Synthesis Of Oxyquinoliziniporphyrins And Pyridoquinoliziniporphyrins

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SYNTHESIS OF OXYQUINOLIZINIPORPHYRINS AND PYRIDOQUINOLIZINIPORPHYRINS

EMMA CRAMER

138 Pages

N-confused porphyrins are porphyrin analogues that introduce a nitrogen outside of the macrocyclic cavity. Two novel N-confused type porphyrins were targeted for this study. Both syntheses use the key intermediate 4-quinolizone. Previous studies of N-confused pyriporphyrin showed that the system is nonaromatic and resembles structurally analogous benziporphyrins. However, modifications to systems of this type can introduce aromatic characteristics. The first system targeted introduced a quinolizone subunit into a porphyrin system. Quinolizone contains a thermodynamically stable amide and this unit disrupts the aromatic pathway. However, dipolar resonance contributors can potentially reinstate some aromatic character. A quinolizone dialdehyde was condensed with tripyrranes under acidic conditions, and following an oxidation step, the first example of oxyquinoliziniporphyrins were isolated. These novel structures were very stable but exhibited only weakly-aromatic properties. Protonation and metalation studies were conducted and these modifications increased the diatropic ring current.

In a related study, the introduction of an antiaromatic pyridoquinolizine unit has been investigated. A pyridoquinolizine diester was prepared from the 4-quinolizone intermediate used in the previous project. However, difficulties were encountered in converting the diester into the dialdehyde required to synthesize the macrocycle. If these problems can be overcome, it is
anticipated that pyridoquinoliziniporphyrins will possess a significant degree of aromatic
coloracter.

KEYWORDS: carbaporphyrin, N-confused porphyrin, aromatic, antiaromatic, metalation
SYNTHESIS OF OXYQUINOLIZINIPORPHYRINS AND PYRIDOQUINOLIZINIPORPHYRINS

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SYNTHESIS OF OXYQUINOLIZINIPORPHYRINS AND PYRIDOQUINOLIZINIPORPHYRINS

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E. C.
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CHAPTER I: INTRODUCTION

Porphyrins 1 are a group of heterocycles that have been studied for many years. They are composed of four pyrrole residues linked by four methine bridges, and they are found virtually everywhere in nature. They play crucial roles in the metabolism of living organisms.\textsuperscript{1,2} Small variations in these macrocycles give these compounds a range of functions. In nature, porphyrins are seen mainly as their metalated derivatives. A few examples include, protoporphyrin IX that binds with iron in hemoglobin and myoglobin to transport oxygen around the body. In higher plants, chlorophylls a and b (3) are dihydroporphyrins with a magnesium bound center that can capture photons to drive photosynthesis, and related structurally diverse chlorophylls are found in algae and photosynthetic bacteria.\textsuperscript{3} Tetrapyrrolic pigments have many other functions and are essential components of cytochromes, peroxidases and catalases.

Figure 1. Porphyrin and its naturally occurring counterparts
In addition to being essential to all life, porphyrins have many applications, one of which is photodynamic therapy (PDT).\(^4\) PDT uses porphyrins to act as photosensitizing agents that can produce reactive oxygen species, such as singlet oxygen, when exposed to light. As porphyrins preferentially accumulate in tumors, this therapy can be used in cancer treatment. Porphyrins contain highly conjugated pathways that allow them to absorb light in the UV-Visible region. This ability to absorb light in the near ultraviolet and visible regions also makes them potential photosensitizers for dye-sensitized solar cells (DSSC).\(^5\) DSSCs are semiconductors that use light absorbing dyes on the surface to create energy.\(^6\)

Porphyrins are near planar, fully conjugated aromatic compounds.\(^7\) The global aromaticity of these macrocycles comes from the presence of an \(18\pi\) electron delocalization pathway that resembles \([18]\text{annulene}\) (4). The delocalization pathway is also responsible for the electronic absorption spectra of porphyrins. Porphyrins are examples of nonbenzenoid aromatic systems, and many studies have been directed to understanding the aromatic properties of these molecules.

![Figure 2. Aromatic pathways of porphyrin and [18]annulene](image)
The aromatic characteristics of porphyrins can be directly observed using X-ray crystallography, nuclear magnetic resonance spectroscopy (NMR), and UV-visible spectroscopy. In X-ray crystallography, the bond lengths do not alternate, which implies the presence of a conjugated pathway around the macrocycle. In NMR spectroscopy, the applied magnetic field induces a diamagnetic ring current over the entire macrocycle. The ring current deshields the external protons causing them to shift downfield in proton NMR spectroscopy, and the meso-protons are commonly observed near 10 ppm. In addition, the internal protons are shielded due to the magnetic field and will therefore shift upfield in the NMR spectra (Figure 3). The internal NH peaks show up at about -4 ppm. The degree of aromaticity in porphyrins can be determined based on the magnitude of these upfield and downfield shifts.

Figure 3. Diamagnetic ring current of porphyrin
Porphyrians exhibit strong absorptions in the near UV and visible regions. Porphyrians give a strong absorption near 400 nm, called the Soret band, and a series of less intense absorptions between 480-700 that are known as the Q bands. As the Q bands fall into the visible region, they are responsible for the intense colors exhibited by the porphyrians.\textsuperscript{1} UV-visible spectroscopy is used extensively to investigate porphyrians and their analogs. Substitutions on a porphyrin system affects the number and intensity of the bands observed, and steric crowding can also modify the chromophore due to distortion of the macrocycle.

Porphyrians contain an internal cavity that possesses four nitrogen atoms, and this is key to the ability of these macrocycles to bind metal cations. Modifications of the internal cavity leads to interesting structures such as heteroporphyrins and carbaporphyrins with altered metal binding properties. Carbaporphyrins are porphyrin analogues where one or more of the nitrogens in the internal cavity have been replaced with a carbon atom.\textsuperscript{10} One way to synthesize these compounds is through the replacement of one of the pyrrole subunits. Porphyrin analogue of this type include structures that replace pyrrole with benzene \textsuperscript{5}, indene \textsuperscript{6}, and azulene \textsuperscript{7}.\textsuperscript{11-13} In addition, structures with inverted pyrrole units that place a carbon within the internal cavity and a nitrogen at the periphery, the so-called N-confused porphyrians \textsuperscript{8}, have been widely studied.\textsuperscript{13}
Carbaporphyrins have a wide range of properties and can have anything from aromatic, to nonaromatic, to even antiaromatic characteristics. For example, benziporphydin could potentially exist as tautomer 9 with an 18π electron pathway. However, synthetic samples of benziporphyrins show no indication of tautomer 9 and DFT studies indicate that it is >40 kcal/mol higher in energy.
than the nonaromatic form. In the first synthesis of a benziporphyrrins, it was suggested that tautomers 10 and 11 were formed and that these structures did not interconvert on the NMR timescale. Later reports showed that the original samples were impure, and better reaction conditions gave only one species 11. Benziporphyrin 11 showed the meso-protons at 6.57 and 7.27 ppm, while the NH resonance appeared downfield at 8.9 ppm, and the internal CH gave a broad triplet at 7.96 ppm. The outer benzene protons gave a 1H triplet at 7.75 ppm and a 2H doublet at 7.98 ppm. These results demonstrated that the arene unit maintains its aromatic character and interrupts global conjugation pathways. The chemical shifts for the internal and external protons are very similar, confirming the absence of an overall aromatic ring current. Addition of TFA to benziporphyrrin afforded a diprotonated dication 12. The proton NMR spectrum of the protonated species showed the presence of a weak diatropic ring current that shifts the internal CH upfield to 5 ppm, and the meso-protons downfield to give two 2H singlets at 6.91 and 7.94 ppm. This weak ring current was attributed to resonance contributors such as 13, or to a contribution from an 18π electron species 14.
Since it is energetically unfavorable for benziporphyrin to lose the aromaticity of the benzene subunit, it was speculated that naphthiporphyrin 15 might be more susceptible to taking on a global aromatic pathway because the resonance stabilization for a benzo-unit within naphthalene is reduced in comparison to benzene. However, the proton NMR spectrum of 15 showed no signs of a ring current. The internal CH was observed at 8.08 ppm. Napthiporphyrin was shown to favor 15 over its tautomers 16 and 17. Naphthiporphyrin could also be protonated with TFA to afford 18. This species exhibited diatropic character similar to benziporphyrin (19-
The internal CH appeared between 4.0 and 4.6, depending on the concentration of TFA. The meso-protons appeared at 7.17, 7.20, 8.29, and 8.81 ppm, values that suggest a slightly larger ring current than protonated benziporphyrin. It was suggested that resonance contributors such as 13 and 19 were favored because these aid in charge delocalization.

Figure 6. Naphthiporphyrin tautomers and resonance contributors for the protonated naphthiporphyrin dication
Benziporphyrrin reacted with nickel(II) acetate or palladium(II) acetate to give the corresponding organometallic species 21 and 22 (Scheme 1). The proton NMR spectrum for 21 showed a significant downfield shift of the meso-protons, which appeared as two 2H singlets at 7.16 and 7.48 ppm. The palladium complex showed a larger diatropic ring current with further downfield shifts to 7.35 and 7.72 ppm. Naphthiporphyrin was also metalated to give the corresponding palladium complex 23 (Scheme 2). The diatropic character of palladium naphthiporphyrin was similar to palladium benziporphyrrin and the meso-protons appeared at 7.27, 7.39, 7.64, and 8.50 ppm. Metalation of these compounds increases the diatropicity of the system but overall, these compounds still remained only weakly aromatic.

Scheme 1. Metalation of Benziporphyrrin
Scheme 2. Metalation of naphthiporphyrin

Unlike benziporphyrin and naphthiporphyrin, dimethoxybenziporphyrins 24a-b have weak diamagnetic ring currents prior to protonation. The proton NMR spectrum of 24a shows the meso-protons are shifted downfield to give two 2H singlets at 7.16 and 8.74 ppm, and the internal CH at a relatively upfield value at 5.07 ppm. In 24b, the diamagnetic ring current is not as large, and the meso-protons showed up at 6.68 and 7.84 ppm. This aromatic character is due to electron-donating methoxy groups affording dipolar resonance contributors such as 25 that have 18π-electron delocalization pathways. This electronic interaction relies on the methoxy units possessing planar sp²-hybridized oxygens. Crowding due to the presence of a methyl group on the benzene in 24b inhibits this interaction, resulting in reduced diatropicity. The aromatic properties of these dimethoxybenziporphyrins are limited because of the requirement for charge separation. Protonation of dimethoxybenziporphyrins further enhanced the aromatic properties. Addition of TFA gave dications 26, and the proton NMR spectrum of 26a showed the internal CH shifted
upfield to -0.68 ppm, while the meso-protons moved downfield to give two 2H singlets at 8.44 and 9.60 ppm. The enhanced aromatic properties of protonated dimethoxybenzoporphyrins are favored because they allow delocalization of positive charge in resonance contributors such as 27 and 28. Nevertheless, the presence of a methyl substituent between the two methoxy groups in 26b reduced the aromatic ring current and the internal CH resonance was only shifted upfield to 4.25 ppm.

