inner protons 21,22-H. The paramagnetic shift, which in the case of **32**−NiCl was large and positive, is now replaced with a small negative value.

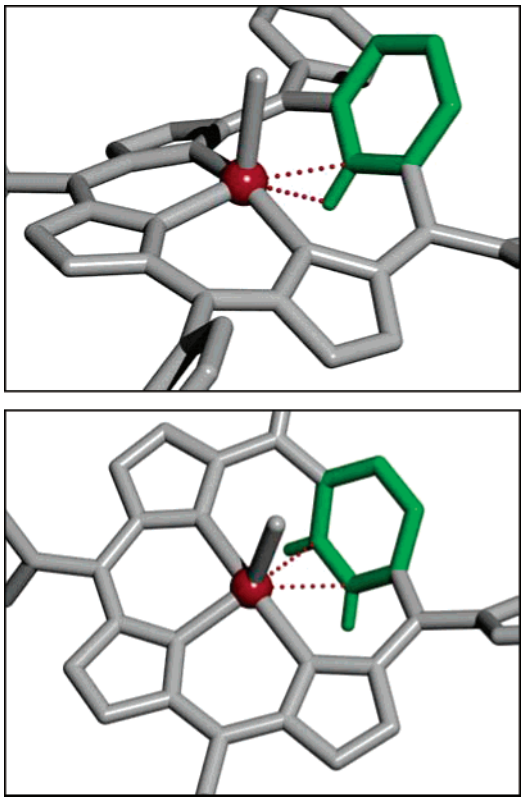


FIGURE 6. Molecular models of complexes **32**−NiCl and **33**−NiCl. Crystal structure coordinates were taken from ref 23.

The conclusions drawn from NMR were confirmed by X-ray analyses of **32**−NiCl and **33**−NiCl (Figure 6). The Ni···H(22) distance in the *m*-benziporphyrin complex was 2.40(3) Å, corresponding to a weak agostic bond, such as could be expected for divalent nickel. The Ni···H(21/22) separations in the *p*-benziporphyrin species are markedly larger (ca. 2.81 Å). Interestingly, the related Ni···C distances vary to a lesser extent (2.55 Å for **32**−NiCl and ca. 2.58 Å for **33**−NiCl).

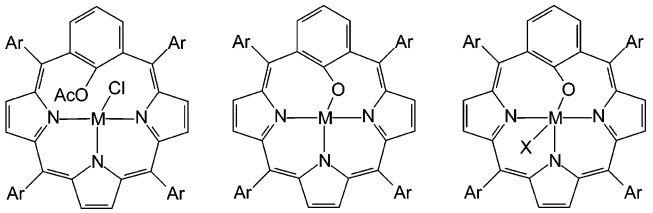
The observations of the agostic mechanism are not restricted to nickel benziporphyrins. An iron(II) complex of N-confused porphyrin was reported to yield a record-breaking chemical shift of the inner proton (1090 ppm at 298 K).[42] In a complementary study on the analogous complex of *m*-benziporphyrin, **32**−FeBr, the 22-H resonance was found at 440 ppm.[35] This smaller value can be explained in terms of the greater flexibility of the benziporphyrin ring, which provides less support for the feeble agostic interaction. Indeed, the Fe···H distances in those two complexes differ substantially. For **32**−FeBr, the separation is 2.44 Å,[42] comparable with **32**−NiCl, whereas in the N-confused porphyrin species it is reduced to only 1.97 Å.[43]

Phenolate Complexes

22-Acetoxy-*m*-benziporphyrin (**23**) can be viewed as a derivative of 22-hydroxy-*m*-benziporphyrin with the internal hydroxy group protected by the ester function. Reactions of the acetoxy compound with a variety of metal salts showed that the latent phenolic donor could frequently be engaged in coordination (Scheme 21).[33]

Depending on the metal ion, it was possible to isolate complex **35**, which preserved the acetoxyl group, or **36**, with the phenolate oxygen coordinated to the metal. Reactions of **23** with $ZnCl_2$ and $CdCl_2$ only yielded the respective **35**−ZnCl and **35**−CdCl species, whereas the use of $NiCl_2$, $PdCl_2$, and $FeCl_2$ led to the cleavage of the ester group and formation of complexes **36**−Ni, **36**−Pd, and **36**−FeCl. In the case of Ni^{II} insertion, it was possible to isolate **35**−NiCl by shortening the reaction time. Apparently, the cleavage reaction is assisted by the metal, and it is not effected by insufficiently acidic ions (Zn and Cd). To obtain **35**−Zn, it was necessary to hydrolyze the acetoxy group of **23** prior to metal insertion.

