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Recent Advances on the Synthesis and Chemistry of Carbaporphyrins and Related Porphyrinoid Systems

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Synthetic methods have been developed for the efficient synthesis of *meso*-unsubstituted carbaporphyrinoid systems, including oxybenziporphyrins, benzocarbaporphyrins, tropiporphyrins, and azuliporphyrins. In addition, *meso*-tetraryl-porphyrinoids are available by using modified Lindsey–Rothemund reaction conditions. These porphyrin analogs show a broad spectrum of aromatic properties that range from nonaromatic benziporphyrins to highly diatropic systems such as benzocarbaporphyrins. Carbaporphyrinoid systems exhibit unusual reactivity and are often capable of generating organometallic derivatives under mild conditions. Many of the trends observed in the carbaporphyrinoid series were also evident for an expanded series of carbasapphyrins as well. Syntheses of dicarbaporphyrinoids have been investigated but it remains to be seen whether these studies will eventually lead to the formation of hydrocarbon analogs of the porphyrins.

Introduction

Porphyrins (**1**) display highly aromatic properties which are commonly attributed to the presence of an 18π electron delocalization pathway (shown in bold),[1] although alternative models have been proposed.[2] In carbaporphyrins, one or more of the internal nitrogen atoms are replaced by carbon atoms (Figure 1).[3,4] In principle, all four nitrogen atoms could be replaced with carbon atoms to give the bridged annulene quatyrin (**2**) while retaining the same type of aromatic characteristics, although a total of six hydrogen atoms would have to be accomodated in the macrocyclic cavity.[3] To date only monocarbaporphyrins **3**[5,6] and *opp*-dicarbaporphyrins **4**[7] have been described, but other intermediary species are possible such as **5** and **6**. Nevertheless, these known carbaporphyrins give unique insights into porphyrinoid aromaticity[5–7] and exhibit unusual reactivity.[8–11] Of particular note, many carbaporphyrinoids have been shown to form organometallic derivatives under mild conditions[10–16] and in some cases stabilize higher oxidation states for transition metal ions.[10,11,14–16] These properties resemble those of the N-confused and double N-confused porphyrins **7**–**9**,[17] which also possess one or more carbon atoms in the macrocyclic core, while providing possibilities for far greater variations in the properties of the coordinating organometallic ligands. Furthermore, also in common with the N-confused porphyrins **7**, carbaporphyrin derivatives often show strong absorptions in the far red that make them potentially good candidates for photosensitizers in photodynamic therapy (PDT).[18]

In a conceptual sense, carbaporphyrins are generated by replacing a pyrrole (ring A) or pyrrolenine unit (ring B) of a regular porphyrin with a cyclopentadienyl moiety (Scheme 1). Clearly, many related molecules can be formed by introducing other cyclic units such as benzene, azulene, indene or cycloheptatriene. Therefore, many types of structurally diverse carbaporphyrinoid systems are possible and

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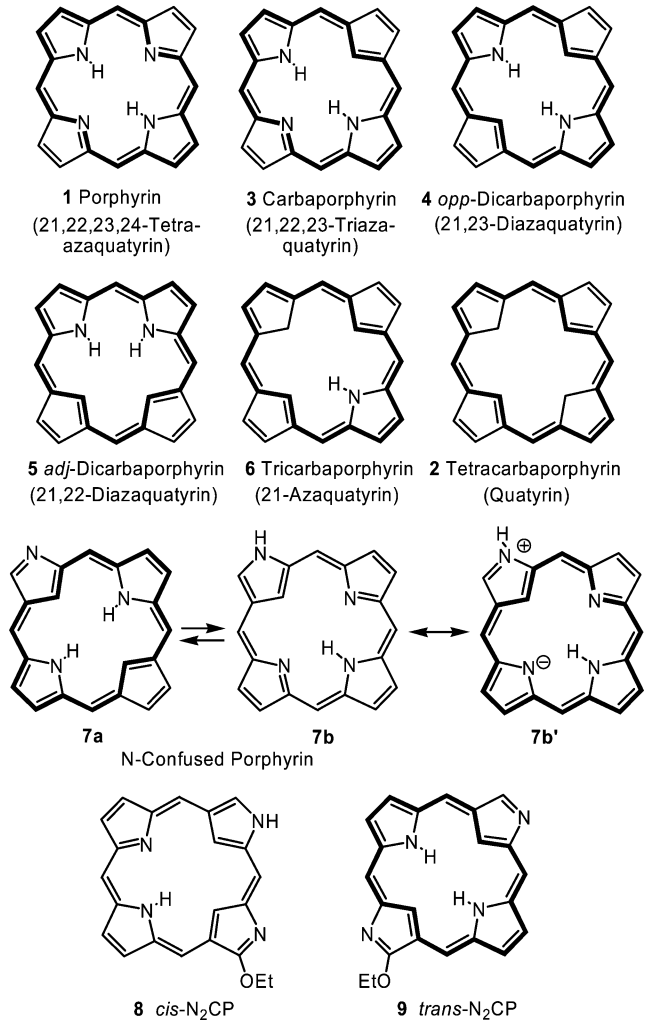


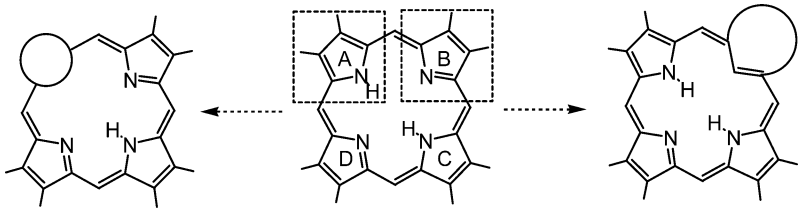
Figure 1. Carbaporphyrins and N-confused porphyrins.

these may have varying degrees of aromatic character.[3,4] In order to investigate these systems, efficient synthetic methods had to be developed.

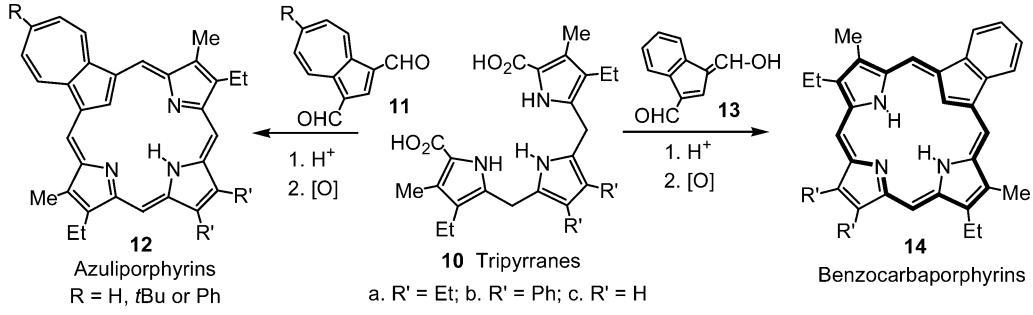
Synthetic Methodologies

The initial syntheses of carbaporphyrinoid systems relied upon the application of a previously little used "3 + 1" variant on the MacDonald condensation (Scheme 2).[19] This method involves the reaction of a tripyrrane **10**[20,21] with aromatic dialdehydes in the presence of an acid catalyst.[19,22] Following oxidation with DDQ, chloranil or ferric chloride, the fully conjugated porphyrinoid is generated.[19,23]

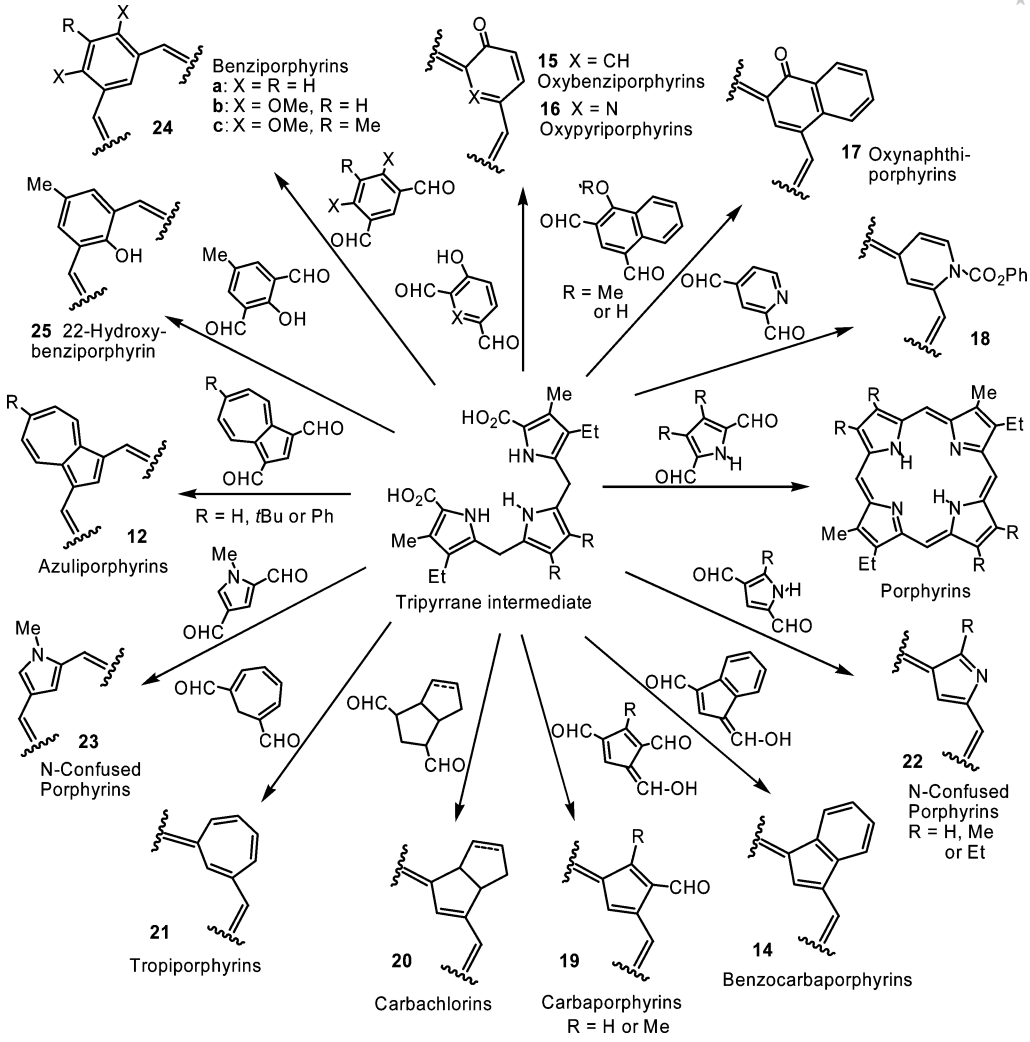
Hence, reaction of **10** with the 1,3-azulenedicarbaldehydes **11** affords the azuliporphyrins **12**,[24–26] while indenedicarbaldehyde **13** gives the benzocarbaporphyrins **14** (Scheme 2).[5,6] This method has been extraordinarily successful in the synthesis of many different classes of porphyrin analogs (Scheme 3), including oxybenziporphyrins **15**,[27,28] oxypyriporphyrins **16**,[28,29] oxynaphthiporphyrins **17**,[14] N-confused pyriporphyrin **18** (trapped in the aromatic form as a phenyl carbamate derivative),[30] carbaporphyrins **19**,[5,6,31] carbachlorins **20**,[32] tropiporphyrins **21**,[16,33] N-confused porphyrins **22**[23] and **23**,[34] benziporphyrins **24** (X = H),[28,35] dimethoxybenziporphyrins **24** (X = OMe),[36] and 22-hydroxybenziporphyrin **25**.[37] The methodology is fairly general, although *meso*-diaryltripyrranes (e.g. **26**) often undergo acidolysis under these reaction conditions and for this reason low yields may be obtained.[38] The di-*tert*-butyl-substituted tripyrrane **27** also gave poor yields of porphyrinoid products apparently because the bulky substituents hinder the formation of a helical conformation that aids in macrocyclic ring closure.[38]



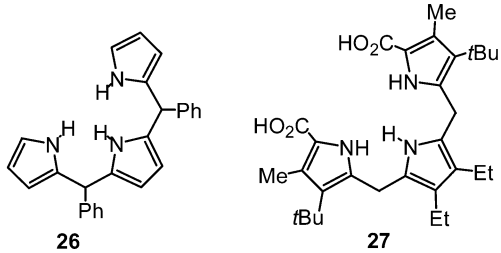
Scheme 1. Conceptual modifications to the porphyrin macrocycle by replacing pyrrole or pyrrolenine units with carbocyclic rings.



Scheme 2. MacDonald "3 + 1" syntheses of azuliporphyrins and benzocarbaporphyrins.

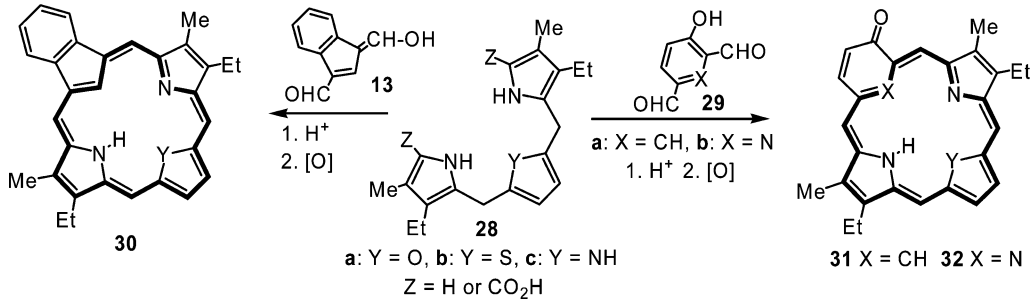


Scheme 3. "3 + 1" syntheses of porphyrin analogs.