Figure 7. Dimethoxybenzoporphyrins and protonated dimethoxybenzoporphyrins and their resonance contributors
As methoxy groups attached to the benzene increased the overall aromatic character due to the introduction of dipolar resonance contributors, a similar effect might be expected with a hydroxy substituent, e.g. structure 29. However, a hydroxy substituent on a benzene ring can also undergo a keto-enol tautomerization process that can generate a keto-unit while introducing a porphyrin-like 18π electron delocalization pathway. Therefore, this keto-enol tautomerization can give a fully aromatic carbaporphyrin, oxybenziporphyrin 30. The 6π arene unit is lost, but 30 has gained a carbonyl unit and a porphyrin-like 18π-electron delocalization pathway that is thermodynamically favored. Oxybenziporphyrin exhibits strong aromatic properties, including porphyrinoid UV-vis absorptions with Soret bands at 428 nm and 465 nm, and Q bands at 548, 590, 636, and 698 nm. The proton NMR spectrum showed a strong diamagnetic ring current, and the internal CH is strongly shifted upfield to -7.2 ppm. This represents an upfield shift of 15 ppm compared to benziporphyrin. The meso-protons were observed at 8.85, 8.98, 8.99 and 10.29 ppm. Protonation of 30 gave a monocation 31 and dication 32 upon a titration with TFA. The second protonation occurs on the carbonyl group to give 32, a species that has significant phenolic character due to resonance contributor 33. This disrupts the aromatic conjugation pathway and drastically reduced the aromatic ring current. The proton NMR spectrum of 32 in TFA-CDCl₃ showed the internal CH at +1.05 ppm, a downfield shift of 8 ppm compared to the free base form 30. Oxybenziporphyrin can act as a trianionic ligand and form silver (III) complexes (Scheme 3). 34b was soluble enough to give a proton NMR spectrum and the meso-protons were observed at 8.87, 9.69, 9.71, and 10.32, demonstrating that the complex retains a diatropic ring current.
similar to the free-base oxybenziporphyrin. The UV-Vis spectra of 34 was also similar to 30, giving a Soret band at 456 nm and Q bands at 524, 608, and 629 nm.

Figure 8. Hydroxybenziporphyrins, oxybenziporphyrins, protonated oxybenziporphyrins, and a phenolic resonance contributor.
Scheme 3. Metalation of oxybenziporphyrin

N-confused porphyrin 8 can be considered to be azacarbaporphyrins and can also form organometallic derivatives. An alternative family of N-confused porphyrins are N-confused pyriporphyrins that are structurally similar to benziporphyrins. N-confused pyriporphyrins 35 and 36 have been investigated where the nitrogen atom is placed at the periphery of the macrocycle. Although meso-unsubstituted pyriporphyrins are unstable, meso-substituted pyriporphyrins have been synthesized and characterized. meso-Substituted pyriporphyrin 37 is nonaromatic and the proton NMR spectrum showed the pyrrolic protons at 6.70 and 7.19 ppm, while the meso-protons appeared at 5.84 and 5.88 ppm, and the internal CH was observed at 8.98 ppm. 37 underwent a metalation reaction with palladium(II) acetate to give organometallic complex 38. The
organometallic complex underwent a protonation with TFA to form cation 39 (Scheme 4). Even upon metalation and protonation, the palladium complex remained nonaromatic.

![Diagram of organometallic complex](image)

Figure 9. N-confused pyriporphyrins

![Scheme 4](image)

Scheme 4. Metalation and protonation of N-confused pyriporphyrin

Although pyriporphyrins without aryl substituents on the pyridine subunit are unstable, an attempt was made to synthesize a dihydro-N-confused pyriporphyrin by trapping it as an aromatic tautomer 40\textsuperscript{20-22} Condensation of 2,4-pyridinedicarbaldehyde with a tripyrrane
generated a dihydroxyriporphyrin and further reaction with phenyl chloroformate afforded 42 as a fully aromatic compound. The external pyridine nitrogen reacted to form a stable carbamate structure. The UV-vis spectrum of 42 gave a Soret band at 420 nm and Q bands at 530, 567, 644, and 709 nm. The proton NMR spectrum of 42 also confirmed that this species has porphyrin-like aromaticity as the internal CH appears at -6.66 ppm, while the meso-protons shifted upfield to give 1H singlets at 8.53, 9.37, 9.49, and 9.56 ppm.

Figure 10. Pyriporphyrins

Many strategies have been developed for the synthesis of porphyrins and related systems. One of the first routes to be reported involved the synthesis of symmetrical porphyrins by the tetramerization of monopyrroles. This approach allows the preparation of tetraphenylporphyrin 43 from pyrrole (44) and benzaldehyde (Scheme 5). Similarly, reaction of 3,4-diethylpyrrole with formaldehyde produces octaethylporphyrin 45 (Scheme 5).
Scheme 5. Tetramerization of monopyrroles to produce porphyrins

Monopyrrole tetramerization works well with pyrroles that have identical 3- and 4- substituents because only one porphyrin product is formed. However, when two different substituents are present (eg. pyrrole 46), scrambling occurs to produce four different porphyrins 47-50 (Scheme 6).\textsuperscript{26-28} Stepwise routes are required to overcome this problem.
Pyrroles readily undergo electrophilic substitution at the $\alpha$-position, and this facilitates the formation of carbon-carbon bonds. MacDonald developed a ‘2+2’ condensation to prepare isomerically pure porphyrins. In this approach, dipyrrylmethane dialdehyde 51 and a dipyrrylmethane 52 are reacted in the presence of an acid catalyst to give a porphodimethene intermediate 53 that can be further oxidized to afford the fully aromatic porphyrin (Scheme 7). The main limitation to this strategy is that one of the dipyrrolic units must be symmetrical or two isomers will be formed. MacDonald and coworkers applied this route to the syntheses of naturally occurring porphyrins. For instance, reaction of 1,9-diformyldipyrrolmethane 54 with 1,9-di-
unsubstituted dipyrrylmethane 55a, or the corresponding dicarboxylic acid 55b, under acidic conditions gave mesoporphyrin IX (56) in excellent yields (Scheme 7).29

![Chemical structures](image_url)

Scheme 7. MacDonald ‘2+2’ condensations

Johnson and coworkers developed a ‘3+1’ variant of the MacDonald condensation to prepare heteroporphyrins, and this methodology was later adapted for the preparation of true porphyrins.30 In this method, tripyrrane 57 is reacted with a pyrrole dialdehyde 58 to give the corresponding porphyrin 59 (Scheme 8). Although this method still requires that one of the intermediates has a plane of symmetry in order to avoid the formation of isomers, this strategy
allows the synthesis of structures that are inaccessible by the ‘2+2’ route. Sessler and coworkers developed a convenient method for preparing tripyrranes in high yields that is now widely used in the synthesis of porphyrins.\(^{31}\)

Scheme 8. ‘3+1’ MacDonald Condensation

The first examples of tripyrranes were reported by Kenner and coworkers, but the initial route was ineffective and difficult to reproduce.\(^{32}\) Sessler and coworkers subsequently developed a practical route to symmetrical tripyrranes by reacting two equivalents of an acetoxyethylpyrrole \(60\) and one equivalent of pyrrole \(61\) under acidic conditions. The pure tripyrrane, \(62\), precipitates from solution in pure form in over 70% yield. Deprotection of the terminal benzyl ester protective groups with Pd/C under an atmosphere of hydrogen affords the corresponding dicarboxylic acids \(63\) (Scheme 9). Tripyrrane \(63\) is then ready for use in the ‘3+1’ syntheses.
Scheme 9: Synthesis of tripyrrane

Johnson and coworkers reacted tripyrranes 64 with furan or thiophene dialdehyde 65 to give heteroporphyrins 66 (Scheme 10). This route is versatile because many different dialdehydes could be reacted with tripyrranes to give alternative macrocyclic systems. Although the potential for this synthetic strategy was not initially recognized, more recent studies have demonstrated that the ‘3+1’ approach can be applied to the synthesis of diverse porphyrin analogue structures, including carbaporphyrinoid systems. ¹⁸
Scheme 10. Synthesis of heteroporphyrins

Core modification determines how these macrocycles act as ligands. Carbaporphyrins are capable of forming metal complexes, although these are comparatively limited compared to naturally occurring porphyrins. Initial attempts to metalate carbaporphyrins such as 67 with nickel(II), palladium(II), and copper(II) were unsuccessful.\textsuperscript{33,34} However later studies showed that benzocarbaporphyrin 67 can form organometallic silver(I) derivatives 68 when reacted with silver(I) acetate.\textsuperscript{35,36} The complexes maintain the diatropic nature of the original carbaporphyrins. In addition, reaction with gold(III) acetate gave the corresponding gold(III) derivatives 69 and these complexes also retained strongly diatropic characteristics (Scheme 11).\textsuperscript{36} True carbaporphyrins like 67 act as trianionic ligands, not only forming complexes with silver(III) and gold(III), but also generating organometallic derivatives with rhodium(III) and iridium(III).\textsuperscript{37}
Scheme 11. Metalation of tetraarylbenzocarbaporphyrin

Benziporphyrin and naphthiporphyrin act as dianionic ligands. As mentioned before, refluxing benziporphyrin and naphthiporphyrin with nickel(II) or palladium(II) acetate affords the corresponding metalloporphyrins (Schemes 1 and 2). Metalation is associated with the emergence of a weak diatropic ring current. Platinum(II) complexes have also been described. Reaction of tetraphenylbenziporphyrin 70 with platinum(II) chloride in benzonitrile gave platinum(II) benziporphyrin 71 (Scheme 12). 38 Benziporphyrin 70 was also reacted with nickel(II) chloride but initially afforded a chloronickel(II) complex 72. However, treatment with base gave the expected nickel(II) benziporphyrin. 39 This chemistry is reversible and addition of HCl to 73 converted it back into 72.