Scheme 21



35–MX
MX = ZnCl, CdCl, NiCl

36–M
M = Ni, Pd, Zn

36–MX
MX = FeCl, FeBr, FeI

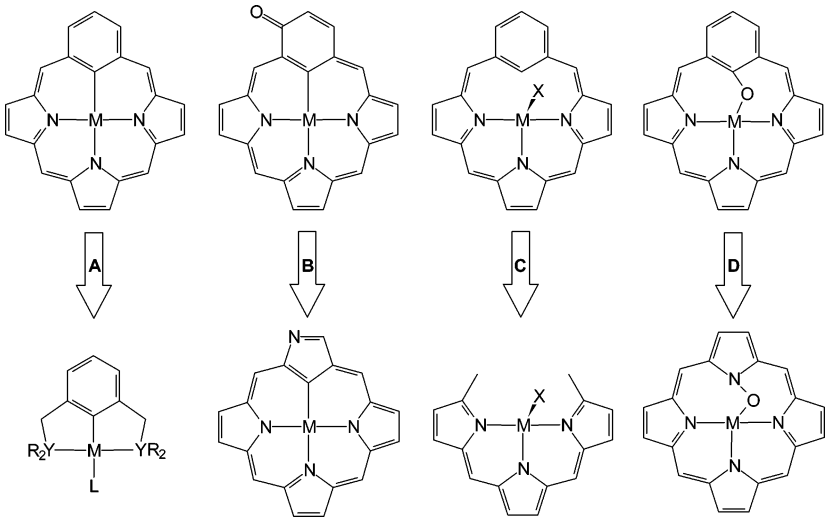
Concluding Remarks

Benziporphyrins are not only versatile ligands but also interesting organic molecules by themselves. In the studies on these macrocycles, several aspects of arene and porphyrin chemistry have been brought together. The aromaticity of benziporphyrins depends on the way the phenylene is incorporated into the macrocycle (*meta* versus *para*) and, in the case of oxybenziporphyrin, also on a tautomeric equilibrium. The case of *m*-benziporphyrin shows that the fusion of structural motifs alters the reactivity of both the arene fragment and the porphyrinic part of the molecule. In particular, the arene is selectively activated toward oxidative substitutions, whereas the tripyrrolic fragment is susceptible to *meso* addition of nucleophiles.

The coordination chemistry of benziporphyrins takes several routes, which differ in the role of the arene moiety. The organometallic derivatives of *m*-benziporphyrin, such as **27**−M, are reminiscent of the large family of pincer ligand complexes, in which the metal−arene bond is supported by two amine or phosphine arms (Scheme 22A).[44,45]

The coordinating properties of oxybenziporphyrin have much in common with the chemistry of N-confused

Scheme 22



porphyrin. The two ligands possess identically charged coordination cores and show an ability to tautomerize upon coordination, which similarly affects their electronic structures (Scheme 22B).

In the *m*- and *p*-benziporphyrin complexes of type **32**−MX and **33**−MX, a weak metal−arene interaction is observed spectroscopically. It is a relatively insignificant bonding contribution compared to the M−N bonds. Consequently, **31**−MX and **32**−MX can be thought of as macrocyclic cousins of tripyrrin complexes, such as those recently studied by the group of Bröring (Scheme 22C).[46]

22-Hydroxy-*m*-benziporphyrin complexes **36**−M provide examples of equatorial coordination by a mixed set of pyrrolic and phenolate donors. In addition, they can be regarded as derivatives of the organometallic species **27**−M with an oxygen atom inserted into the M−C bond. Interestingly, this type of modification is also found in the world of regular porphyrins. Metal complexes of porphyrin *N*-oxides were synthesized that bear an obvious structural analogy to **36**−M (Scheme 22D).[47] Complexes of phenoxy pincer ligands are also known.[48]

In the chemistry presented in this Account, there is much opportunity for future exploration. This is equally true for the organic and inorganic aspects of benziporphyrin research. The *meso*-substituted macrocycles, which can be easily synthesized in a variety of modifications, are especially suited for systematic study. Their properties can be fine-tuned to match particular purposes, for instance, to activate arene C−H bonds, stabilize arene π interactions with the metal, or generate unusual coordination modes in the macrocyclic core.

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