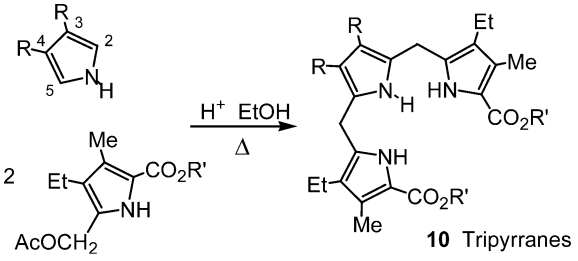


Even though the "3 + 1" approach has been remarkably successful, the initial bust of synthetic studies summarized in Scheme 3 only allowed the synthesis of porphyrin analogs with one exotic ring. In much earlier work by Johnson and co-workers, furan and thiophene analogs of the porphyrins were prepared from oxa- and thiatripyrranes,[39] and these intermediates were shown to be equally well suited for the synthesis of carbaporphyrinoid systems (Scheme 4).[40,41] A matched set of nine porphyrin analogs were prepared by reacting the tripyrranes **28a**–**c** with the aldehydes **13**, **29a** and **29b** to give the benzocarbaporphyrin **30a** and its oxa- and thiaanalogs **30b** and **30c**, and the related oxybenziporphyrins **31** and oxypyriporphyrins **32**.[40] Nevertheless, even more divergent structures were of interest and these required the availability of further modified tripyrrane-type intermediates. Tripyrranes are commonly prepared by reacting 2,5-diunsubstituted pyrroles with 2 equiv. of an acetoxymethylpyrrole in the presence of an acid catalyst (e.g., refluxing acetic acid in ethanol; Scheme 5).[20,21] This chemistry relies upon the reactivity of pyrroles towards electrophilic substitution at the 2- and 5-positions. Azulene has comparable reactivity towards electrophiles at the analogous 1- and 3-positions and has been shown to react with 2 equiv. of an acetoxymethylpyrrole in refluxing acetic acid in 2-propanol to afford the azulitripyrrane **33a** (Scheme 6).[25,42]

The azulitripyrrane was prepared with terminal *tert*-butyl ester protective groups and these were readily cleaved with TFA. Following dilution of the solution with dichloromethane, dialdehydes were added, and after an oxidation step the azuliporphyrins **34a** and the related heteroanalogs **34b**–**d** were isolated in good overall yields.[25,42] Related azuliporphyrinoids have been prepared from 6-*tert*-butyl-



Scheme 4. Heteroanalogs of benzocarba-, oxybenzi- and oxypyriporphyrins.

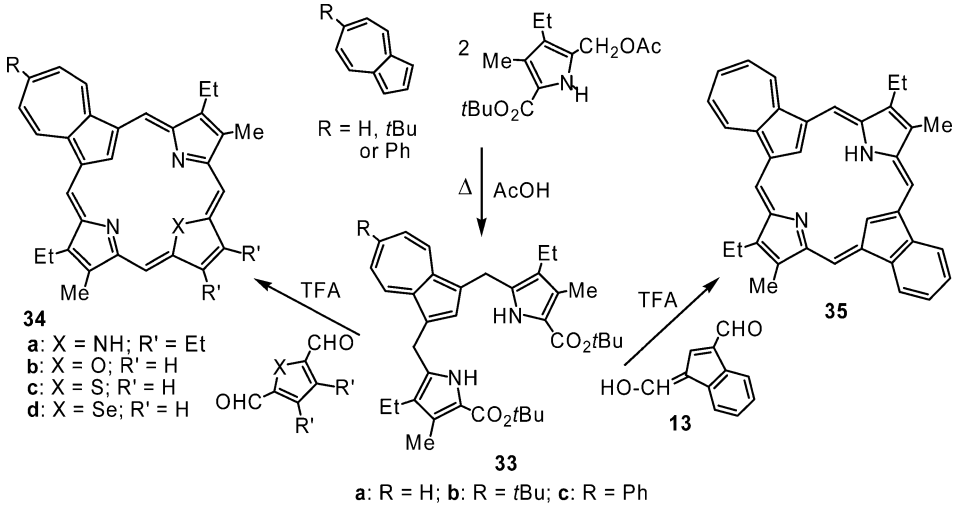


Scheme 5. Synthesis of tripyrranes.

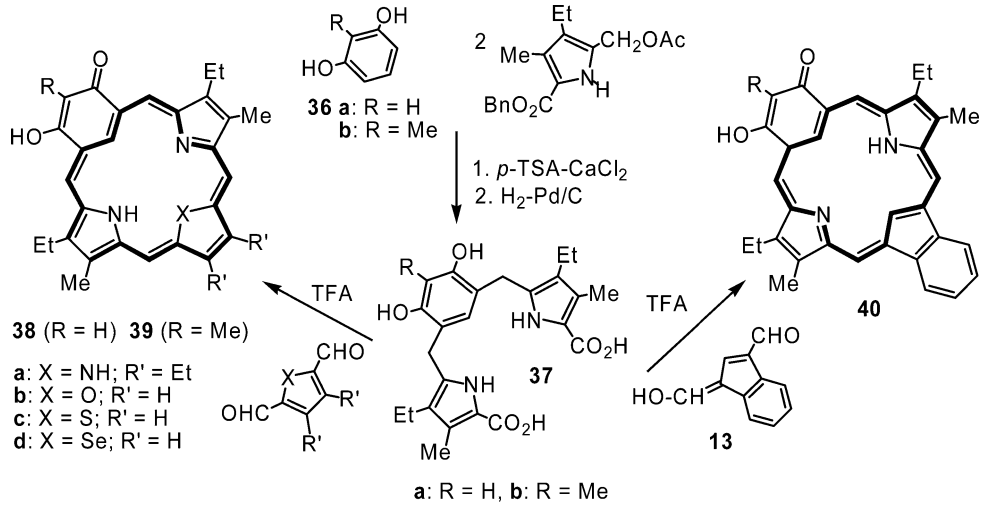
and 6-phenylazulene.[26] In addition, reaction of **33a** with indenedicarbaldehyde **13** afforded the dicarbaporphyrinoid system **35**.[42] This strategy could also be applied to the synthesis of carbaporphyrinoids from resorcinol (**36a**) and 2-methylresorcinol (**36b**) (Scheme 7).[15] Hence, reaction of **36a** or **36b** with 2 equiv. of an acetoxymethylpyrrole in the presence of *p*-toluenesulfonic acid and calcium chloride gave the related benzitripyrrane and following hydrogenolysis over 10% Pd/C, the corresponding dicarboxylic acids **37** could be isolated. Subsequent "3 + 1" condensation with pyrrole-, furan-, thiophene-, or selenophene-dicarbaldehydes afforded the hydroxyoxybenziporphyrins **38** and **39**. Similarly, reaction of **37a** or **37b** with **13** afforded the dicarbaporphyrinoids **40** in moderate yields.[43]

The synthesis of pyridine analogs of the porphyrins had been little studied until recently,[44] due in part to the poor stability of *meso*-unsubstituted pyriporphyrins.[45] We have developed a general route for the synthesis of the diphenylpyritripyrranes **41** from readily available pyridine dicarboxylic acids **42** (Scheme 8).[30] Following conversion of **42a**–**c** into the corresponding diacyl chlorides, Friedel–Crafts acylation of benzene with $AlCl_3$ gave the dibenzoylpyridines **43**. Reduction with sodium borohydride afforded quantitative yields of the related dicarbinols, and these were converted into the corresponding dimesylate derivatives and reacted with excess pyrrole to give the tripyrrane analogs **41**.[30] Further reaction with pyrroledicarbaldehyde **44** in dichloromethane with TFA as the catalyst, and oxidation with DDQ, gave the diphenylpyriporphyrins **45** in good yields.[30]

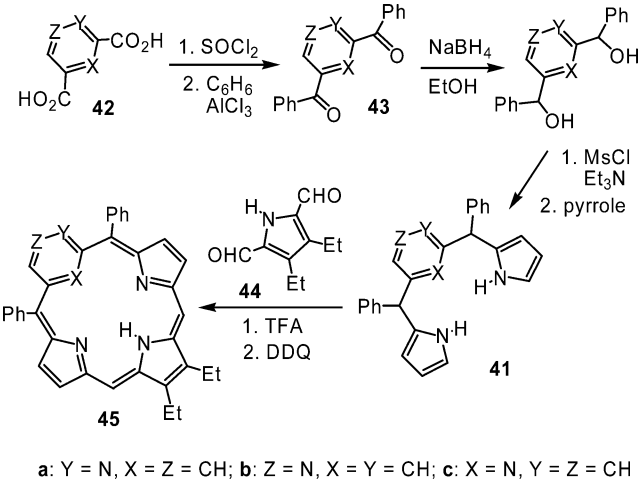
Syntheses of *meso*-tetraarylcarbaporphyrinoids were also developed, in part to provide more direct routes to these systems.[46] In addition, *meso*-tetrasubstituted porphyrinoids are often more soluble in organic solvents and are generally more robust compounds that are less prone towards side reactions.[11] The reactivity and regioselectivity of azulene towards electrophilic substitution made it a potential substitute for pyrrole in macrocyclic syntheses (Scheme 9). Initially, the synthesis of calix[4]azulene **46a**



Scheme 6. Back-to-front syntheses of azuliporphyrins and related systems.



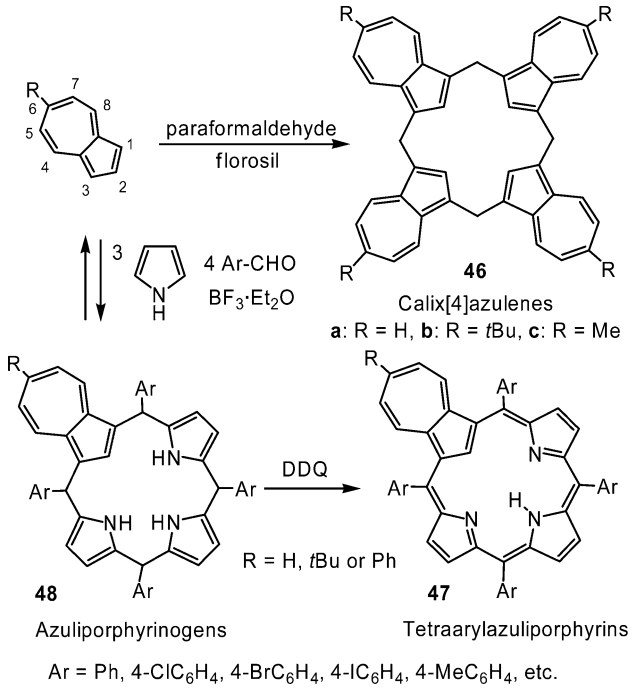
Scheme 7. Synthesis of benziporphyrinoids from resorcinols.



Scheme 8. Synthesis of diphenylpyriporphyrins.

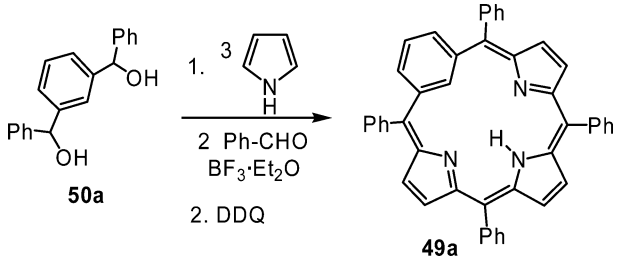
was investigated by reacting azulene with paraformaldehyde in the presence of an acid catalyst.[47] Following an extensive survey of many acid catalysts and solvents, many reaction conditions were found that gave low yields of **46a** with some calix[5]azulene.[47] However, when azulene and paraformaldehyde were treated with florisil in dichloromethane, >70% yields of pure calix[4]azulene were obtained.[47] The chemistry can be applied to some substituted azulenes, but attempts to react azulene with other aldehydes or ketones gave no macrocyclic products under the conditions that we investigated.[47] Calixazulene **46** has the same carbon framework as quatyrin and may provide an entry towards this ultimate carbaporphyrinoid system. However, the chemistry involved in this synthesis is very similar to the reaction of pyrroles and aldehydes under Lindsey's conditions for the Rothemund reaction.[48,49] We speculated that mixtures of pyrrole, benzaldehyde and azulene could react under Lindsey–Rothemund conditions to afford tetraphenylazuliporphyrin **47a**.[46] In the Lindsey reaction conditions, pyrrole and benzaldehyde are reacted in the presence of a catalytic amount of boron trifluoride–diethyl ether in dichloromethane to generate a porphyrinogen, and subsequent oxidation with DDQ then affords the *meso*-tetraphenylporphyrin (TPP) product.[49] The initial formation of the macrocycle at the porphyrinogen level is complicated by the fact that all of the carbon–carbon bond forming reactions are reversible, and the intially formed product can open to form smaller fragments or oligomers. The advantage of Lindsey's methodology is that it separates the condensation and oxidation phases of the chemistry, and this allows the conditions to be better optimized taking into account concentration, solvent, catalyst, temperature, time, and many other factors.[49] In the synthesis of *meso*-tetramesitylporphyrins, chloroform was found to be a superior solvent apparently due to modifications to the reactivity of the BF_3 catalyst that are caused by the presence of ca. 0.8% ethanol as a stabilizer.[50] We have also found that chloroform is a superior solvent in the synthesis of other sterically crowded porphyrin systems.[51–53] When we reacted azulene, pyrrole and benzaldehyde in a ratio of 1:3:4 in the presence of boron trifluoride–diethyl ether in dichloromethane, very little azuliporphyrin was formed.[46] However, much better results were obtained in chloroform. In the synthesis of TPP, optimal results were obtained when the reaction products were oxidized after 30 min. However, virtually no azuliporphyrin was formed when the reaction was terminated at < 2 h, and TPP was isolated as the major product. Nevertheless, if the reaction time was extended to 16 h, and the products treated with DDQ for 1 h, tetraphenylazuliporphyrin was isolated in 10–13% yield.[46,54] Significant quantities of TPP were still formed but this by-product was easily separated by column chromatography. The results suggest that the porphyrinogen precursor to TPP is generated rapidly but can fragment to regenerate open chain pyrrolic species. An azuliporphyrinogen **48** must accumulate over longer time periods, possibly due to thermodynamic factors, and on oxidation the azuliporphyrin framework is fixed in place as acidolytic cleavage can no longer occur for the conjugated species.[54] A series of *meso*-tetraarylazuliporphyrins were synthesized by this approach and in some cases >20%

yield of azuliporphyrin could be isolated from this one-pot procedure.[54] This approach was also used in the synthesis of the substituted azuliporphyrins **47** (R = *t*Bu or Ph) from 6-*tert*-butyl- or 6-phenylazulene (Scheme 9).[55]



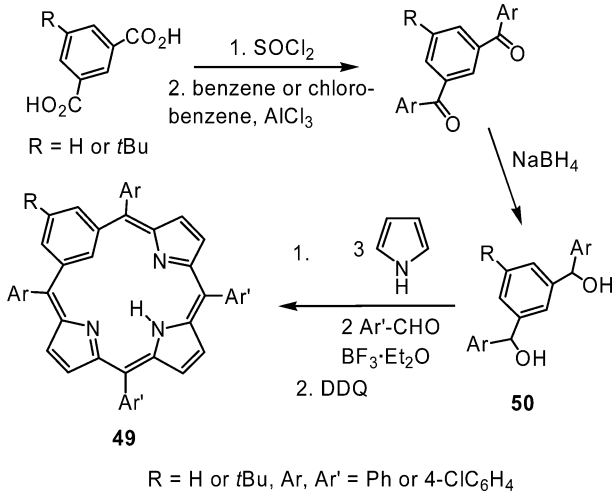
Scheme 9. Synthesis of calix[4]azulenes and tetraarylazuliporphyrins.