Tetraphenylbenziporphyrin 70 reacted with [Rh(CO)\(_2\)Cl\(_2\)] to form a six-coordinate rhodium(III) benziporphyrin 74. When 74 was dissolved in dichloromethane and placed on a silica column for 12 hours, it formed an unstable aromatic benziporphyrin 75. However, when 74 was run through an alumina column it formed rhodium(III) carbaporphyrins 76a-c instead (Scheme 12). 40 These complexes were strongly aromatic in character and the chemistry demonstrates that
the arene unit in benziporphyrin can undergo a ring contraction to form a cyclopentadiene moiety. Although these complexes were generated in low yields, and this chemistry does not provide a practical route to carbaporphyrin derivatives, important insights into the reactivity of benziporphyrins were obtained.

Scheme 12. Metalation of tetraphenylbenziporphyrin
N-confused pyriporphyrins have similar coordination cavities to those found in benziporphyrins. N-confused pyriporphyrin 77 was reacted with FeBr$_2$ and collidine in THF to give the iron(II) complex 78 (Scheme 13). Further reaction of 78 with bromine and exposure to oxygen afforded 79 with a five-coordinate iron center. Another metalation done with N-confused pyriporphyrins involved the reaction of pyriporphyrin 37 and palladium(II) acetate in acetonitrile to give the palladium(II) complex 38 (Scheme 4).

![Scheme 13. Metalation of N-confused pyriporphyrins](image)

Carbaporphyrinoid systems have been studied extensively over the last 25 years. The aromaticity, reactivity and spectroscopic properties of these systems vary considerably, and the availability of new structural analogues can further extend our understanding of these macrocycles. Although carbaporphyrins replace one or more of the internal nitrogens with carbon atoms, it is also possible to introduce heteroatoms at the exterior of the macrocycle. This is the
case for N-confused porphyrins and pyriporphyrins, but few other examples of this type are currently known.

In this thesis, extended structures related to N-confused pyriporphyrins have been explored to better understand the aromaticity and spectroscopic properties of systems of this type. Adding subunits where the heteroatom is at the exterior of the macrocycle may lead to porphyrin analogues systems with unusual properties. This approach has been applied to the introduction of a 4-quinolizone subunit to a porphyrinoid macrocycle and the aromatic properties of the new system have been assessed. Metalation and protonation of this system has also provided valuable insights. The use of 4-quinolizone to access antiaromatic pyridoquinolizones has been investigated but the formation of porphyrin analogues incorporating this antiaromatic subunit has not yet been achieved.
Pyridine analogs 81 of phthalocyanines 80 were first discovered in 1950 by Linestad (Figure 11), but the first synthesis of pyriporphyrin 82 was not attempted until 1994.\textsuperscript{11,42-45} Initially, 2,6-pyridinicarbaldehyde 83a was reacted with a tripyrrane 63a using the ‘3+1’ method in the presence of an acid catalyst, followed by an oxidation with DDQ, but the desired pyriporphyrin 82a could not be detected. Instead, several related structures were isolated. However, the related hydroxy pyridine dialdehyde 83b gave excellent yields of the aromatic porphyrin 82b (Scheme 14). The ‘3+1’ method was also used to prepare other pyriporphyrins.\textsuperscript{42,20} Modifications to N-confused pyriporphyrin systems are of interest since these drastically alter the aromatic properties. The addition of an embedded N-confused type subunit within structure 84 was targeted for this investigation due to the potential for this system to exist in several tautomeric forms. In principle, this porphyrinoid may be prepared from dialdehyde 85 (Scheme 15). The thermodynamic stability of the amide component of the quinolizone unit could block the 18π electron conjugation pathway in oxyquinoliziniporphyrs 84, but dipolar resonance contributors might reinstate a degree of macrocyclic aromaticity (Scheme 16).
Figure 11. Phthalocyanine 80 and dipyrrithalocyanine 81

\[
\begin{align*}
\text{80} & \quad \text{M} = \text{2H, Cu, Ni} \\
\end{align*}
\]

Scheme 14. Syntheses of pyriporphyrins
Scheme 15: Retrosynthetic analysis of oxyquinolizinoporphyrins

Scheme 16. Oxyquinolizinoporphyrins resonance contributors
In addition to dialdehyde 85, the key intermediates for the synthesis of oxyquinoliziniporphyrins are tripyrranes (see Scheme 9). Tripyrranes can be prepared from pyrrolic precursors. The central pyrrole unit is derived from 3,4-diethylpyrrole 61. This is prepared using the Barton-Zard reaction from ethyl isocyanoacetate 86. Reaction of glycine ethyl ester hydrochloride 87 and triethylamine and refluxing methyl formate gave N-formylglycinate 88. This was dehydrated with phosphorous oxychloride and triethylamine at 0 °C to afford the desired isocyanide 86 (Scheme 17).

Scheme 17. Synthesis of ethyl isocyanoacetate 86

The second precursor needed for the Barton Zard synthesis is acetoxy nitrohexane 89. This was prepared in two steps from propionaldehyde 90. Reaction of 1-nitropropane with 90 in the presence of potassium fluoride gave the corresponding nitro alcohol 91. Subsequent treatment of 91 with acetic anhydride under acidic conditions afforded the desired nitroacetate 89 (Scheme 18).

Scheme 18. Preparation of acetoxy nitrohexane 89
Condensation of acetoxy nitrohexane 89 and ethyl isocyanoacetate 86 in the presence of two equivalents 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) produced pyrrole ester 92. Crude 92 was then decarboxylated with sodium hydroxide in ethylene glycol at 190 °C to form diethylpyrrole 61 (Scheme 19).

Scheme 19. Preparation of 3,4-diethylpyrrole 61

Two different tripyrranes were used in these studies, and these were prepared from benzyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate 60a and benzyl 5-acetoxymethyl-4-butyl-3-methylpyrrole-2-carboxylate 60b. In order to synthesize these pyrrolic precursors, ethyl esters 93a-b were first prepared in a Knorr-type condensation of diethyl aminomalonate 94 and β-diketones 95a-b in the presence of acetic acid (Scheme 20).

Scheme 20. Knorr-type synthesis of ethyl 4-ethyl-3,5-dimethyl-2-carboxylate 93a and ethyl 4-butyl-3,5-dimethyl-2-carboxylate 93b
Diethyl aminomalonate 94 and diketones 95a-b were prepared from commercially available diethyl malonate and 2,4-pentanedione, respectively. Diethyl malonate and sodium nitrite were reacted in the presence of acetic acid to give diethyl oximinomalonate 96. Reduction with hydrogen over 10% Pd/C then gave diethyl aminomalonate 94 (Scheme 21).

\[
\text{EtO} \quad \text{EtO} \\
\text{NaNO}_2 \quad \text{AcOH} \\
\text{EtO} \quad \text{EtO} \\
96 \\
\text{H}_2 \quad \text{Pd/C} \\
\text{EtO} \quad \text{EtO} \\
94
\]

Scheme 21. Preparation of diethyl aminomalonate 94.

Alkylation of 2,4-pentanedione with ethyl iodide or n-butyl bromide and potassium carbonate in refluxing acetone gave the required diketones 95a and 95b (Scheme 22).

\[
\text{R} \quad \text{R} \\
\text{EtI or BrBu} \quad \text{K}_2\text{CO}_3 \\
95 \text{a. R = Et} \\
\text{b. R = Bu}
\]

Scheme 22. Synthesis of 3-ethyl-2,4-pentadione 95a and 3-butyl-2,4-pentadione 95b

Pyrrole 93a,b were transesterified with benzyl alcohol in the presence of sodium benzyloxide to give the corresponding benzyl esters 97a,b. Selective oxidation with lead tetraacetate in acetic acid then gave acetoxymethyl pyrroles 60a-b. (Scheme 23).
Scheme 23. Synthesis of 60a-b

Two equivalents of acetoxyethylpyrroles 60a-b were reacted with 3,4-diethylpyrrole (61) in refluxing ethanol with acetic acid to give the corresponding tripyrrane dibenzyl esters 62a-b. Hydrogenolysis of the benzyl esters over Pd/C afforded the required dicarboxylic acid derivatives 63a-b (Scheme 24).

Scheme 24. Synthesis of tripyrranes 63a-b

In order to synthesize the targeted oxyquinolinizinoporphyrin system, dialdehyde 85 was required. This was prepared in four steps from 2-picoline (98). Lithium diisopropylamide (LDA) was added to a solution of 2-picoline and diethyl carbonate in THF at -78°C. The reaction was quenched with saturated ammonium chloride and following workup, ethyl 2-pyridylacetate (99) was isolated (Scheme 25).
Scheme 25. Synthesis of ethyl 2-pyridylacetate 99

The next step in this synthesis involves the formation of the quinolizone subunit. Ethyl 2-pyridylacetate was heated with diethyl ethoxymethylene malonate (100) at 180 °C for 8 hours to give diester 101. The esters were cleaved by refluxing 101 in HCl to give 4-quinolizone 102 (Scheme 26).46

Scheme 26. Synthesis of 4-quinolizone 103

The final step involves the functionalization of the quinolizone subunit to introduce the dialdehyde units. 4-Quinolizone 102 undergoes a Vilsmeier-Haack reaction with POCl₃ and DMF, and the reaction mixture was quenched with aqueous sodium carbonate to give quinolizone dialdehyde 85 (Scheme 27).47
Scheme 27. Synthesis of 4-quinolizone-1,3-dicarbaldehyde 85

The ‘3+1’ MacDonald condensation was carried out by reacting tripyrranes 63a-b with dialdehyde 85 in the presence of trifluoroacetic acid under dilute conditions. The condensation was followed by an oxidation with DDQ, to give the desired porphyrin products 84a-b in 36-54% yields (Scheme 28). The porphyrins were purified by column chromatography on alumina followed by recrystallization with dichloromethane and hexanes to give dark green solids.