A similar synthesis of *meso*-tetraphenylbenziporphyrin **49a** from the dicarbinol **50a** was developed independently by Stepien and Latos-Grazynski (Scheme 10).[56] In the synthesis of TPP from pyrrole and benzaldehyde, or in the analogous synthesis of azuliporphyrin **47**, eight carbon–carbon bonds must be formed. In the dicarbinol approach, the two bonds to the benzene unit are already in place and only six more bonds are required to generate the macrocycle. The dicarbinol **50a** was prepared by reacting isophthalaldehyde with phenylmagnesium bromide. Further reaction with pyrrole and benzaldehyde in the presence of $BF_3{\cdot}Et_2O$ in dichloromethane, followed by oxidation with DDQ, gave the benziporphyrin **49a** in up to 15% yield.[56] The reactivity of this system has been extensively investigated and examples of metallo derivatives have been reported.[57] We have recently developed a more convenient route to the required dicarbinol intermediates **50** from dicarboxylic acids and

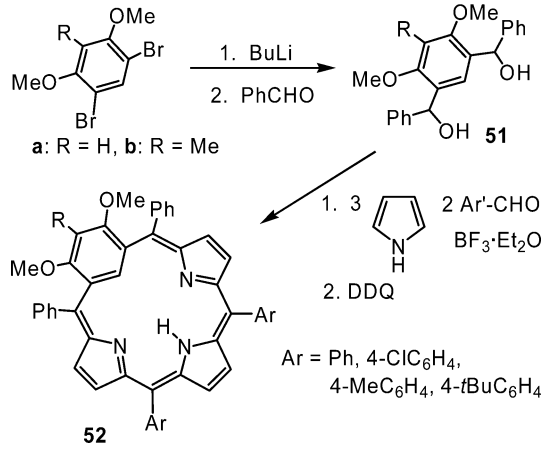


Scheme 10. Synthesis of tetraphenylbenziporphyrin.

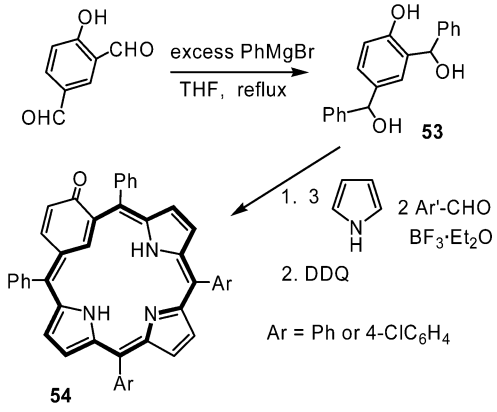
have investigated the influence of the substituents on the yields of the benziporphyrin products **49** (Scheme 11).[58] In some cases the yields were raised to >30%.[58] In addition, dicarbinols **51** were easily obtained from dibromo(dimethoxy)benzenes by metal–halogen exchange, followed by reaction with benzaldehyde (Scheme 12).[59] These dimeth-



Scheme 11. Improved synthesis of tetraarylbenziporphyrins.



Scheme 12. Synthesis of tetraaryldimethoxybenziporphyrins.



Scheme 13. Synthesis of tetraaryloxybenziporphyrins.

oxybenzenedicarbinols also gave good yields of tetraarylbenziporphyrins **52** and by varying the aldehydes used in these syntheses, mixed aryl substituents could easily be introduced.[59] Reaction of excess phenylmagnesium bromide with 5-formylsalicylaldehyde gave the related phenolic dicarbinol **53** and this reacted with aryl aldehydes and pyrrole in the presence of $BF_3{\cdot}Et_2O$, followed by oxidation with DDQ, to give the fully aromatic oxybenziporphyrins **54** (Scheme 13).[60] Interestingly, benziporphyrins **49** were only obtained in good yields when dichloromethane was used as a solvent, but superior results in the synthesis of dimethoxybenziporphyrins **52** or oxybenziporphyrin **54** necessitated the use of chloroform as the reaction solvent.[59,60]

Benzocarbaporphyrins

Most of the work that has been carried out on carbaporphyrins has dealt with the benzo[*b*]carbaporphyrins **14** because this system is easily prepared from indenedicarbaldehyde **13** (Scheme 2).[5,6] The carbaporphyrins **14** have UV/Vis spectra that closely resemble the spectra of true porphyrins with strong Soret bands near 420 nm and a series of four Q bands (Figure 2). The aromatic nature of this system is evident from the high degree of diatropic character in the proton NMR spectra for these porphyrin analogs. The internal CH and NH protons resonate upfield at –7 and –4 ppm, respectively, while the *meso*-carbon atoms give singlets downfield near +10 ppm (Figure 3). The NMR spectroscopic data indicate that a single tautomer is favored in solution where the two NHs flank the central nitrogen and thereby optimize intramolecular hydrogen bonding interactions (Scheme 14).[6,61,62] As the aromatic character of these carbaporphyrins is believed to be derived from the [18]-annulene substructure highlighted in bold, the outer double bond of the pyrrolenine ring (labeled as ring C in Figure 4) should have more alkene character than the equivalent carbon–carbon bonds in the two pyrrole units (rings B and D).[61] Allylic coupling to methyl substituents in alkenes is generally ca. 2 Hz, but the equivalent ^4J coupling in aromatic systems is usually <1 Hz and this difference can be used as a measure of aromatic character.[63] Although the coupling constants are also affected by ring size and bond angles, similar studies have been conducted on porphyrins and these data allow for meaningful comparisons to be made.[63] In order to assess the ^4J coupling constants in benzocarbaporphyrins, the compounds **55** and **56** were prepared and careful proton NMR studies were conducted.[61] In compound **55**, the C ring ^4J coupling was found to be 1.3–1.4 Hz while carbaporphyrin **56** gave a ^4J coupling constant of 0.9–1.0 Hz for rings B and D. These data imply that the C ring double bond has more olefinic character than the B and D rings and this supports the proposed 18π electron pathway model for this system.[61]

The benzocarbaporphyrin **14** is protonated in the presence of trace amounts of TFA to give the monocation **57** and this can be further *C*-protonated with excess TFA to

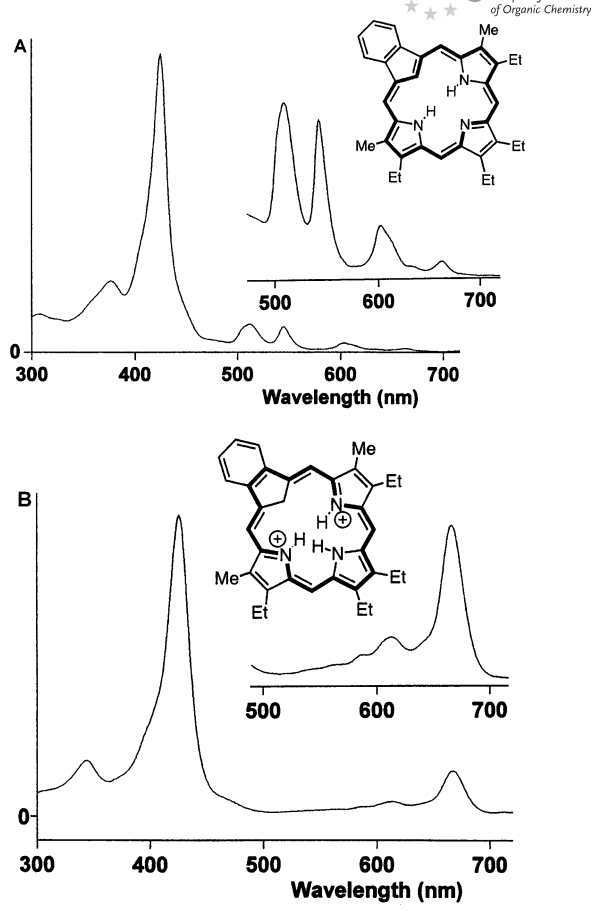


Figure 2. UV/Vis spectra of benzocarbaporphyrin **14a**. A. Free base in 1% Et_3N/chloroform. B. Dication **58a** in 50% TFA/chloroform.[5,6]

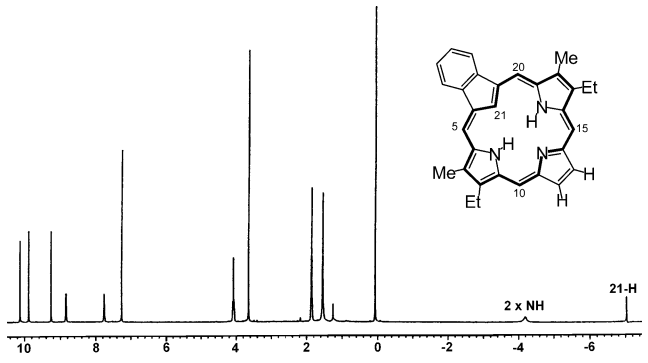
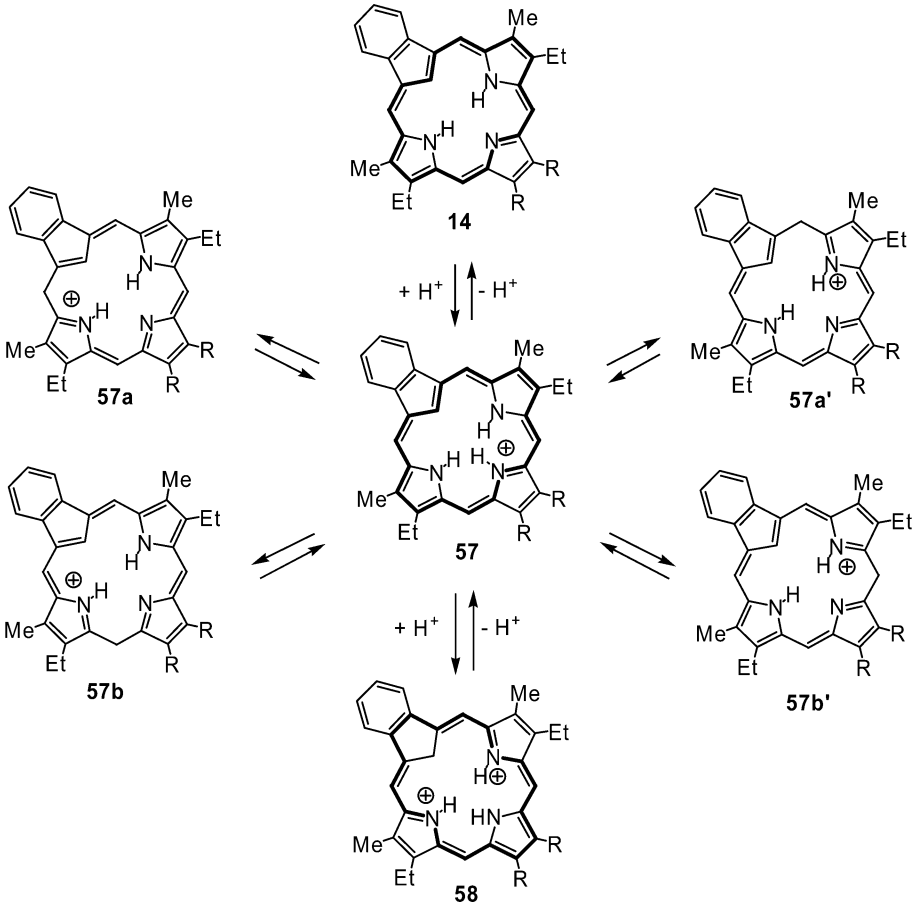


Figure 3. 400 MHz proton NMR spectrum of a benzocarbaporphyrin in $CDCl_3$.[41]

give the dication **58** (Scheme 14).[5,6] The latter species is formed in equilibrium with **57**, but in 50% TFA/$CDCl_3$ this is the only species that shows up in the proton NMR spectra.[6] The proton NMR spectroscopic data for **57** and **58** support the retention of an aromatic ring current, and in the case of the dication **58** the internal CH_2 and NH groups show up at –5.14 and –1.4 ppm, respectively, while the *meso*-protons where shifted further downfield to give two 2 H singlets at δ = 10.45 and 11.05 ppm. The benzo protons adjacent to the macrocycle gave particularly insightful in-



Scheme 14. Protonation of benzocarbaporphyrins.

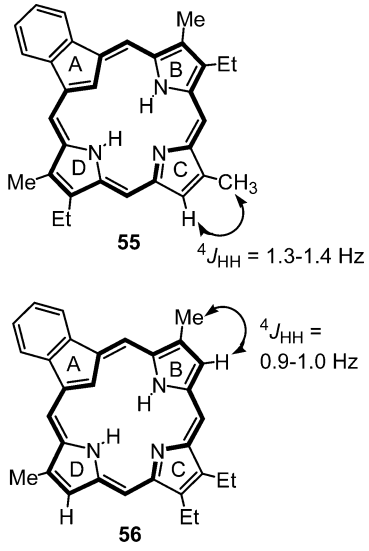
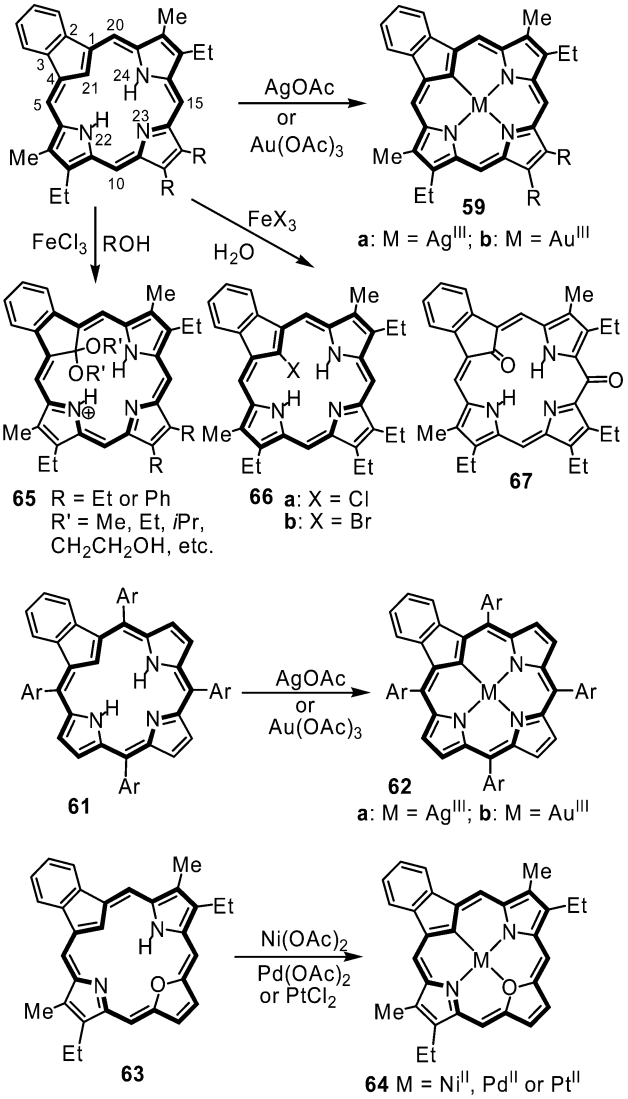


Figure 4. ^4J Coupling constants for benzocarbaporphyrins.

formation, resonating at 8.83, 8.69 and 10.13 ppm, for the free base **14**, the monocation **57**, and the dication **58**, respectively. The substantial downfield shift of this resonance in **58** indicates that the 18π electron delocalization pathway has been relocated through the benzene ring and for this reason this species can be considered to be a benzo[18]annulene.[6] Addition of d-TFA to solutions of **14** in $CDCl_3$ showed slow deuterium exchange at the *meso* positions and this indicates that *C*-protonated species such as **57a** and **57b** are also in equilibrium with **57** and **58** (Scheme 14).[6]

The carbaporphyrin cavity has a CH–NH–N–NH arrangement that could potentially act as an organometallic ligand. Although initial attempts to metalate this system with transition-metal salts such as nickel(II) or copper(II) acetate were unsuccessful,[8] carbaporphyrin **14** was later shown to react with silver(I) acetate to give the related silver(III) complex **59** in excellent yields (Scheme 15).[10,11] This compound gave orange solutions and was substantially less polar than the corresponding free base benzocarbaporphyrin **14**. The proton NMR spectroscopic data also showed that the silver(III) complex retained highly diatropic character. X-ray crystallography for the free base form of the diphenylcarbaporphyrin **14b** shows that the macrocycle is reasonably planar although the indene unit is significantly tilted by 15.5° from the mean macrocyclic plane (Figure 5, A).[6] This was attributed to steric crowding due to the three interior hydrogen atoms. By comparison, the X-ray crystal structure for the silver complex **59a** shows that the macrocycle is near planar presumably because the three hydrogen atoms are no longer present and the sil-

ver(III) cation is an excellent fit for the porphyrinoid cavity (Figure 5, B).[10] Gold(III) acetate also reacted with **14**, although the yields of gold(III) carbaporphyrins **59b** were low.[11] Tetraarylbenzocarbaporphyrins **61** were better suited to this chemistry and gave good yields of both the silver(III) complexes **62a** and the gold(III) derivatives **62b** (Scheme 15).[11] Hence, carbaporphyrins are capable of acting as trianionic ligands and form stable derivatives with metals in relatively high oxidation states. On the other hand, 23-oxacarbaporphyrin **63** is a dianionic ligand and readily forms nickel(II), palladium(II) and platinum(II) organometallic derivatives **64** (Scheme 15).[40] During the earlier investigations on **14**, reactions with a large excess of ferric chloride in methanol/chloroform were shown to give the dimethoxy carbaporphyrin ketals **65** (R = Me).[8] When other alcohol solvents were used such as ethanol, 2-propanol and ethylene glycol, similar carbaporphyrin ketals with R = Et, *i*Pr or CH_2CH_2OH, respectively, were generated.[9] The ketals were isolated in a monoprotonated form (usually as hydrochloride salts) and the free bases were rather unstable.[9] Nevertheless, these oxidations were regioselective and gave good yields. The diatropic nature of these porphyrinoids was retained and the dimethoxy ketals showed the OMe resonance as a 6 H singlet at –1.3 ppm.[8,9] It is also worth noting that these ketals, in common with carbaporphyrin dications, are examples of benzo[18]annulenes.[8,9] Addition of TFA-generated dications that also retained diatropic characteristics. The ketals **65** are polar molecules that show strong absorptions in the far red (Figure 6), and for this reason could potentially be used as photosensitizers in photodynamic therapy.[8,9] In addition, ketals **65** have been shown to be highly active against leishmania.[64] Oxidation of **14a** with ferric chloride in water gave a 21-chloro derivative **66a** as the major product, although a nonaromatic diketone **67** was formed with longer reaction times.[9] The presence of the chlorine atom causes the indene unit in **66a** to tilt by nearly 30° from the mean [18]annulene plane (Figure 5, C), but the proton NMR spectroscopic data showed that the chlorocarbaporphyrin retains nearly all of its diatropicity.[9] The NH resonance for **66a** was upfield to –4.1 ppm, while the *meso*-protons still gave rise to two downfield 2 H singlets at δ = 9.75 and 9.91 ppm. Benzocarbaporphyrin **14a** gave the corresponding bromo deriva-



Scheme 15. Chemistry of benzocarbaporphyrins.

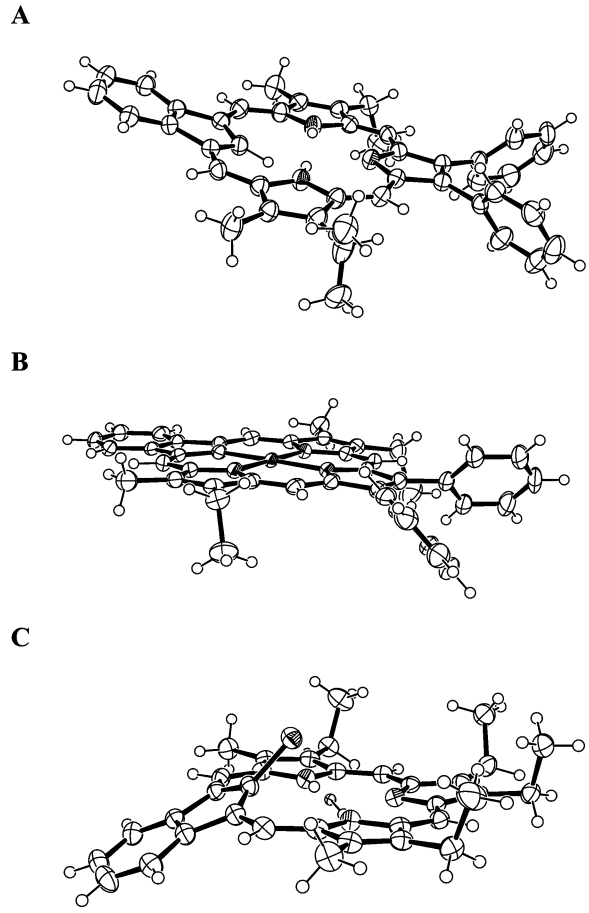


Figure 5. Single-crystal X-ray structures (ORTEP-III) of diphenylbenzocarbaporphyrin **14a** (A),[6] silver(III) complex **59a** (B),[10] and 21-chlorobenzocarbaporphyrin **66** (C).[9]

tive **66b** with ferric bromide, albeit in only 7% yield, and even this species showed a comparable diatropic ring current.[9]

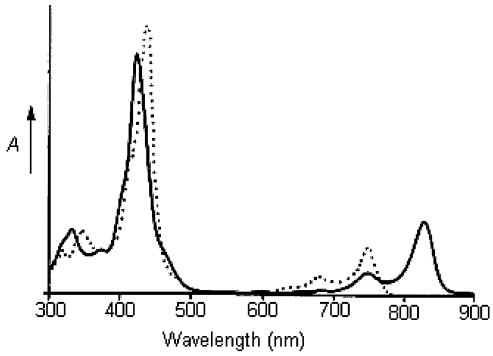


Figure 6. UV/Vis spectra of carbaporphyrin diketal **65** (R = Et; R′ = Me) in chloroform (bold line, monocation) and 10% TFA/chloroform (dotted line, dication $\mathbf{65}H_2^{2+}$).[8,9]

Azuliporphyrins

Azuliporphyrins **12** are significantly less aromatic than the carbaporphyrins **14**, showing the internal CH near 3 ppm, while the external *meso*-protons are observed as two 2 H singlets at 8 and 9 ppm.[24–26] The UV/Vis spectra for azuliporphyrins are also quite different from porphyrins or carbaporphyrins showing 4 bands between 350 and 500 nm and a broad absorption extending to 800 nm (Figure 7).[24,25] Addition of TFA gives a dication **68** (Scheme 16) that shows significantly increased diatropicity where the interior CH shifts upfield to give a resonance at –3 ppm, while the *meso*-protons appear further downfield as two 2 H singlets near 10 ppm.[24,25] The UV/Vis spectrum for the dication is also somewhat more porphyrin-like giving two Soret-type bands at 368 and 466 nm (Figure 7). The aromatic character of **12** derives from dipolar resonance contributors that simultaneously gives the system tropylium-ion character and an 18π electron delocalization pathway.[24,25] This cooperative interaction is limited by the need for charge separation, but in the dication the same type of resonance interaction becomes more favorable because it aids in charge delocalization. Similar properties were observed for heteroazuliporphyrins **34b**–**d** (Scheme 6).[25,42] Azuliporphyrins **12** have also been shown to act as organometallic ligands, generating stable nickel(II), palladium(II) and platinum(II) complexes **69** (Scheme 16).[12,13]

The tropylium ion character of the seven-membered ring makes this unit susceptible to nucleophilic attack, and this appears to be the trigger for oxidative ring contraction reactions that yield benzocarbaporphyrins.[65] Reaction of **14** with *tert*-butyl hydroperoxide under basic conditions gives mixtures of the benzocarbaporphyrins **14** and **70** (Scheme 17).[25] Initial attack by a *tert*-butyl peroxide anion would give the carbaporphyrin adduct **71** and this can then undergo a Cope rearrangement to generate **72**. Subsequent elimination of *tert*-butoxide would afford aldehydes **70**,

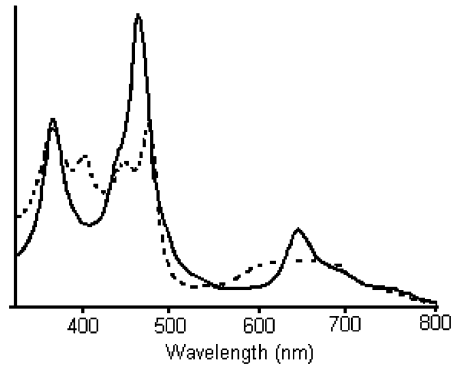
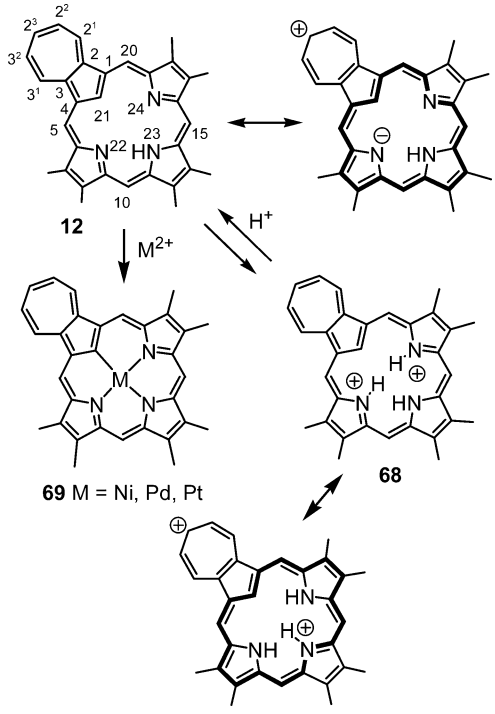