Scheme 28. Synthesis of carbaporphyrins 84a,b.
The proton NMR spectrum of the free base forms could only be obtained for 84b due to the poor solubility of 84a. The free base of 84b in CDCl₃ showed that this species has some aromatic character and the meso-protons showed up at 7.62, 7.63, 8.13, and 9.04 ppm (Figure 12). The internal protons of this species did not resolve in the proton NMR spectra, but the downfield shifts for the meso-protons indicate that a diatropic ring current is present.
Porphyrrins 84a-b were also assessed using UV-Vis spectroscopy. In 1% TEA 84a showed strong absorption bands at 332, 406, 462, and 489 nm as well as some broad bands absorption bands around 610 and 655 nm. A similar absorption spectrum was obtained for 84b.
The spectra closely resemble the electronic absorption spectra for azuliporphyrins, a well-studied class of carbaporphyrinoids that also exhibit intermediary aromatic characteristics (Scheme 29). Addition of 1 equivalent of TFA afforded a new species that was attributed to the monoprotonated species 103a (Scheme 30). At higher concentrations of TFA, a new species corresponding to a dication 104a was formed and this gave a very strong Soret-type band at 464 nm, and more pronounced Q bands at 638, 667, and 711 nm (Figure 13). This spectrum is more typical of an aromatic porphyrinoid species.

Figure 13. UV-vis spectra of oxyquinolizinoporphyrin 84a in 1% triethylamine-dichloromethane (free base, blue line) and 10% TFA-dichloromethane (104a, red line)
As expected oxyquinoliziniporphyrin 84b gave a similar electronic spectra to 84a.

In 1% TEA, 84b showed strong absorption bands at 332, 409, 462, and 489 nm and broader absorption bands at 610 and 656 nm. Upon addition of TFA, a strong absorption emerged at 464 nm and Q bands appeared at 638, 667, and 713 nm (Figure 14).
Protonation of benziporphyrins has been shown to give a degree of macrocyclic aromaticity. The UV-vis spectra for these carbaporphyrinoid systems indicates that this is also true for this structure. The proton NMR spectra were also consistent with the formation of a strongly aromatic structure.
Scheme 30. Protonation of oxyquinoliniziporphyrins 84a-b

The proton NMR spectra of the protonated species 104b in CDCl₃ with 1 drop of TFA showed the presence of a strong diatropic ring current (Figure 15). The meso-protons shifted downfield to 10.32, 10.03, 9.17 and 9.14 ppm, while the internal CH appeared upfield at -2.82 ppm. The proton NMR spectra could also be obtained for 104a due to an increase in solubility upon protonation. This spectrum was similar to 104b with the meso-protons 9.18, 9.21, 10.05, and 10.35 ppm, and the internal CH at -2.93 ppm (Figure 16). This increase in aromatic character can be attributed to electron-donation from the quinolizone nitrogen to give resonance contributors such as 105 with 18π electron delocalization pathways (Scheme 31).
Figure 15. Downfield region of the $^1$H NMR spectra for oxyquinolizinoporphyrin 84b (top spectrum) and dication 104b (bottom spectrum)
Figure 16. $^1$H NMR spectrum of protonated oxyquinoliziniporphyrin dication 104a in TFA-CDCl$_3$

Scheme 31. Resonance contributors for oxyquinoliziniporphyrin dications.
Metalation of quinoliziniporphyrins \textbf{84a-b} were also investigated with palladium(II) and nickel(II) acetate. Oxyquinoliziniporphyrins \textbf{84a-b} were reacted with palladium(II) acetate in acetonitrile and chloroform for 15-60 min. The reaction mixtures were diluted with dichloromethane and washed with water. The solution was evaporated, and the residue was purified by column chromatography. Recrystallization from chloroform-hexanes gave the palladium complexes in 32\% yield for \textbf{106a} and 85\% for \textbf{106b}. Reaction with Ni(OAc)$_2$ gave the corresponding nickel complexes, and these were purified by chromatography to give \textbf{107a} in 72\% yield and \textbf{107b} in a 43\% yield (Scheme 32).

\begin{center}
\includegraphics[width=\textwidth]{scheme32.png}
\end{center}

\textbf{Scheme 32. Metalation of oxyquinoliziniporphyrins 84a-b}

The proton NMR spectra of the palladium and nickel complexes showed that metalation effects the degree of aromaticity in these ring systems. The proton NMR spectrum of palladium(II) complex \textbf{106a} showed the \textit{meso}-protons at 8.29, 8.35, 8.66, and 9.62 ppm. The \textit{meso}-protons of nickel complex \textbf{107a} did not shift as far downfield and showed up at 7.96, 7.98, 8.04, and 8.96 ppm (Figure 17).
Figure 17. Downfield region of the $^1$H NMR of palladium oxyquinoliniporphyrin 106a (top spectrum) and nickel quinoliziniporphyrin 107a (bottom spectrum).
The proton NMR spectra of the metal complexes of 84b gave similar results (Figure 18). In palladium complex 106b, the *meso*-protons shifted substantially downfield compared to free base 84b appearing at 7.95, 8.25, 8.36, and 9.51 ppm. In nickel complex 107b the shifts were less drastic, and the corresponding resonances appeared at 7.97, 8.00, 8.16, and 8.96 ppm. Nevertheless, these values are still significantly downfield compared to 104b. The enhanced aromatic character of the palladium complexes may be due to the macrocycle taking on a more planar conformation. Nickel(II) porphyrinoids are often distorted to enable coordination to the relatively small nickel(II) cation.
Figure 18. Downfield region of the $^1$H NMR spectra of oxyquinolinizinoporphyrin 84b (middle spectrum), palladium complex 106b (top spectrum), and nickel complex 107b (bottom spectrum)
The metalated derivatives were also examined by UV-vis spectroscopy to further assess the changes to these systems. The Ni(II) and Pd(II) complexes of 84a show significant differences in their absorption spectra. Palladium complex 106a showed strong absorptions at 347, 409, and 465 nm, with an equally strong broad absorption at 649 nm. Nickel complex 107a gave strong absorptions at 359 and 411 nm with a shoulder at 472 nm, and an equally strong absorption at 661 nm (Figure 19).

Figure 19. UV-vis spectra of oxyquinoliniziporphyrin 84a (black line), palladium(II) complex 106a (red line), and nickel(II) complex 107a (blue line)

The metal complexes of oxyquinoiliziniporphyrin 84b gave similar UV-Vis spectra. Palladium(II) complex 106b showed strong absorptions at 347, 408, and 466 nm and an equally strong broad absorption at 648 nm, while nickel(II) complex 107b gave strong absorptions
at 357 and 416 nm, with a shoulder at 454 nm, and an equally strong broad absorptions at 660 nm (Figure 20).

Figure 20. UV-vis spectra of oxyquinoliziniporphyrin 84b (black line), palladium(II) complex 106b (red line), and nickel(II) complex 107b (blue line)

Oxyquinoliziniporphyrins give further insights into the reactivity and aromatic properties of carbaporphyrins. Specifically, N-confused pyriporphyrins are relatively unstable and nonaromatic but the structurally related quinolizone subunit considerably alters the properties of this system. This investigation showed that structures of these types can have global aromatic character, especially upon protonation as seen in the proton NMR spectra and UV-Vis spectra. The proton NMR spectra of the protonated oxyquinoliziniporphyrins show internal CH peaks at ca. -2.9 ppm, and the UV-vis spectra give Soret and Q bands similar to those seen in aromatic
porphyrinoid systems. Metalation of oxyquinolizinoporphyrins was also achieved, and the introduction of a metal cation also enhanced the aromatic characteristics of these structures.
Experimental:

Melting points are uncorrected. NMR spectra were recorded using a 400 or 500 MHz NMR spectrometer and were run at 302 K unless otherwise indicated. $^1$H NMR values are reported as chemical shifts $\delta$, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak) and coupling constant ($J$). Chemical shifts are reported in parts per million (ppm) relative to CDCl$_3$ ($^1$H residual CHCl$_3$ singlet $\delta$ 7.26 ppm, $^{13}$C CDCl$_3$ triplet $\delta$ 77.23 ppm) or d$_6$-DMSO ($^1$H residual d$_5$-DMSO pentet $\delta$ 2.49 ppm, $^{13}$C d$_6$-DMSO septet $\delta$ 39.7 ppm) and coupling constants were taken directly from the spectra. NMR assignments were made with the aid of $^1$H-$^1$H COSY, HSQC, DEPT-135 and nOe difference proton NMR spectroscopy. 2D-NMR experiments were performed using standard software.

Ethyl 2-Pyridylacetate (99) A mixture of 2-picoline (9.9 mL) and diethyl carbonate (36.3 mL) was treated with LDA (105 mL) in THF (100 mL) at -78°C for 3 hours under nitrogen. The mixture was then cooled to room temperature and stirred for another 30 min. The solution was treated with ammonium chloride (50 mL) in water (200 mL) and the aqueous layer was extracted with diethyl ether. The ether was dried with magnesium sulfate, filtered, and the filtrate was evaporated under reduced pressure to yield ethyl 2-pyridyl acetate (13.492 g, 81.7% yield) as a dark brown liquid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.12 (3H, t, $J$ = 7.1 Hz, OCH$_2$CH$_3$), 3.71 (2H, s, py-CH$_2$), 4.05 (2H, q, $J_{HH}$ = 7.1 Hz, OCH$_2$CH$_3$), 7.00-7.05 (1H, m, py), 7.15-7.18 (1H, m, py), 7.47-7.53 (1H, m, py), 8.39-8.43 (1H, m, 6-H).
Diethyl 4-quinolizone-1,3-dicarboxylate (101) A mixture of ethyl 2-pyridylacetate (3.404 g, 20.0 mmol) with diethyl ethoxymethylenemalonate (4.325 g, 20.0 mmol) was heated at 180 °C for 8 hours while distilling off ethanol. After 8 hours, a minimal amount of hot acetone was added, and the solution was allowed to cool. Recrystallization with acetone yielded the quinolizone diester (3.691 g, 63.8%) as brown-yellow crystals, mp 123-124°C (lit mp46 123-129°C). \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 1.43 (6H, m, 2 x OCH\(_2\)C\(_3\)H), 4.40 (2H, q, J = 7.1 Hz, OCH\(_2\)CH\(_3\)), 4.44 (2H, q, J = 7.1 Hz, OCH\(_2\)CH\(_3\)), 7.36 (1H, dt, J = 1.4, 6.9 Hz), 7.85-7.90 (1H, m) (7,8-H), 9.17 (1H, s, 2-H), 9.36-9.39 (1H, m, 9-H), 9.52-9.55 (1H, m, 6-H). \(^1^3\)CNMR (125 MHz, CDCl\(_3\)): δ 14.38, 14.44 (2 x OCH\(_2\)CH\(_3\)), 61.04, 61.18 (2 x OCH\(_2\)CH\(_3\)), 117.0 (7 or 8-C), 124.4 (9-C), 130.4 (6-C), 136.7 (7 or 8-C), 144.4 (2-C), 147.0, 155.5, 164.8, 165.4.