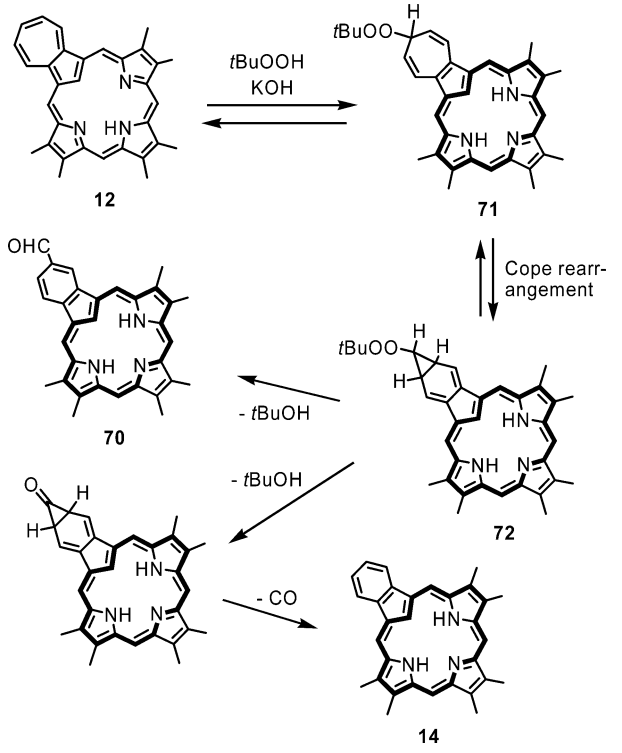
Figure 7. UV/Vis spectra of azuliporphyrin **12b** in chloroform (dotted line, free base) and 1% TFA/chloroform (bold line, dication).[24,25]



Scheme 16. Protonation and metalation of azuliporphyrins.

while loss of tBuO$^-$ and decarbonylation would yield **14**. This type of rearrangement has also been observed for thia- and selenaazuliporphyrins **34** (X = S or Se), and this chemistry allows an alternative synthetic entry to benzocarbaporphyrins.[25] Interestingly, it is difficult to sterically inhibit this chemistry and *tert*-butyl-substituted azuliporphyrins **34a** (Scheme 6; R = tBu) still undergo ring contractions to afford benzocarbaporphyrins.[26,55]

meso-Tetraarylazuliporphyrins **47** also show borderline aromatic characteristics that are enhanced for the dications **73** (Scheme 18).[46,54] The seven-membered ring remains susceptible to nucleophilic attack and reversibly forms adducts (e.g. **74**) with nucleophiles such as pyrrolidine or thiophenol.[46,54] Reactions with tBuOOH and KOH again yields benzocarbaporphyrins, and this remains the only route available to synthesizing the *meso*-tetraaryl versions

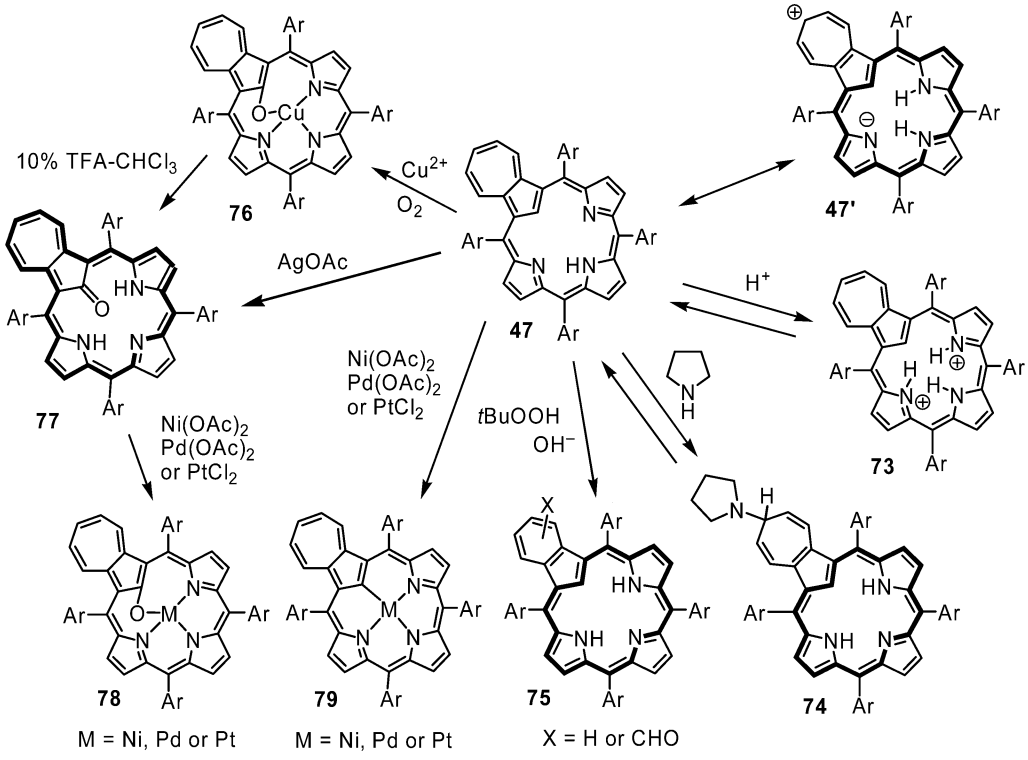


Scheme 17. Conversion of azuliporphyrins to benzocarbaporphyrins.

75 of this system.[46,54] Reaction of **47** with copper(II) salts resulted in a rather different oxidation reaction where the internal carbon is oxidized and the copper(II) ion forms a highly distorted metalated species **76**.[66] Demetalation with 10% TFA in chloroform gave a ketone **77** that has a 20π electron delocalization pathway. Although the azulene protons were shifted abnormally upfield to give two triplets at 5.38 (1 H) and 5.69 ppm (2 H), and a doublet at δ = 5.16 ppm (2 H), the data were consistent with a nonaromatic species rather than a paratropic or antiaromatic macrocycle.[66] The ketone could easily be remetalated to give the related nickel(II), palladium(II) or platinum(II) complexes **78** (Scheme 18). The parent tetraarylazuliporphyrins **47** are also superior organometallic ligands readily forming nickel(II), palladium(II) and platinum(II) metallo derivatives **79**.[13]

Tropiporphyrins

The cycloheptatriene porphyrin analog "tropiporphyrin" **21** is also an aromatic porphyrinoid, although the seven-membered ring cannot so easily accommodate a reasonably planar [18]annulene substructure.[16,33] In the proton NMR spectrum of **21** in $CDCl_3$, the internal CH is shifted upfield to –7.3 ppm but the *meso*-protons are less affected than in carbaporphyrins giving two 2 H singlets at 8 and 9 ppm. The UV/Vis absorption spectrum for **21** is porphyrin-like showing a Soret band at 395 nm, but this absorption is relatively weak and broadened (Figure 8). Addition of TFA gave rise to a green monoprotonated species **80** (Scheme 19) where the Soret band shifted to 439 nm. The diatropicity of **80** was similar to the free base form, with the internal CH resonating at –6.5 ppm and the NHs giving resonances at



Scheme 18. Reactivity of tetraarylazuliporphyrins.

–4.1 (1 H) and –1.4 ppm (2 H). In addition, the *meso*-protons are shifted further downfield giving two 2 H resonances at δ = 8.5 and 9.5 ppm, but this can be primarily attributed to the positive charge that is present in **80**. It is noteworthy that fully aromatic porphyrinoids like **14** show *meso*-proton resonances at δ = 10 ppm, and the implication is that tropiporphyrin has diminished aromaticity.[16,33] Further addition of TFA leads to a nonaromatic dication **81** due to *C*-protonation of a *meso*-carbon bridge. This species can now take on tropylium ion character but, unlike the case for azuliporphyrins, this is only possible when the porphyrinoid aromaticity has been lost.[33]

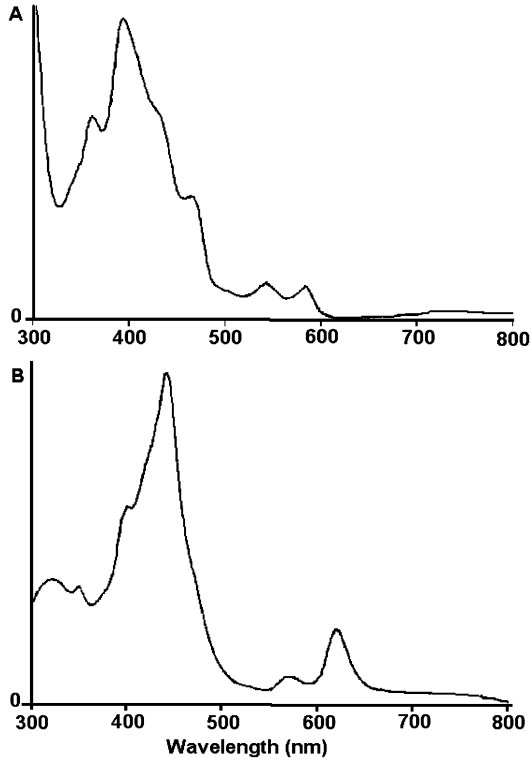
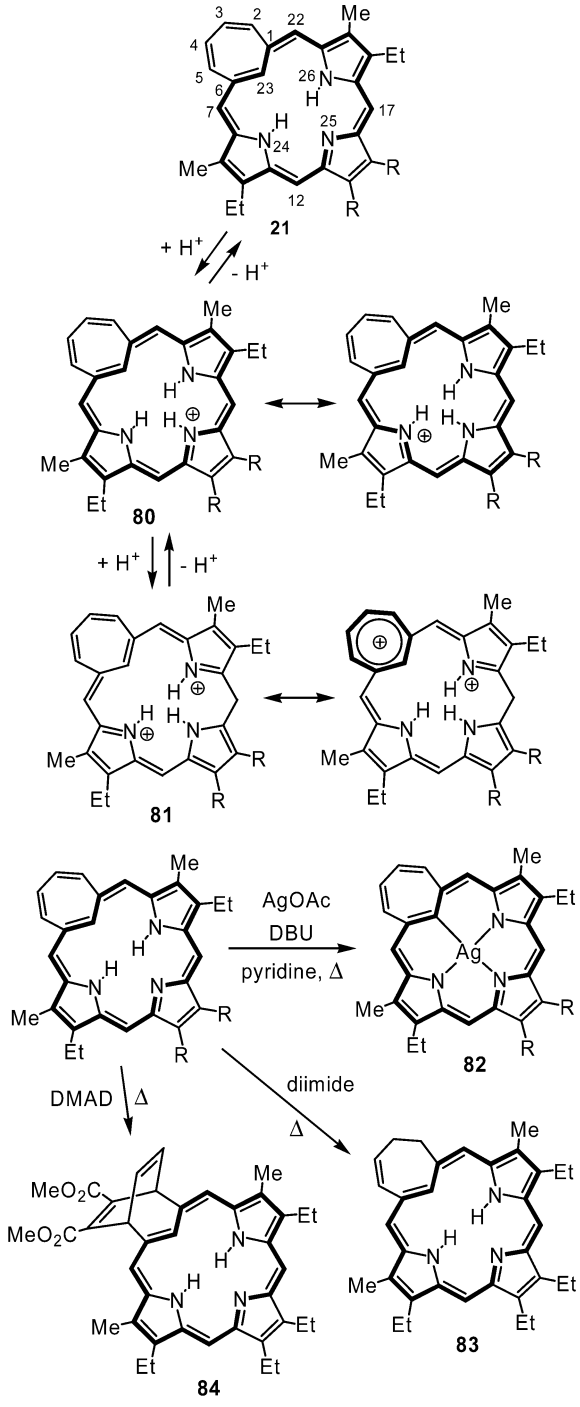


Figure 8. UV/Vis spectra of tropiporphyrin **21a**. A. Free base in 1% Et_3N/chloroform. B. Monocation **80** in trace TFA/chloroform.[16,33]

Tropiporphyrins have the same arrangement of core atoms as benzocarbaporphyrins, and can similarly act as trianionic ligands generating silver(III) complexes **82** when **21** is reacted with silver(I) acetate and DBU in refluxing pyridine (Scheme 19).[33] Although other carbaporphyrin silver complexes were generated under milder conditions, silver(III) derivatives **82** were quite stable and showed comparable diatropicity to free base tropiporphyrin. One of the silver(III) derivatives afforded crystals that were suitable for X-ray diffraction analysis and the data confirmed that the macrocycle is significantly distorted from planarity and showed that the cycloheptatriene unit is severely twisted (Figure 9).[33] Although free base tropiporphyrins **21** may have a different conformation from the silver derivatives, it is clear that the cycloheptatriene unit induces severe distortions in this case as well. Tropiporphyrin **21a** underwent a regioselective reduction with diimide to give a dihydrotropi-



Scheme 19. Protonation and chemistry of tropiporphyrins.