4-Quinolizone (102) A solution of diethyl 4-quinolizone-1,3-dicarboxylate (2.550 g, 8.8 mmol) in 50 mL of concentrated hydrochloric acid was refluxed for one hour. The solution was neutralized over ice with solid potassium carbonate. The solution was extracted with ether until it was no longer colored. The ether was dried, filtered, and evaporated under reduced pressure. The residue was columned on silica with 70:30 toluene-ethyl acetate to give the product as the second broad yellow fraction (0.787 g, 62.4%) as large yellow crystals, mp 72-73°C (lit mp46 71-72°C). \(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 6.57-6.62 (2H, m, 1,9-H), 6.93-6. (1H, m 7-H), 7.27-7.31 (1H, m), 7.41-7.44 (1H, m, 3-H), 7.62 (1H, dd, J = 7.6 Hz, 2-H), 9.09 (1H, m, 6-H). \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): δ 103.1, 109.1 (1,9-C), 114.9 (7-C), 125.4 (3-C), 127.3 (6-C), 129.2 (8-C), 138.0 (2-C), 142.7, 158.6.
4-Quinolizone-1,3-dicarbaldehyde (85) POCl₃ (12 mL) was added dropwise to DMF (12 mL) over ice and kept under 10 °C throughout addition. 4-Quinolizone (0.700 g, 4.8 mmol) was added and the solution was stirred at 50 °C for three hours. After the three hours, the solution was poured over ice, and neutralized with sodium carbonate and a solid formed. The solid was filtered to afford the dialdehyde (0.860 g, 89.1%) as a yellow powder mp 239-240 °C (lit mp47 231-232 °C). ¹H NMR (400 MHz, CDCl₃): δ 7.60 (1H, dt, J = 1.3, 7.0 Hz), 8.12-8.16 (1H, m) (7,8-H), 8.63 (1H, s, 2-H), 9.58-9.60 (1H, m, 9-H), 9.62-9.65 (1H, m, 6-H), 9.93 (1H, s, 1-CHO), 10.42 (1H, s, 3-CHO).

¹³CNMR (125 MHz, CDCl₃): δ 120.1 (7 or 8-C), 124.7 (6-C), 130.4 (9-C), 140.5 (7 or 8-C), 145.1 (2-C), 180.46, 180.56, 188.1, 188.6.

Oxyquinoliziniporphyrin (84a) In a pear-shaped flask, tripyrrane dicarboxylic acid 63 (261 mg, 0.578 mmol) was dissolved in TFA (2 mL) and stirred under nitrogen for 10 minutes. Dichloromethane (200 mL) was added followed by dialdehyde 85 (119mg, 0.591 mmol). The flask was covered in aluminum foil to protect the reactants from light, and the solution was stirred overnight under nitrogen. After stirring overnight, the solution was neutralized with triethylamine and DDQ (135 mg, 0.594 mmol) was added. After stirring for an additional hour, the resulting solution was washed with water, and the organic layer was evaporated under reduced pressure. The residue was purified by recrystallization with chloroform and hexanes to give the carbaporphyrinoid product (165.0 mg, 54.9%) as a dark green powder, mp >300°C. UV-vis (1% Et₃N-CH₂Cl₂): λ max/nm (log ε): 332 (4.55), 406 (4.56), 462 (4.62), 489 (4.71), 565 (sh,
3.79), 610 (4.17), 655 (4.42), 714 (sh, 3.80). UV-vis (1 eq TFA-CH₂Cl₂): λₘₐₓ/nm (log ε): 334 (4.54), 355 (4.52), 397 (4.47), 440 (sh, 4.63), 465 (4.95), 485 (sh, 4.39), 595 (sh, 3.96), 637 (4.62), 699 (sh, 4.16), 761 (sh, 4.17). UV-vis (10% TFA-CH₂Cl₂): λₘₐₓ/nm (log ε): 368 (4.58), 399 (4.58), 440 (sh, 4.72), 464 (5.10), 482 (sh, 4.67), 638 (4.44), 667 (4.48), 711 (sh, 4.01).

1H NMR (500 MHz, CDCl₃-TFA): δ -2.93 (1H, s, 22-H), -1.36 (1H, br s, NH), 1.55 (6H, dt, J = 1.5, 7.7 Hz, 13,14-CH₂CH₃) 1.68 (6H, q, J = 7.9 Hz, 9,18-CH₂CH₃), 3.27 (3H, s, 8-CH₃), 3.31 (3H, s, 19-CH₃), 3.64-3.71 (4H, m, 13,14-CH₂CH₃) 3.75 (4H, q, J = 7.9 Hz, 9,18-CH₂CH₃), 8.03 (1H, dt, J = 1.5, 6.9 Hz, 3²-H), 8.70-8.75 (1H, m, 4²-H), 9.18 (1H, s, 9.21 (1H, s) (11,16-H), 9.36 (1H, d, J = 8.8 Hz, 4¹-H), 10.03-10.04 (1H, m, 3¹-H), 10.05 (1H, s, 6-H), 10.35 (1H, s, 21-H).

13C NMR (125 MHz, CDCl₃-TFA): δ 10.6, 10.8 (13,14-CH₃), 14.8, 14.9 (13,14-CH₂CH₃), 15.9 (9,18 CH₂CH₃) 18.50, 18.54, 18.59, 18.60 (9,13,14,18-CH₂CH₃), 92.6, 93.2 (11,16-C), 110.0, 110.2, 111.5 (6-C), 112.4, 112.5, 114.74 (21-C), 115.0, 117.0, 118.3 (22-C), 122.3 (3²-C), 126.4 (4¹-C), 134.4 (3¹-C), 138.2, 139.0, 140.0, 144.3 (4²-C), 147.42, 147.44, 151.0, 159.8. HRMS (ESI) m/z: [M+H]⁺ calcd for C₃₅H₃₆N₄O 529.2967; found 529.2958.

**Palladium(II) Complex 106a.** Oxyquinolinizinoporphyrin 84a (10.2 mg, 0.019 mmol) and palladium(II) acetate (11.2 mg, 0.050 mmol) in chloroform (5 mL) and acetonitrile (5 mL) were refluxed for 2 hours. The residue was cooled, chloroform (20 mL) was added, and the mixture was washed with water and evaporated under reduced pressure. The residue was columned on grade 3 neutral alumina and the product eluted with dichloromethane. A dark green band was collected and recrystallized with dichloromethane and hexanes to give the palladium complex as a dark
green solid (3.9 mg, 32.0%), mp >300°C. UV-vis (CH$_2$Cl$_2$): $\lambda_{\text{max}}$/nm (log $\varepsilon$): 347 (4.39), 409 (4.41), 444 (sh, 438), 465 (4.46), 605 (sh, 4.13), 649 (4.43), 705 (sh, 3.93). $^1$H NMR (500 MHz, CDCl$_3$): 1.56-1.67 (12H, m, 9,13,14,18-CH$_2$C$_3$H$_3$), 2.87 (3H, s), 3.13 (3H, s) (11,16-CH$_3$), 3.35-3.45 (8H, m, 9,13,14,18-CH$_2$C$_3$H$_3$), 7.14-7.18 (1H, m, 3$_2$-H), 7.53-7.57 (1H, m, 4$_2$-H), 8.29 (1H, s), 8.35 (1H, s) (11,16-H), 8.47-8.51 (1H, m, 4$_1$-H), 8.66 (1H, s, 6-H), 9.32-9.35 (1H, m, 3$_1$-H), 9.62 (1H, s, 21-H). $^{13}$C NMR (partial data from HSQC, CDCl$_3$): 11.1 (8,19-CH$_3$), 16.1, 17.4 (9,13,14,18-CH$_2$C$_3$H$_3$), 19.4 (9,13,14,18-CH$_2$C$_3$H$_3$), 95.9 (11,16-C), 113.3 (6-C), 116.0 (3$_2$-C), 118.4 (21-C), 123.7 (4$_1$-C), 130.9 (3$_1$-C), 135.3 (4$_2$-C). HRMS (ESI) m/z: [M]$^+$ calced for C$_{35}$H$_{34}$N$_4$OPd 632.1767; found 632.1741.

**Nickel (II) complex (107a)** Oxyquinoliziniporphyrin 84a (25.0 mg, 0.047 mmol) and nickel(II) acetate (25.5 mg, 0.102 mmol) in chloroform (12 mL) and acetonitrile (12 mL) were refluxed for 1 hour. The residue was cooled, chloroform (20 mL) was added, and the mixture was washed with water and evaporated under reduced pressure. The residue was columned on grade 3 neutral alumina, eluting dichloromethane. A dark green band was collected and evaporated down to give the nickel complex as a dark green solid (20.0 g, 72.2%), mp >300°C. UV-vis (CH$_2$Cl$_2$): $\lambda_{\text{max}}$/nm (log $\varepsilon$): 359 (4.33), 411 (4.43), 472 (sh, 4.33), 620 (sh, 4.18), 661 (4.40). $^1$H NMR (500 MHz, CDCl$_3$): 1.44-1.52 (6H, m, 9,13,14,18-CH$_2$C$_3$H$_3$), 1.54-1.60 (6H, m, 9,18-CH$_2$CH$_3$ or 13,14-CH$_2$CH$_3$), 2.60 (3H, s, 8-CH$_3$), 2.85 (3H, s, 19-CH$_3$), 3.18-3.34 (8H, m, 9,18-CH$_2$CH$_3$ and 13,14-CH$_2$CH$_3$), 6.75-6.80 (1H, m, 3$_2$-H), 7.03-7.08 (1H, m, 4$_2$-H), 7.73-7.77 (1H, m, 4$_1$-H), 7.96 (1H, s), 7.98 (1H, s) (11,16-H), 8.04 (1H, s, 6-H), 8.96 (1H, s, 21-H), 8.97-9.00 (1H, m, 3$_1$-H). $^{13}$C
NMR (125 MHz, CDCl₃-TFA): δ 10.7, 11.0 (8,19-CH₃), 16.30, 16.35, 17.25, 17.31 (9,13,14,18-CH₂CH₃), 18.98, 19.02, 19.08, 19.14 (9,13,14,18-CH₂CH₃), 94.9, 95.1 (11,16-C), 111.4 (6-C), 113.7, 114.7 (21-C), 123.3 (4¹-C), 129.8 (3¹-C), 134.4 (4²-C), 137.6, 139.0, 140.9, 141.49, 141.55, 142.9, 143.6, 143.9, 147.9, 148.1, 149.9, 151.1, 151.3, 162.0. HRMS (ESI) m/z: [M]+ calcd for C₃₅H₃₄N₄O₉Ni 584.2086; found 584.2072.

**Oxyquinoliziniporphyrin (84b)** In a pear-shaped flask, tripyrrane dicarboxylic acid 63b (103 mg, 0.202 mmol) was dissolved in TFA (1 mL) and stirred under nitrogen for 10 minutes. Dichloromethane (100 mL) was added, followed by dialdehyde 85 (50 mg, 0.249 mmol) The flask was covered in aluminum foil to protect the solution from light, and the mixture stirred overnight under nitrogen. The solution was neutralized with triethylamine and DDQ (70 mg, 0.308 mol) was added and the mixture stirred for an additional hour. The resulting solution was washed with water and the organic layer evaporated under reduced pressure. The residue was purified on a grade 3 neutral alumina column, eluting with a 70:30 mixture of toluene and acetone. The product was collected as a dark green band. Recrystallization with acetone and hexanes gave the oxyquinoliziniporphyrin (43 mg, 0.074 mmol, 36.4%) as a dark green powder, mp >300°C. UV-vis (1% Et₃N-CH₂Cl₂): λ_max/nm (log ε): 332 (4.60), 364 (sh, 4.45), 409 (4.58), 462 (4.67), 489 (4.76), 558 (sh, 3.76), 610 (4.21), 656 (4.47). UV-vis (5 eq TFA-CH₂Cl₂): λ_max/nm (log ε): 348 (4.58), 361 (4.59), 440 (sh, 4.71), 465 (5.07), 484 (sh, 4.62), 640 (4.57), 670 (4.47). UV-vis (10% TFA-CH₂Cl₂): λ_max/nm (log ε): 368 (4.61), 439 (sh, 4.77), 464 (5.16), 482 (sh, 4.72), 638 (4.48), 667 (4.52), 713 (sh, 4.05). ¹H NMR (500 MHz, CDCl₃): δ 1.02-1.06 (6H, m, 2 x CH₂CH₂CH₂CH₃),
1.51-1.62 (10H, m, 2 x CH₂CH₂CH₂CH₃ and 13,14-CH₂CH₃), 1.82-1.91 (4H, m, 2 x CH₂CH₂CH₂CH₃), 2.69 (3H, s, 8-CH₃), 2.84 (3H, s, 19-CH₃), 3.15 (4H, q, J = 8.0 Hz, 2 x CH₂CH₂CH₂CH₃), 3.28 (4H, q, J = 7.6 Hz, 13,14-CH₂CH₃), 7.00-7.05 (1H, m, 3²-H), 7.38-7.42 (1H, m, 4²-H), 7.62 (1H, s), 7.63 (1H, s) (11,16-H), 8.13 (1H, s, 6-H), 8.39 (1H, d, J = 9.1 Hz, 4¹-H), 9.04 (1H, s, 21-H), 9.29-9.32 (1H, m, 3¹-H). ¹³C NMR (125 MHz, CDCl₃): δ 11.1 (C-8), 11.2 (C-19), 14.13, 14.14 (2 x CH₂CH₂CH₂CH₃), 16.67, 16.69 (2 x 13,14-CH₂CH₃), 18.55 (2 x 13,14-CH₂CH₃), 22.80, 22.84 (2 x CH₂CH₂CH₂CH₃), 25.27, 25.29 (2 x CH₂CH₂CH₂CH₃), 33.81, 33.85 (2 x CH₂CH₂CH₂CH₃), 93.0, 93.2 (11,16-H), 109.8 (6-C), 114.2 (21-C), 117.4 (3²-C), 122.5 (4¹-C), 130.6 (3¹-C), 134.8 (4²-C), 139.1, 139.4, 139.7, 139.8, 141.0, 142.0, 147.4, 160.7. ¹H NMR (500 MHz, CDCl₃-TFA): δ -2.82 (1H, s, 22-H), -1.12 (1H, br s, NH), 1.03 (6H, overlapping triplets, 2 x CH₂CH₂CH₂CH₃), 1.51-1.60 (4H, m, 2 x CH₂CH₂CH₂CH₃), 1.69 (6H, overlapping triplets, 13,14-CH₂CH₃), 1.86-1.94 (4H, m, 2 x CH₂CH₂CH₂CH₃), 3.26 (3H, s), 3.30 (3H, s) (8,19-CH₃), 3.61-3.68 (4H, m, 13,14-CH₂CH₃) 3.72 (4H, overlapping quartets, 2 x CH₂CH₂CH₂CH₃), 8.00-8.04 (1H, m, 4²), 8.69-8.74 (1H, m, 3²-H), 9.14 (1H, s), 9.17 (1H, s) (11/16-H), 9.36 (1H, d, J = 8.5 Hz, 4¹-H), 10.01-10.05 (2H, m, 3¹-H/6-H), 10.32 (1H, s, 21-H). ¹³C NMR (125 MHz, CDCl₃): δ 11.79, 11.97 (8,9-CH₃), 14.00, 14.02 (2 x CH₂CH₂CH₂CH₃), 16.8 (13,14-CH₂CH₃), 19.6 (2 x CH₂CH₂CH₂CH₃), 22.98, 23.00 (2 x CH₂CH₂CH₂CH₃), 25.9 (13,14-CH₂CH₃), 33.67, 33.71 (2 x CH₂CH₂CH₂CH₃), 93.8, 94.3 (11,16-C), 112.6 (6-C), 113.3, 113.5, 115.8 (21-C), 116.1, 119.6 (22-C), 123.1 (4²-C), 127.4 (4¹-C), 135.3 (3¹-C), 139.3, 139.50, 139.55, 140.0, 143.2, 143.8, 144.3, 144.5, 144.7, 145.1 (3²-C), 152.0, 160.9. HRMS (ESI) m/z: [M+H]⁺ calcd for C₃₉H₄₄N₄O 585.3593; found 585.3571.
**Palladium (II) Complex (106b)** Oxyquinoliziniporphyrin 84b (10.1 mg, 0.017 mmol) and palladium(II) acetate (10.2 mg, 0.045 mmol) in chloroform (5 mL) and acetonitrile (5 mL) were stirred for 10 min at room temperature. Chloroform was added (20 mL) and solution washed with water and evaporated under reduced pressure. The residue was columned on a grade 3 neutral alumina column, eluting with dichloromethane. A dark green band was collected and recrystallized with dichloromethane and hexanes to give the palladium complex as a dark green solid (11.8 mg, 84.9%), mp >300°C. UV-vis (CH$_2$Cl$_2$): $\lambda_{\text{max}}$ (log e): 347 (4.60), 408 (4.62), 445 (sh, 4.59), 466 (4.67), 602 (sh, 4.32), 648 (4.65), 708 (sh, 4.16). $^1$H NMR (500 MHz, CDCl$_3$): 1.07 (3H, t, $J$ = 7.5 Hz), 1.11 (3H, t, $J$ = 7.4 Hz) (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 1.57-1.64 (2H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 1.64-1.72 (8H, m, CH$_2$CH$_2$CH$_2$CH$_3$ and 13,14-CH$_2$CH$_3$), 1.93 (2H, p, $J$ = 7.4 Hz), 2.03 (2H, p, $J$ = 7.5 Hz) (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 2.52 (3H, s, 8-CH$_3$), 3.05 (3H, s, 19-CH$_3$), 3.29 (2H, t, $J$ = 7.7 Hz, CH$_2$CH$_2$CH$_2$CH$_3$), 3.38-3.47 (6H, m, CH$_2$CH$_2$CH$_2$CH$_3$ and 13,14-CH$_2$CH$_3$), 6.64-6.70 (1H, m, 3$^2$-H), 6.79-6.85 (1H, m, 4$^1$-H), 7.53-7.58 (1H, m, 4$^1$-H), 7.95 (1H, s, 6-H), 8.25 (1H, s), 8.36 (1H, s) (11/16-H), 8.83-8.87 (1H, m, 3$^1$-H), 9.51 (1H, s, 21-H). $^{13}$C NMR (125 MHz, CDCl$_3$): 10.8, 11.5 (8,19-C), 14.34, 14.40 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 17.50, 17.55 (13,14-CH$_2$CH$_3$), 19.24, 19.28 (13,14-CH$_2$CH$_3$), 23.14, 23.17 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 25.74, 25.91 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 34.10, 34.26 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 95.7, 96.3 (11,16-C), 109.8, 113.5 (6-C), 114.6, 116.6 (3$^2$-C), 118.3 (21-C), 122.7 (4$^1$-C), 129.9 (3$^1$-C), 135.0 (4$^2$-C), 136.8, 137.7, 138.1, 139.0, 140.1, 141.7, 142.48, 142.56, 147.3, 147.5, 148.08, 148.20, 149.2, 149.4, 160.2. HRMS (ESI) m/z: [M]$^+$ calcd for C$_{39}$H$_{44}$N$_4$OPd 688.2393; found 688.2379.
Nickel(II) Complex (107b) Oxyquinolizinoporphyrin 84b (11.2 mg, 0.019 mmol) and nickel(II) acetate (13.8 mg 0.055 mmol), in chloroform (5 mL) and acetonitrile (5 mL) were refluxed for 1 hour. The solution was cooled to room temperature and diluted with chloroform (20 mL). The solution was washed with water and solvent evaporated under reduced pressure. The residue was run through a grade 3 neutral alumina column eluting with dichloromethane. A dark green band was collected and evaporated under reduced pressure to give the nickel complex (5.6 mg, 42.7%) as a dark green solid, mp >300 °C. UV-vis (CH$_2$Cl$_2$): $\lambda_{\text{max}}$ (log $\varepsilon$): 357 (4.32), 416 (4.39), 454 (sh, 4.32), 620 (sh, 4.15), 660 (4.34). $^1$H NMR (500 MHz, CDCl$_3$): 1.00-1.05 (6H, m, 2 x CH$_2$CH$_2$CH$_2$CH$_3$), 1.52-1.59 (10H, m, 2 x CH$_2$CH$_2$CH$_2$CH$_3$ and 13,14-CH$_2$CH$_3$), 1.81-1.90 (4H, m, 2 x CH$_2$CH$_2$CH$_2$CH$_3$), 2.68 (3H, s, 19-CH$_3$), 2.82 (3H, s, 8-CH$_3$), 3.16-3.24 (4H, m, 13,14-CH$_2$CH$_3$), 3.24-3.31 (4H, m, 2 x CH$_2$CH$_2$CH$_2$CH$_3$), 6.99-7.03 (1H, m, 4$_{2}$-H), 7.35-7.40 (1H, m, 3$_{2}$-H), 7.97 (1H, s), 8.00 (1H, s) (11,16-H), 8.05-8.09 (1H, m, 4$_{1}$-H), 8.16 (1H, s, 6-H), 8.96 (1H, s, 21-H), 9.14-9.17 (1H, m, 3$_{1}$-H). $^{13}$C NMR (125 MHz, CDCl$_3$): 11.0 (8-CH$_3$), 11.2 (19-CH$_3$), 14.3 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 17.16, 17.21 (13,14-CH$_2$CH$_3$), 19.00, 19.03 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 23.05, 23.07(2 x CH$_2$CH$_2$CH$_2$CH$_3$), 25.48, 25.53 (13,14-CH$_2$CH$_3$) 29.9, 33.92, 33.97 (2 x CH$_2$CH$_2$CH$_2$CH$_3$), 95.27, 95.39 (11,16-C), 111.3 (6-C), 113.9, 114.7 (21-C), 117.1 (4$_{2}$-C), 123.6 (3$_{2}$-C), 130.1 (3$_{1}$-C), 134.4 (4$_{1}$-C), 138.1, 139.7, 139.8, 140.2, 141.9, 143.0, 143.9, 148.1, 148.3, 150.0, 151.4, 151.8, 152.0, 162.1. HRMS (ESI) m/z: [M]$^+$ calcd for C$_{39}$H$_{44}$N$_4$ONi 640.2712; found 640.2684.
Porphyridionoquinoliziporphyrin are important examples of nonbenzenoid aromatic compounds. German chemist Erich Hückel proposed a theory to predict when a compound is aromatic. This stated that a cyclic structure must be continuously conjugated, planar, and have $4n+2 \pi$ electrons, in order for it to be considered aromatic. Aromatic compounds are generally very stable compounds and possess diamagnetic ring currents that can be observed in proton NMR spectroscopy. In addition, Hückel determined that antiaromatic systems also need to be planar and continuously conjugated, but possess $4n \pi$ electrons (in both cases, $n$ is an integer). Antiaromatic compounds are known to be relatively unstable and include cyclobutadiene (108), the cyclopentadienyl cation (109), pentalene (110), and pyridoquinoline (111) (Figure 21). Unlike the diamagnetic ring current seen in aromatic compounds, antiaromatic compounds have a paramagnetic ring current, which may be observed by proton NMR spectroscopy, where the external protons will be shifted upfield and the internal protons will be shifted downfield. This is the reverse of what is seen in aromatic compounds. Antiaromatic systems are intriguing and the effect of incorporating a subunit of this type into a porphyrin-like framework would provide insights into the properties of porphyrinoid structures. Antiaromatic tricycle 111 can be synthesized from the common intermediate 4-quinolizone (102) and its incorporation into a porphyrinoid system has been investigated.
In order to synthesize a porphyrin-like system 112 that incorporates 111 using the ‘3+1’ method, a related dialdehyde intermediate 113 is required. The synthesis of this key intermediate might be possible starting with quinolizone 102. Initially, 4-quinolizone was refluxed in phosphorus oxychloride for 30 minutes. The resulting solid was dissolved in water, perchloric acid was added, and the perchloric acid salt 114 was obtained. The chloroquinolizininium cation is prone to nucleophilic aromatic substitution reactions, including with malonate derived enolate ions. Treatments of perchloric salt with the tert-butyl ethyl malonate and sodium hydride resulted in
nucleophilic addition and loss of chloride to give \( t \)-butyl ethyl 4H-quinolizin-4-malonate (115) (Scheme 34).\(^{49}\)