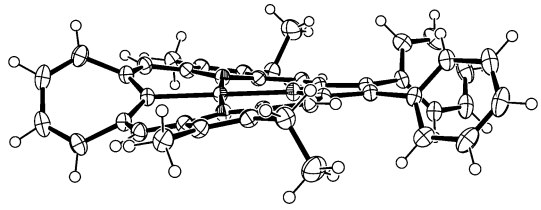


Figure 9. Single-crystal X-ray structure (ORTEP-III) of silver(III) diphenyltropiporphyrin **82b** showing the highly twisted carbocyclic ring.[16]

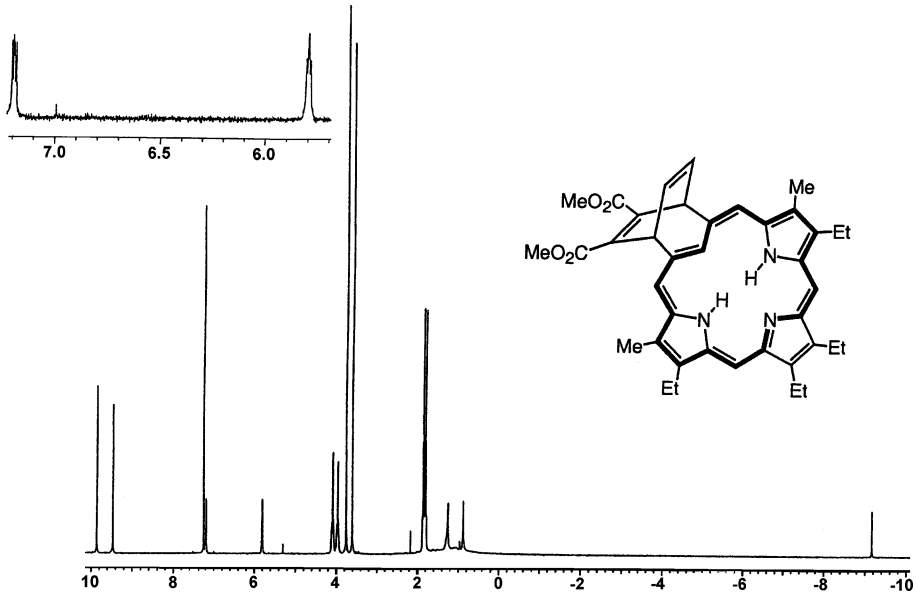
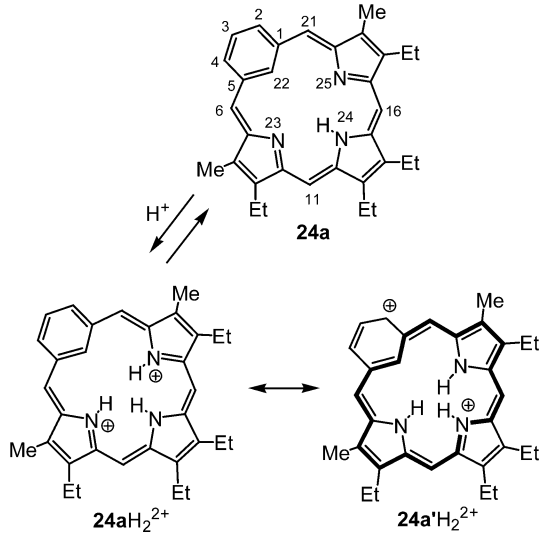


Figure 10. 400 MHz proton NMR spectrum of Diels–Alder adduct **84** in $CDCl_3$ showing the greatly enhanced diamagnetic ring current for this porphyrinoid system.[16]

porphyrin **83**, but this system showed greatly enhanced diatropic character.[33] The internal CH shifted upfield to –8.3 ppm, and equally significantly the *meso*-protons shifted downfield to give three singlets between 9.2 and 9.8 ppm. As the aromatic character of these systems is derived from the [18]annulene substructure, only this portion of the molecule needs to be reasonably planar. The reduced tropiporphyrin has a more flexible carbocyclic ring that can more easily accommodate this requirement. Neither of the two exterior double bonds in the seven-membered ring are required for aromaticity, and tropiporphyrin can potentially act as a diene in Diels–Alder reactions while retaining porphyrinoid characteristics. Reaction of **21a** with dimethyl acetylenedicarboxylate gave the unusual Diels–Alder adduct **84** with a cage-like unit replacing the cycloheptatriene ring.[33] This adduct showed a dramatically increased diatropic ring current with the internal CH shifted upfield to nearly –9.2 ppm, while the *meso*-protons gave rise to two 2 H singlets at δ = 9.47 and 9.86 ppm (Figure 10). Although no crystallographic data are available for **84**, the cage structure most likely allows the internal double bond to flatten out and optimize delocalization for the 18π electron pathway.[33] The UV/Vis spectra for **83** and **84** are also far more porphyrin-like. For instance, **84** shows a strong Soret band at δ = 408 ppm and four Q bands at 497, 533, 592 and 649 nm. Addition of TFA to solutions of **83** and **84** gave the corresponding monoprotonated species and these also showed highly diatropic properties.[33]

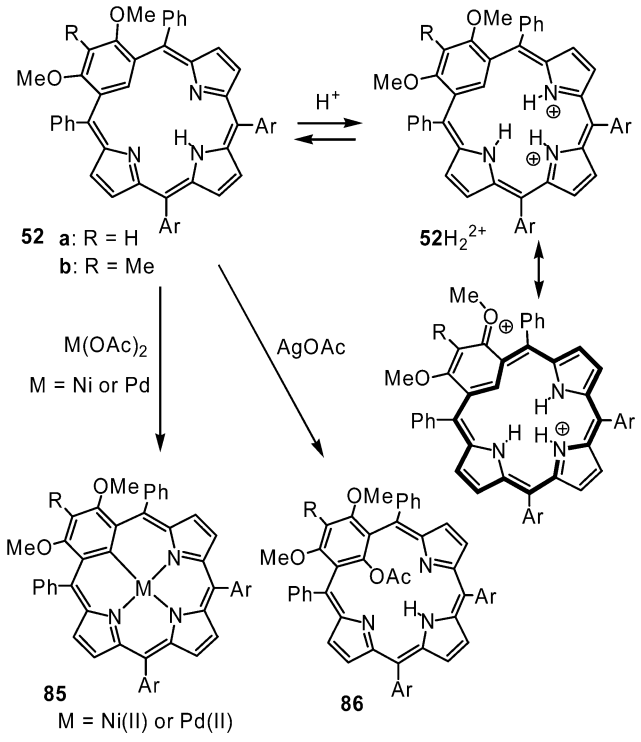
Benziporphyrins

The first example of a benziporphyrin, **24a**, was obtained by reacting isophthalaldehyde with tripyrrane **10** using the "3 + 1" methodology.[28,35] The benzene unit interupts the porphyrinoid conjugative pathway and the proton NMR spectrum for **24a** shows no indication of macrocyclic aromaticity (Scheme 20).[28] The internal CH of benziporphyrin gave a resonance at δ = 7.96 ppm, while the external benzene protons appeared at 7.75 (t, 1 H) and 7.98 ppm (2 H, dd).[28] In addition, the NH proton was downfield at 8.9 ppm, and the *meso*-protons gave two 2 H singlets at δ = 6.6 and 7.3 ppm. The UV/Vis spectrum for benziporphyrin also shows little similarity to the spectra obtained for aromatic porphyrinoids, giving a moderately strong peak at 384 nm and broad weak absorptions between 550 and 750 nm.[28] Addition of TFA gave a related dication **24a**H_2^{2+} that appears to show a small diatropic ring current.[28] The *meso*-protons shift downfield to give singlets at δ = 7.0 and 8.0 ppm, an effect that could be due to the positive charges of the macrocycle, but the internal CH



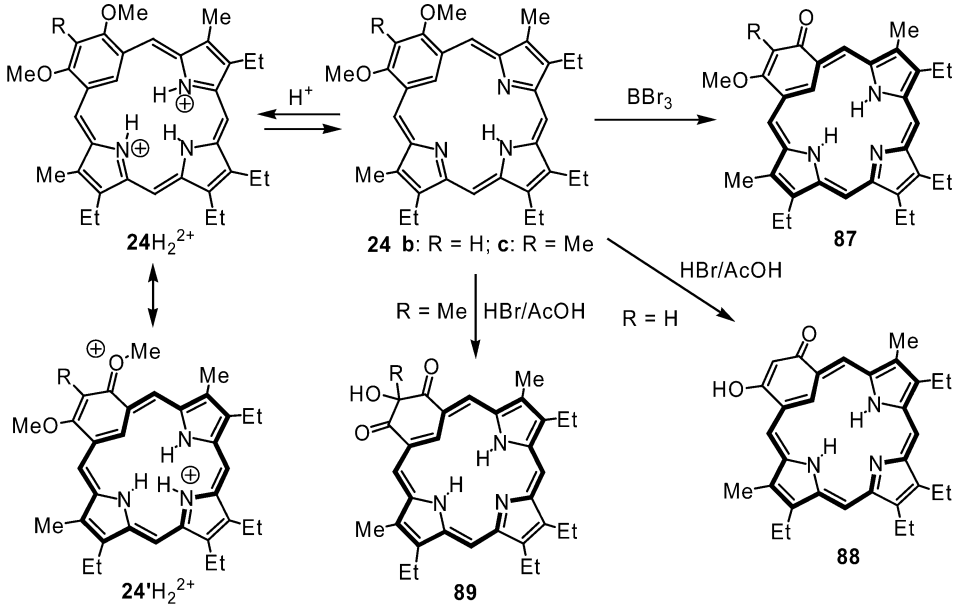
Scheme 20. Protonation of benziporphyrin.

shifts upfield to 5.24 ppm while the outer benzene protons resonate further downfield as a 1 H triplet at δ = 7.96 ppm and a 2 H doublet of doublets at δ = 7.98 ppm.[28] This small diatropic ring current can be attributed to contributions from canonical forms such as **24a′**H_2^{2+}.[28,67] The presence of electron-donating groups in dimethoxybenziporphyrins **24b** and **24c** (Scheme 3 and Scheme 22) increases this effect,[36] and similar results were subsequently noted for tetraphenyl-dimethoxy-benziporphyrins **52** (Scheme 21).[59] Although the internal CH for tetraphenylbenziporphyrin **49** (Scheme 10) gives a peak at 7.3 ppm in its proton NMR spectrum, the equivalent resonances for dimethoxybenziporphyrins **52a** and **52b** are 5.8 and 6.4 ppm, suggesting the presence of a small diatropic ring current.[59] This effect is increased for the corresponding dications, which give this resonance for **49**, **52a** and **52b** at 5.5, 3.5 and 4.7 ppm, respectively.[59] The electron-donating methoxy units stabilize canonical forms that allow for an 18π electron delocalization pathway, and this effect is more favored for the dications where this is beneficial for charge delocalization.[59] In this respect, these benziporphyrins resemble azuliporphyrins[25] and the non-aromatic tautomer of N-confused porphyrins **7b** (Figure 1),[17] although the effect is somewhat smaller. The oxygen atoms of the methoxy groups need to take on a degree of sp^2 character to donate electrons into the π-system and this requires that the methyl group lies in the plane of the benzene ring. The presence of a methyl substituent in **52b** sterically inhibits the methoxy units from taking on the required geometry and for this reason the diatropic character is diminished for **52b** compared to **52a**.[36,59]



Scheme 21. Protonation and chemistry of dimethoxybenziporphyrins.

Dimethoxybenziporphyrins **52** undergo similar chemistry to tetraphenylbenziporphyrin **49**,[57] readily forming organometallic derivatives **85** with nickel(II) acetate or palladium(II) acetate (Scheme 21).[59] Benziporphyrins **52** can also be selectively oxidized with silver(I) acetate to form the 22-acetoxy derivatives **86** (Scheme 21).[59] Interestingly, addition of TFA to solutions of **86** afforded dications that had similar diatropicity to the parent benziporphyrin dications and this demonstrates that the internal acetate group does not significantly disrupt π conjugation in these species.[59] Treatment of etio-series dimethoxybenziporphyrins **24** with boron tribromide selectively cleaved one of the ether units



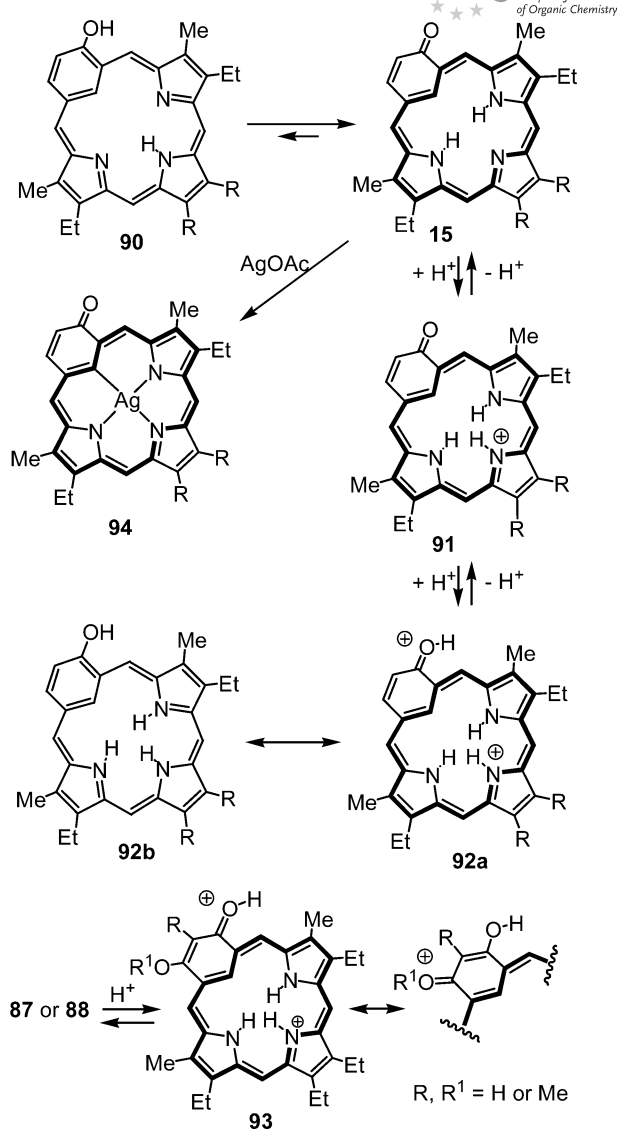
Scheme 22. Protonation of dimethoxybenziporphyrins **24b** and **24c** and their conversion to oxybenziporphyrins.

to give methoxyoxybenziporphyrins **87** (Scheme 22).[36] When **24b** was treated with HBr in refluxing acetic acid, the second methoxy unit was cleaved to give corresponding hydroxyoxybenziporphyrin **88**, but **24c** underwent an additional oxidation process to give the carbaporphyrinoid diketone **89**.[36]

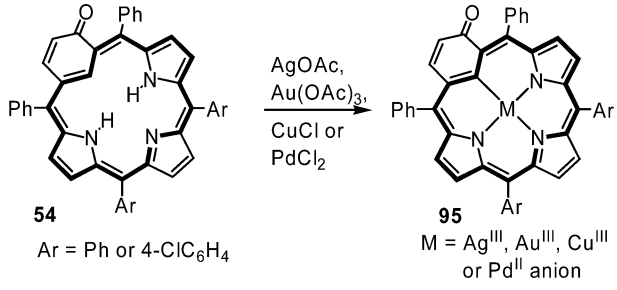
2-Hydroxybenziporphyrin **90** has been shown to favor the fully aromatic keto tautomer oxybenziporphyrin **15** (Scheme 23).[27] Unlike benziporphyrins **24**, **15** shows a highly diatropic ring current by proton NMR spectroscopy where the internal CH resonates near –7 ppm.[28] In addition, the UV/Vis spectrum for **15** is similar to true porphyrins with a strong Soret band at 428 nm ($\log_{10}\varepsilon = 5.18$), a secondary Soret band at 456 nm, and a series of four Q bands at 548, 590, 636 and 698 nm. Addition of trace amounts of TFA to solutions of **15** gives the aromatic monocation **91** but further protonation affords a dication **92** that retains only a fraction of the original diatropic character.[28] The inner CH for **92** in 10% TFA/$CDCl_3$ was shifted downfield to +1 ppm, while the NHs appeared as a broad resonance at +5.5 ppm, indicating that this species has significant phenolic character (Scheme 23). However, the related 4-hydroxy- or 4-methoxyoxybenziporphyrins **87** and **88** retain most of their diatropicity in the presence of TFA due to favorable charge delocalization in the dications **93** that does not compete with macrocyclic aromaticity (Scheme 23).[36] Oxybenziporphyrins **15** can act as trianionic ligands affording silver(III) complexes **94** under mild conditions (Scheme 23),[14] and as dianionic ligands forming palladium(II) derivatives.[68] Oxynaphthiporphyrins **17** (Scheme 3) show similar properties to **15**, again generating stable silver(III) complexes with silver(I) acetate.[14]

Tetraaryloxybenziporphyrins **54** (Scheme 24) have somewhat smaller diamagnetic ring currents and the inner CH resonates at –3 ppm for proton NMR spectra run in $CDCl_3$.[60] Addition of TFA gave the related dication which showed a greatly diminished ring current where the 22-CH resonance shifted to 4.25 ppm. These effects are attributed to the presence of *meso*-substituents that disrupt the planarity of the macrocycle and this factor is also known to play a role for azuliporphyrins,[47,55] benzocarbaporphyrins[47,55] and N-confused porphyrins.[23,69] On the other hand, tetraarylporphyrinoids **54** are superior organometallic ligands forming a series of metallo derivatives **95** with silver(III), gold(III), copper(III) and palladium(II) (Scheme 24).[60,70]

Although the hydroxyoxybenziporphyrin **38a** (Scheme 7) is a highly insoluble compound, the dication generated in TFA/$CDCl_3$ is reasonably soluble and shows a strong aromatic ring current that shifts the 22-CH resonance to –2.5 ppm.[15] The related 3-methyl-4-hydroxy-2-oxybenziporphyrin **39a** and heteroanalogs **39b**–**d** (Scheme 25) proved to be relatively unstable and are prone to oxidation. However, these compounds can be cleanly oxidized with $PhI(OAc)_2$ to give the stable highly diatropic porphyrinoids **96a**–**d**;[15] a closely related diketone **89** (Scheme 22) had been obtained in an earlier study.[36] Alternatively, reaction of **39a** with bromine in acetic acid gave the bromo-derivative **97**.[15] These porphyrinoids show enhanced ring currents and the inner CH resonance for both **96a** and **97** in $CDCl_3$ appears at –8.0 ppm. The porphyrin analogs **96a** and **97** also show strong porphyrin-like Soret bands at 417 and 400 nm, respectively, and a series of Q bands in the visible region.[15] The related oxa-, thia- and selena-porphyrinoids **96b**–**d** were also highly diatropic and showed porphyrin-like UV/Vis absorption spectra. Porphyrinoid **96a**

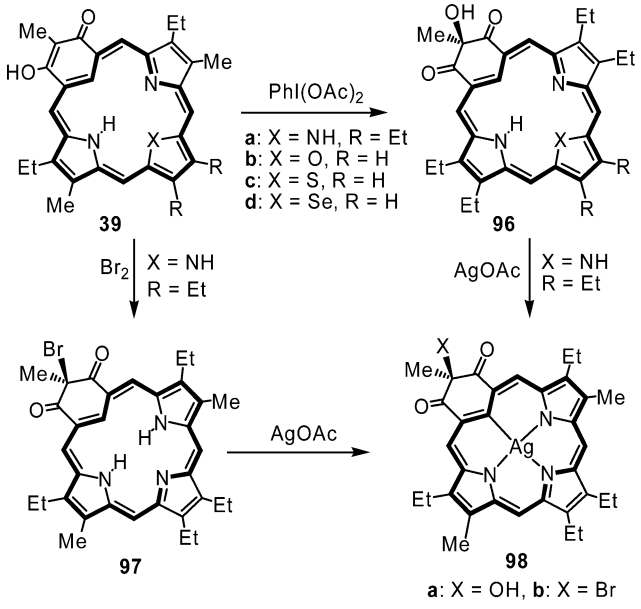


Scheme 23. Protonation and metalation of oxybenziporphyrins.



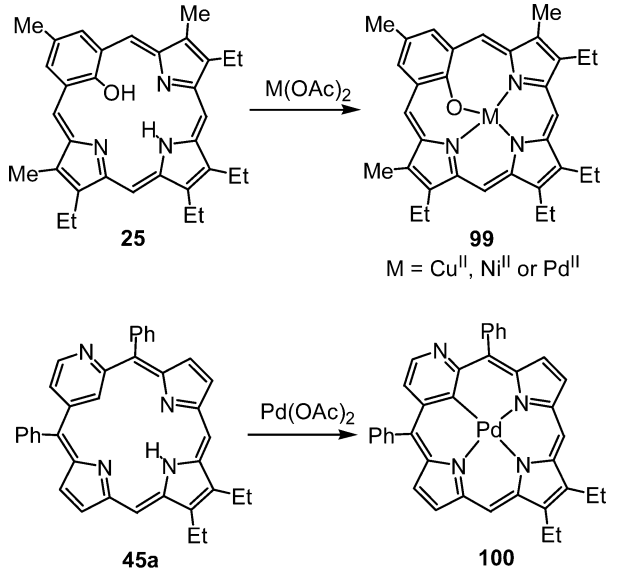
Scheme 24. Metalation of tetraaryloxybenziporphyrins.

cleanly reacted with silver acetate to give the silver(III) complex **98a** in 87% yield (Scheme 25). Bromo-derivative **97** also gave a silver complex **98b**, but in this case the yield was only 9%. This poor result was attributed to the high affinity of silver(I) ions for bromine that can lead to side reactions.[15]



Scheme 25. Benziporphyrin diketones.

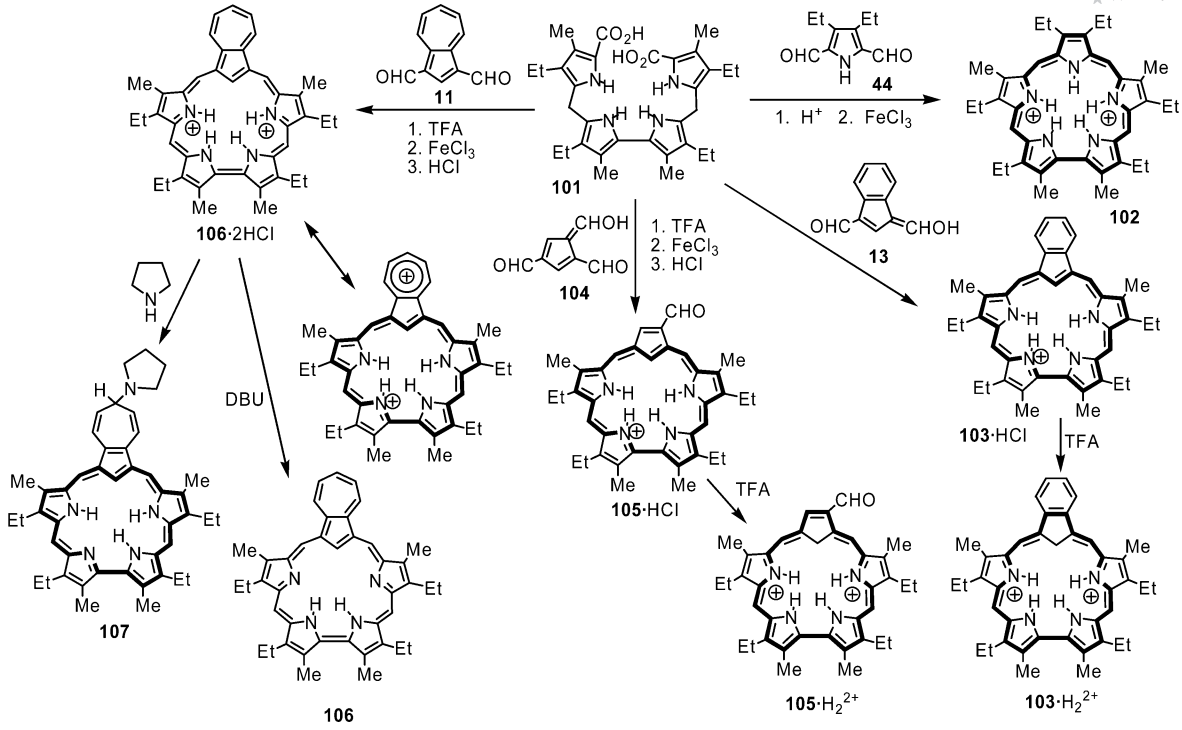
The 22-hydroxybenziporphyrin **25** (Scheme 26) only gave clear NMR spectroscopic data in TFA/$CDCl_3$, and as expected the dication has no diatropic character.[37,71] This system forms coordination complexes **99** (Scheme 26)[72] with copper(II), palladium(II) and nickel(II) salts that resemble those obtained from oxyazuliporphyrin **77** (Scheme 18).[66] A more extensive study on the metalation of a related tetraphenylbenziporphyrin has also been reported.[73] The N-confused pyriporphyrin **45a** can be considered to be a 2-azabenziporphyrin, and this system has also been shown to act as an organometallic ligand generating the palladium(II) complex **100** (Scheme 26).[30]



Scheme 26. Metalation reactions.

Expanded Carbaporphyrinoid Systems

The broad range of characteristics exhibited by carbaporphyrinoids suggests that equally interesting results could be obtained with further modifed structures. The analogs described above all have four cyclic subunits connected by single carbon bridges, but expanded porphyrinoid frameworks can also be investigated. Using a "4+1" strategy, a series of carbasapphyrins have been synthesized (Scheme 27).[74–77] Tetrapyrrole **101** reacted with pyrroledicarbaldehyde **44**, followed by oxidation with ferric chloride, to give sapphyrin **102** in 50% yield.[74–76] Reaction of **101** with the indenedicarbaldehyde **13** gave benzocarbasapphyrin **103** in 38% yield, while the tricarbaldehyde **104** gave carbasapphyrin **105** in 7–12% yield.[75,76] Azulenedicarbaldehyde **11** also reacted with **101** to give the expanded azuliporphyrinoid **106** in 35% yield.[76] Benzocarbasapphyrin **103** was isolated as a hydrochloride salt and this gave a UV/Vis spectrum with a strong Soret band at 476 nm, a secondary band at 496 nm, and a series of Q bands at 613, 669, 708 and 788 nm. The free base form was generated in 1% DBU/chloroform and this showed a weaker Soret band at 470 nm and Q bands at 596, 645, 710 and 793 nm. However, the free base carbasapphyrin was unstable and gradually degraded in solution. In 1% TFA/chloroform, a *C*-protonated dication $\mathbf{103}H_2^{2+}$ was formed (Scheme 27) with a strong Soret band at 482 and several minor peaks at higher wavelengths.[76] *C*-protonation was also observed for benzocarbaporphyrins **14**, but these only fully generate the dication in 50% TFA/chloroform solutions.[6] The dication $\mathbf{103}H_2^{2+}$ presumably forms more easily because the larger sapphyrin system can more readily delocalize the positive charge, although the larger cavity will also more easily accommodate the internal CH_2 unit. The proton NMR spectrum for $\mathbf{103}H^+$ in $CDCl_3$ showed the internal CH at –7.9 ppm and the NH resonances at –5.1 and –4.4 ppm. The diatropic ring current was also evident from the *meso*-proton resonances at δ = 11.1 and 11.3 ppm. In TFA/$CDCl_3$, $\mathbf{103}H_2^{2+}$ showed the CH_2 resonance at –3.75 and two broad 2 H singlets for the NHs at –0.56 and +0.67 ppm, while the external *meso*-protons appeared at δ = 10.37 and 11.05 ppm. Although the shifts for the dication are slightly reduced, it retains a powerful diamagnetic ring current due to the presence of a 22π electron delocalization pathway. In the monocation, the benzo unit gives two multiplets at δ = 7.96 and 9.35 ppm, but these are shifted downfield in $\mathbf{103}H_2^{2+}$ to 8.72 and 10.00 ppm, respectively. These shifts are consistent with the aromatic delocalization pathway being relocated through the fused benzo unit[76] and this result is similar to those obtained for benzocarbaporphyrins **14**.[6]



Scheme 27. "4 + 1" syntheses of sapphyrins, carbasapphyrins and an azulisapphyrin.