\[
\begin{array}{c}
\text{N} \\
\text{POCl}_3 \\
\text{HClO}_4 \\
\end{array} \quad \begin{array}{c}
\text{N} \\
\text{Cl} \\
\text{ClO}_4^- \\
\end{array} \quad \begin{array}{c}
\text{EtO}_2\text{C} \\
\text{CO}_2\text{t-Bu} \\
\end{array} \quad \begin{array}{c}
\text{N} \\
\text{CO}_2\text{Et} \\
\end{array}
\]

Scheme 34. Synthesis of \( t \)-butyl ethyl 4H-quinolizin-4-malonate (115)

Compound 115 was reacted with hydrogen chloride gas in toluene to cleave the \( \text{tert} \)-butyl group and this gave ethyl 4H-quinolizin-4-ylideneacetate (116) (Scheme 35).

\[
\begin{array}{c}
\text{EtO}_2\text{C} \\
\text{CO}_2\text{t-Bu} \\
\end{array} \quad \begin{array}{c}
\text{EtO}_2\text{C} \\
\text{CO}_2\text{Et} \\
\end{array}
\]

Scheme 35. Synthesis of ethyl 4H-quinolizin-4-ylideneacetate (116)

In order to construct the tricyclic pyridoquinolizine system, 116 was refluxed with ethyl propiolate and potassium carbonate in nitrobenzene for 8 minutes. This involves a cycloaddition, followed by an oxidation to give the fully conjugated ring system. Purification by column chromatography on grade 3 neutral alumina, eluting with 80:20 toluene-hexanes, diethyl pyrido[2,1,6-de]quinolizine-1,3-dicarboxylate (117) was isolated in 42% yield (Scheme 36)
Now that 117 was available, it is necessary to convert the ester units into aldehydes. A one step reaction was attempted using DIBAL-H but this proved to be unsuccessful. When the reaction was conducted at low temperatures or even room temperature, no conversion was observed and starting material was isolated. The low reactivity of the ester moieties can be attributed to the electron donating nitrogen atom. Attempts to fully reduce the esters to the alcohols with lithium aluminum hydride (LiAlH₄), followed by an oxidation with pyridinium chlorochromate, also proved to be unsuccessful due to the instability of the dialcohol species. In fact, the presence of electron withdrawing carbonyl groups appear to be essential for stabilizing the antiaromatic system. Hence, an alternative route was explored using the nonaromatic dihydro species 118. This can be prepared from 116 and ethyl propiolate when the reaction is carried out at 160 °C for one minute (Scheme 37).
Scheme 37. Synthesis of 3a,4-dihydropyrido[2,1,6-de]quinolizine 118

It had been hoped that 118 would be more stable than 117. However, all attempts to convert 118 into a dialdehyde species were unsuccessful. Direct conversion of 118 to dialdehyde species 113 with DIBAL-H failed. Similar to what was seen with 117, at low temperatures and room temperature there was no reaction and starting material was collected. Attempts to reduce 118 with LiAlH₄, followed by an oxidation with PCC, were also unsuccessful and led to decomposition. Further attempts to prepare dialdehyde 113 from 116 are currently under investigation.
**Experimental:**

Melting points are uncorrected. NMR spectra were recorded using a 400 or 500 MHz NMR spectrometer and were run at 302 K unless otherwise indicated. \(^1\)H NMR values are reported as chemical shifts \(\delta\), relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak) and coupling constant \(J\). Chemical shifts are reported in parts per million (ppm) relative to CDCl\(_3\) (\(^1\)H residual CHCl\(_3\) singlet \(\delta 7.26\) ppm, \(^{13}\)C CDCl\(_3\) triplet \(\delta 77.23\) ppm) or d\(_6\)-DMSO (\(^1\)H residual d\(_5\)-DMSO pentet \(\delta 2.49\) ppm, \(^{13}\)C d\(_6\)-DMSO septet \(\delta 39.7\) ppm) and coupling constants were taken directly from the spectra. NMR assignments were made with the aid of \(^1\)H-\(^1\)H COSY, HSQC, DEPT-135 and nOe difference proton NMR spectroscopy. 2D-NMR experiments were performed using standard software.

**4-Chloroquinolizinylum Perchlorate (114)** 4-Quinolizone (102) (1.995 g, 0.014 mol) in phosphorus oxychloride (4ml) was stirred on a steam bath for 1 hour. The solid was filtered off and dissolved in water. Perchloric acid was added to the ice-cold solution until the perchlorate salt fully precipitated. The precipitate was suction filtered and vacuum dried overnight to give bright yellow crystals.

**tert-Butyl ethyl 4H-quinolizin-4-ylidenemalonate (115)** tert-Butyl ethyl malonate (3.420 g, 0.018 mol) in distilled THF (30 mL) was stirred under nitrogen, powdered sodium hydride (1.089 g in mineral oil) was added in portions, and the mixture heated at 50 °C for 3 hours. 4-Chloroquinolizininium perchlorate (114) (2.396 g 0.009 mol) was added in small portions to the ice
cooled solution, keeping the temperature below 20 °C, and the resulting solution was refluxed overnight. The solvent was evaporated under reduced pressure. The residue was dissolved in chloroform and filtered. Any remaining solid was unreacted perchlorate. The filtrate was concentrated and loaded onto a grade 3 alumina column. An orange band eluted with chloroform, the solvent evaporated and the residue recrystallized from acetone to give tert-butyl ethyl 4-quinolizin-4-ylidenemalonate as an orange powder (1.581g, 55.0%), mp 171-172 °C (lit. mp\textsuperscript{49} 187-188 °C). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): 1.25 (3H, t, $J = 7.1$ Hz OCH\textsubscript{2}CH\textsubscript{3}), 1.40 (9H, s, OCCH\textsubscript{3}), 4.16 (2H, q, $J = 7.1$ Hz OCH\textsubscript{2}CH\textsubscript{3}), 7.46 (1H, dt, $J = 1.6$, 7.0 Hz, 7-H), 7.64-7.68 (1H, m, 3-H), 7.76-7.81 (1H, m, 8-H), 7.88-7.92 (1H, m, 2-H), 7.93-7.97 (1H, m, 2-H), 8.10 (1H, dd, $J = 1.5$, 8.0 Hz, 1-H), 9.01-9.04 (1H, m, 6-H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): 15.1 (OCH\textsubscript{2}CH\textsubscript{3}), 29.1 (OCCH\textsubscript{3}), 58.7 (OCH\textsubscript{2}CH\textsubscript{3}), 77.6, 119.3 (7-C), 119.8 (3-C), 126.3 (9-C), 129.2 (1-C), 132.3 (8-C), 135.3 (2-C), 142.9, 155.1, 167.2, 168.2.