The formylcarbasapphyrin **105** was also isolated as the hydrochloride salt (Scheme 27) and this showed a Soret band at 480 nm and Q bands at 612, 671, 755 and 844 nm.[75,76] The proton NMR spectroscopic data for **105**H^+ demonstrated that this carbaporphyrinoid is also highly diatropic and the inner CH gave a resonance at –8.5 ppm. Addition of TFA again readily formed the dication **105**H_2^{2+}, but unlike the situation for the benzocarbasapphyrin **103**, this species showed an increased diatropic ring current. The internal CH_2 was observed at –7.1 ppm and the *meso*-protons shifted downfield to values >11 ppm. The increased diatropicity of **105**H_2^{2+} compared to **103**H_2^{2+} is unlikely to be due to the presence of an electron-withdrawing formyl group as this would destabilize the diprotonated species. However, in **103**H_2^{2+} two of the benzo-carbon atoms are used in the 22π electron delocalization pathway and this compromises some the benzene unit's aromatic character, a factor that is not relevant for carbasapphyrin dication **105**H_2^{2+}.[76] Similar trends have been noted for carbaporphyrins **14** and **19**.[6]

The azulisapphyrin **106** was isolated as a dihydrochloride salt (Scheme 27). The UV/Vis spectrum for the diprotonated species **106**H_2^{2+} somewhat resembled the free base forms of azuliporphyrins **12** (Figure 11).[76] In this case, four moderately strong bands were observed at 420, 455, 481 and 511 nm together with an additional broad band centered on 742 nm. The free base form was generated in 1% Et_3N/chloroform but this was unstable and rapidly decomposed. Addition of pyrrolidine to a solution of **106**·2HCl afforded a porphyrin-like UV/Vis spectrum with a Soret band at 480 nm and a series of Q bands, and this was attributed to the formation of a pyrrolidine adduct **107** (Figure 11).[76] However, this species was also unstable and could not be further characterized. Nevertheless, this nucleophilic addition is otherwise very similar to the ones previously noted for azuliporphyrins.[25] The proton NMR spectrum of **106**·2HCl in [D_4]methanol showed the *meso*-protons as two 2 H singlets at δ = 10.1 and 10.7 ppm, while the internal CH gave an upfield resonance at –8.2 ppm. Although these shifts are solvent dependent, they demonstrate

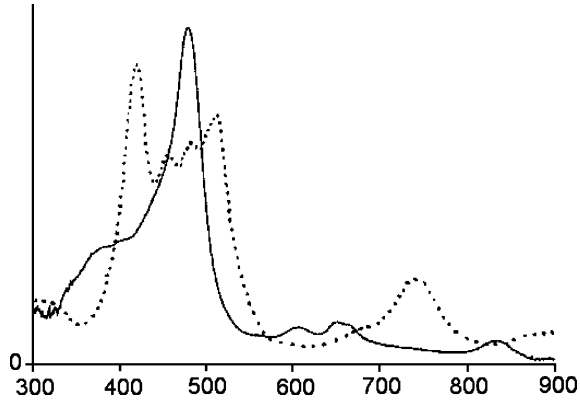
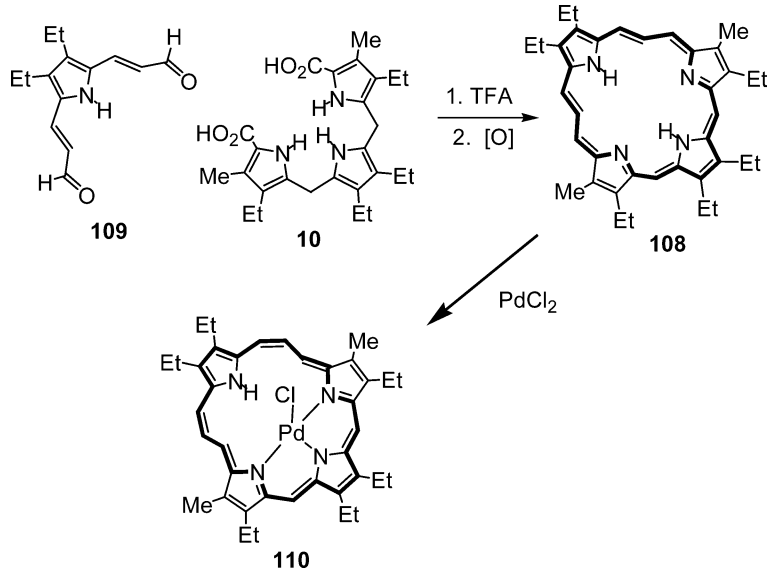


Figure 11. Dotted line: UV/Vis spectrum of azulisapphyrin **106**·2HCl in chloroform showing an absorption spectrum that closely resembles those obtained for azuliporphyrins. Bold line: azulisapphyrin **106** in 1% pyrrolidine/chloroform solution showing a porphyrin-like UV/Vis spectrum attributable to the pyrrolidine adduct **107**. This spectrum disappears after several minutes due to the instability of this species.[76]



109 10 108 110

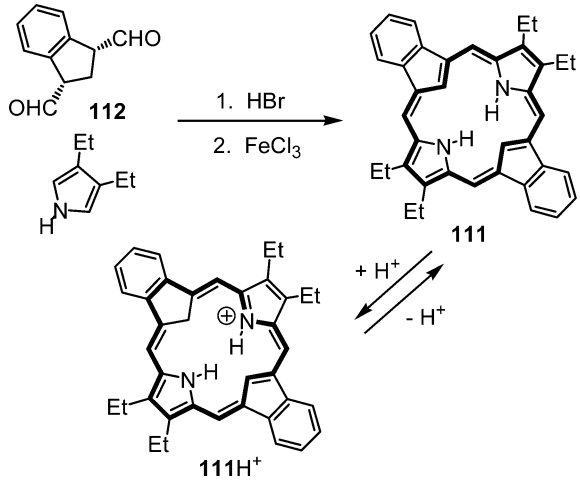
Scheme 28. Synthesis and metalation of a [22]porphyrin-(3.1.1.3).

that tropylium-containing canonical forms are major contributors for this species (Scheme 27).[76]

The presence of internal carbon atoms in carbaporphyrinoid species can also be achieved for vinylogous porphyrinoids with extended bridges between the pyrrolic subunits.[78] Recently, we reported the synthesis of a new vinylogous porphyrinoid system **108** by the "3 + 1" condensation of the stretched pyrroledicarbaldehyde **109** with tripyrrane **10** (Scheme 28).[79] The presence of two adjacent three carbon bridges in [22]porphyrin-(3.1.1.3) **108** could disrupt the planarity of this system, but the proton NMR spectrum in TFA/$CDCl_3$ shows a strong diamagnetic ring current. In particular, the middle CH of the 3 carbon bridging units is orientated inside the porphyrinoid cavity and gives a triplet at –10.2 ppm. The flanking CHs give rise to two doublets at δ = 12.7 and 12.8 ppm, while the isolated *meso*-carbon atoms gave a 2 H singlet at δ = 12.4 ppm. This system readily forms a palladium complex **110** where the macrocyclic framework has been reorganized to accommodate the metal cation. It remains to be seem whether carbon–metal bonds can also be generated in this expanded porphyrinoid system.[79]

Dicarbaporphyrins and Related Macrocycles

The formation of quatyrin, the hydrocarbon analog of the porphyrins, has not yet been accomplished but significant advances have been made on the synthesis of dicarbaporphyrins. The first example of a dicarbaporphyrin (**111**) was obtained by reacting 3,4-diethylpyrrole with diformylindane (**112**) in the presence of HBr, followed by oxidation with ferric chloride (Scheme 29).[7] The dibenzodicarbaporphyrin **111** was diatropic by proton NMR spectroscopy, showing the *meso*-protons downfield as a 4 H singlet at +9.8 ppm, while the internal CH and NH resonances were observed at –5.7 and –4.8 ppm, respectively. This system also gave a porphyrin-like UV/Vis spectrum with a Soret band at 442 nm, followed by Q bands at 522, 556, and 643 nm.[7] Addition of TFA gave a *C*-protonated cation **111**H^+ where the interior CH_2, CH and NH units gave resonances at –4.3 (2 H), –3.3 (1 H) and –0.95 ppm (2 H), respectively, again attesting to the aromatic character of this species.[7] *C*-protonation occurs easily for **111** with trace amounts of TFA, whereas this type of protonation only goes to completion in 50% TFA/chloroform for benzocarbaporphyrins **14**.[6] This is primarily due to the *C*-protonated species for **111** only bearing a single positive charge that can more easily be delocalized over the porphyrinoid system than is the case for the *C*-protonated dication derived from **14**. Unfortunately, **111** proved to be somewhat unstable and this has limited further study.[7]

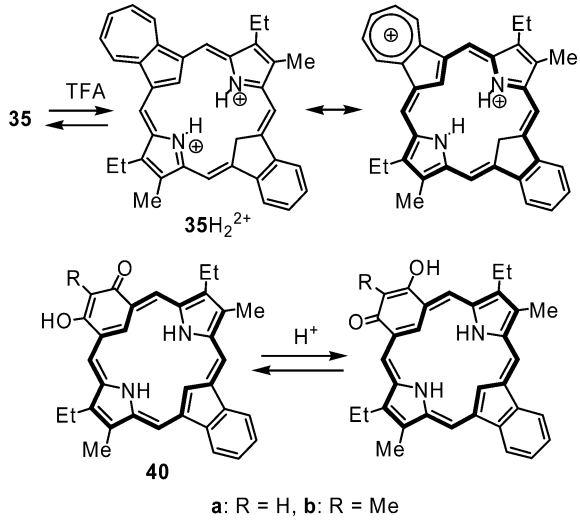


112 111 111H+

Scheme 29. Synthesis of an *opp*-dicarbaporphyrin.

Rational syntheses of *opp*-dicarbaporphyrins have also been developed and reaction of indenedicarbaldehyde **13** with carbatripyrranes (Scheme 6 and Scheme 7) gave dicar-

baporphyrinoids **35** and **40**.[42,43] Carbaazuliporphyrin **35** (Scheme 30) is significantly diatropic, showing the internal CH and NH resonances at δ = 0.52, 1.25 and 1.99 ppm for proton NMR spectra run in $CDCl_3$.[42] Addition of trace TFA gave a monocation that showed much larger shifts, and the two CHs moved upfield to –3.68 and –2.37 ppm, while the NHs were observed as a broad 2 H singlet at –1.16 ppm. Further addition of TFA gave a *C*-protonated dication with diminished diatropicity where the internal CH_2 gave a 2 H singlet at –0.9 ppm and the inner azulene proton resonated at +1.49 ppm, while the NHs were observed as a broad peak at 4.3 ppm.[42] In the more dilute solutions used to run the UV/Vis spectra, only the free base and dicationic forms could be observed.[42] Free base **35** gave broad absorptions at 494 and 675 nm, but the dication **35**H_2^{2+} gave a more porphyrin-like spectrum with a strong Soret band at 481 nm and smaller absorptions at 529, 623 and 670 nm.[42] Resorcinol-derived dicarbaporphyrins **40a** and **40b** (Scheme 30) are very polar compounds that do not dissolve well in most organic solvents and good NMR spectroscopic data could only be obtained in [D_6]DMSO.[44] The proton NMR spectra again showed that these porphyrinoids were very diatropic and **40b** showed the two internal CHs at –5.11 and –4.82 ppm.[43] The NMR spectra for both of the dicarbaporphyrinoids indicates that there was no plane of symmetry (Figure 12), suggesting that the tautomerization process shown in Scheme 30 only occurs slowly at room temperature. Addition of TFA increased the rate of tautomerization and the NMR spectroscopic data were simplified due to the apparent presence of a plane of symmetry in the macrocycle. The UV/Vis data for these dicarbaporphyrinoids were very porphyrin-like but showed considerably variations with solvent due to aggregation in solution.[43]



Scheme 30. Protonation and tautomerization of *opp*-dicarbaporphyrinoids.

The synthesis of *adj*-dicarbaporphyrinoids requires the development of a new synthetic strategy that allows for the linkage of two carbocyclic units. We are developing a new

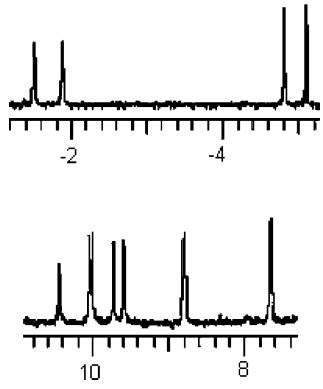
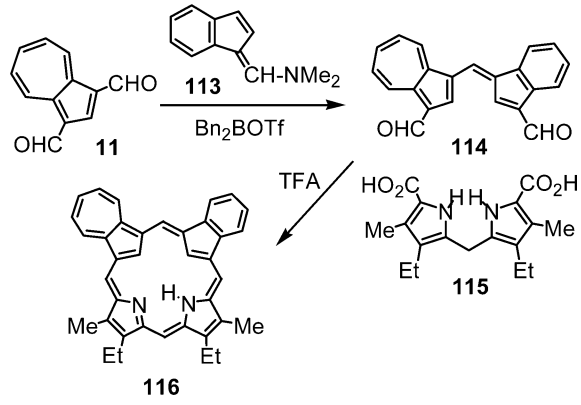


Figure 12. Upfield and downfield regions of the 400 MHz proton NMR spectrum for dicarbaporphyrin **40b** in [D_6]DMSO. The spectra illustrate both the presence of a highly diatropic ring current in this system and the lack of macrocyclic symmetry due to slow rates for tautomerization.[43]

methodology for synthesizing systems of this type using fulvene intermediates (Scheme 31). Azulenedicarbaldehyde **11** reacted with indene enamine **113** in the presence of dibutylboron triflate to give the diformylfulvene **114** and this was treated with dipyrrylmethane **115** in dichloromethane with TFA as a catalyst to give the *adj*-dicarbaporphyrinoid product **116** in 19% yield.[80] This system shows similar properties to the isomeric dicarbaporphyrinoid **36**, but **116** is a far more stable compound and this should allow the reactivity of this novel porphyrinoid to be explored in detail. Further studies are in progress to fully develop this fulvenedicarbaldehyde methodology.



Scheme 31. Synthesis of an *adj*-dicarbaporphyrinoid.

Conclusions

Efficient routes for the synthesis of carbaporphyrinoid systems have been developed. These porphyrin analogs show considerable variations in their physical, spectroscopic and chemical properties. They range from highly aromatic systems to borderline aromatic or nonaromatic macrocycles, and the proton NMR spectroscopic data for these porphyrinoids provide significant insights into the limits to porphyrinoid aromaticity.[25,59] Many of these structures

form stable organometallic derivatives under mild conditions and can act as dianionic or trianionic ligands. In the latter category, carbaporphyrins can stabilize metals in relatively high oxidation states (e.g. Ag^{III})[14,81] and may find applications as catalysts. Carbaporphyrins could potentially find medicinal applications as photosensitizers in photodynamic therapy,[9] and carbaporphyrin ketals are being investigated as possible agents for treating leishmaniasis.[64] The replacement of two pyrrole units with carbocyclic rings has proven to be more of a challenge but several dicarbaporphyrinoid systems have now been synthesized and characterized.[7,42,43,80] Further progress on the synthesis of tri- or tetracarbaporphyrinoid systems is likely to be even more challenging but may ultimately lead to the synthesis of the theoretically important hydrocarbon system quatyrin.

Acknowledgments

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