**Ethyl 4H-quinolizin-4-ylidenenacetate (116)** Hydrogen chloride gas was passed through a rapidly stirring solution of tert-butyl ethyl 4H-quinolizin-4-ylidenenacetate (1.081g, 3.45 mmol) in toluene (40 mL) for 30 minutes. The gas flow was stopped, and the solution was heated at 50 °C until the reaction no longer produced CO\textsubscript{2} gas (50 min.) The mixture was cooled to 0 °C, the toluene was decanted off and dichloromethane (40 mL) was added. The mixture was added to an ice salt bath and 6M NaOH was added (2 mL) slowly. The organic layer was separated, and the water was extracted with more dichloromethane (20 mL). The combined organic layers were evaporated down to give a bright red residue (0.670 g, 91%) that formed crystals with refrigeration, mp 45-
46 °C (Lit. m. p. 80-81°C). $^1$H NMR (500 MHz, CDCl$_3$): 1.30 (3H, t, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.18 (2H, q, $J = 7.2$ Hz, OCH$_2$CH$_3$), 4.96 (1H, s, 4'-H), 6.40-6.46 (1H, m, 3-H), 6.75-6.81 (1H, m, 8-H), 7.03-7.08 (1H, m, 1-H), 7.22-7.29 (overlapping CDCl$_3$, m, 2-H and 7-H), 7.91-7.95 (1H, m, 9-H), 8.57-8.66 (1H, m, 5-H). $^{13}$C NMR (partial data from HSQC, CDCl$_3$): 14.4 (OCH$_2$CH$_3$), 57.5 (OCH$_2$CH$_3$), 74.5 (4'-C), 105.9 (3-C), 114.9 (8-C), 115.9 (6-C), 126.2 (1-C), 126.8 (2-C or 7-C), 128.1 (9-C), 131.3 (2-C or 7-C).

**Diethyl Pyrido[2,1,6-de]quinolizine-1,3-dicarboxylate (117)** Ethyl 4H-quinolizin-4-ylidene acetate 116 (0.696 g, 3.236 mmol) was dissolved in nitrobenzene (25 mL). The solution was purged with nitrogen, and ethyl propiolate (0.400 g, 4.077 mmol) and potassium carbonate (0.500 g, 3.618 mmol) were added. The solution was stirred under reflux for 8 minutes under nitrogen. After 6 minutes the nitrobenzene was removed using a steam distillation, the remaining water was extracted with chloroform and the residue was dried on a vacuum pump overnight to remove traces of nitrobenzene. The residue was first run through a neutral alumina column, eluting with chloroform to remove any tarry biproduct. The product was further purified on neutral alumina eluting with 80:20 toluene-hexanes. A bright yellow band was collected and this gave the pyridoquinoline product 117 (0.276 g, 41.9 %). $^1$H NMR (500 MHz, CDCl$_3$): 1.20 (6H, t, $J = 7.2$ Hz, 2 x OCH$_2$CH$_3$), 4.01 (4H, q, $J = 7.2$ Hz, 2 x OCH$_2$CH$_3$), 5.19-5.22 (2H, m, 5,8-H), 6.08 (2H, t, $J = 8.3$ Hz, 7,6-H), 6.65-6.68 (2H, m, 4,9-H).
CHAPTER IV: CONCLUSION

Modifications to porphyrinoid systems allows the effects this has on the macrocycle to be investigated. Each new system can potentially alter the degree of aromaticity that is observed. Changes to the internal cavity, achieved by inserting different rings into the system, provide valuable insights. Furthermore, metalation or protonation can further influence the degree of aromatic character. Carbaporphyrinoids are common porphyrin analogues that replace one of the internal nitrogen atoms with a carbon atom. One type of carbaporphyrin that has been extensively studied is benziporphyrin. Benziporphyrin replaces one pyrrole subunit with a benzene subunit. This system is nonaromatic and has no diatropic ring current present. Likewise, N-confused pyriporphyrin, which is structurally similar to benziporphyrin, replaces a pyrrole subunit with a pyridine moiety where the nitrogen is on the exterior of the macrocycle instead of the internal cavity. N-confused pyriporphyrins are also nonaromatic, although certain modifications to this system can reinstate some of the aromatic properties.

The work reported in this thesis explored the effects of inserting an N-confused-type structure, 4-quinolizone, into a porphyrin system. Quinolizone contains a thermodynamically stable amide, and this unit disrupts the aromatic pathway. However, the proton NMR spectra, along with its UV-Vis data, showed a degree of global aromaticity that can be attributed to dipolar resonance contributors that possess $18\pi$ electron delocalization pathways. Metalation and protonation studies were also conducted on this system, and these resulted in significant increases to the diatropic ring current.
Preliminary investigations into the synthesis of a porphyrin analogue incorporating an antiaromatic pyridoquinolizine unit are also reported. Pyridoquinolizine introduces another N-confused type unit that is likely to have a profound effect on the resulting porphyrinoid system. Specifically, electron-donation from the antiaromatic unit is expected to lead to enhanced macrocyclic aromaticity. However, difficulties have been encountered in converting a pyridoquinolizine diester into the key dialdehyde intermediate required for the synthesis. Alternative routes to the dialdehyde are currently under investigation. Access to new porphyrinoid systems of these types gives insights into the aromatic properties of macrocyclic structures and provides access to novel organometallic derivatives.
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Figure A-1. 400 MHz $^1$H NMR spectrum of ethyl 2-pyridylacetate 99 in CDCl$_3$
Figure A-2. 500 MHz $^1$H NMR spectrum of diethyl 4-quinolizone-1,3-dicarboxylate 101 in CDCl$_3$
Figure A-3. $^1$H-$^1$H COSY NMR spectrum of diethyl 4-quinolizone-1,3-dicarboxylate 101 in CDCl$_3$
Figure A-4. 125 MHz $^{13}$C NMR spectrum of diethyl 4-quinolizone-1,3-dicarboxylate 101 in CDCl$_3$
Figure A-5. HSQC NMR spectrum of diethyl 4-quinolizone-1,3-dicarboxylate 101 in CDCl₃
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Figure A-9. HSQC NMR spectrum of 4-quinolizone 102 in CDCl$_3$
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Figure A-12. 125 MHz $^{13}$C NMR spectrum of 4-quinolizone-1,3-dicarbaldehyde 85 in CDCl$_3$
Figure A-13. HSQC NMR spectrum of 4-quinolizone-1,3-dicarbaldehyde 85 in CDCl₃
Figure A-14. 500 MHz $^1$H NMR spectrum of oxyquinoliziniporphyrin $84a$ in CDCl$_3$-TFA
Figure A-15. $^1$H-$^1$H COSY NMR spectrum of oxyquinolinizinoporphyrin 84a in CDCl$_3$-TFA
Figure A-16. 125 MHz $^{13}$C NMR spectrum of oxyquinolizinoporphyrin 84a in CDCl$_3$-TFA
Figure A-17. DEPT-135 NMR spectrum of oxyquinoliziniporphyrin 84a in CDCl₃-TFA
Figure A-18. HSQC NMR spectrum of oxyquinolizinoporphyin 84a in CDCl₃-TFA
Figure A-18. ESI Mass Spectrum of oxyquinoliziniporphyrin 84a CHCl₃

Figure A-19. UV-Vis Spectra of oxyquinoliziniporphyrin 84a 1%TEA-CH₂Cl₂
Figure A-20. UV-Vis Spectra of oxyquinoliziniporphyrin 84a 1 eq TFA-CH$_2$Cl$_2$

Figure A-21. UV-Vis Spectra of oxyquinoliziniporphyrin 84a 10% TFA-CH$_2$Cl$_2$
Figure A-22. 500 MHz $^1$HNMR spectrum of palladium(II) complex 106a in CHCl$_3$
Figure A-23. $^1$H-$^1$H COSY NMR spectrum of palladium(II) complex 106a in CDCl$_3$
Figure A-24. HSQC NMR spectrum of palladium(II) complex 106a in CDCl₃

Figure A-25. UV-Vis Spectra of palladium(II) complex 106a in CH₂Cl₂
Figure A-26. ESI Mass spectrum of palladium(II) complex 106a in CHCl₃
Figure A-27. 500 MHz $^1$H NMR spectrum of nickel(II) complex 107a in CHCl$_3$
Figure A-28. $^1$H-$^1$H COSY NMR spectrum of nickel(II) complex $107a$ in CDCl$_3$
Figure A-29. 125 MHz $^{13}$C NMR spectrum of nickel(II) complex 107a in CDCl$_3$
Figure A-30. DEPT-135 NMR spectrum of nickel(II) complex 107a in CDCl₃
Figure A-31. HSQC NMR spectrum of nickel(II) complex 107a in CDCl₃

Figure A-32. UV-Vis Spectrum of nickel(II) complex 107a in CH₂Cl₂
Figure A-33. ESI Mass spectrum of nickel (II) complex 107\textit{a} in CDCl$_3$
Figure A-34. 500 MHz $^1$H NMR spectrum of oxyquinioliziniporphyrin 84b in CDCl$_3$
Figure A-35. $^1$H-$^1$H COSY NMR spectrum of oxyquinoxaliniporphyrin 84b in CDCl$_3$
Figure A-36. 125 MHz $^{13}$C NMR spectrum of oxyquinoliniporphyrin $84b$ in CDCl$_3$. 
Figure A-37. DEPT-135 NMR spectrum of oxyquinoliziniporphyrin 84b in CDCl$_3$
Figure A-38. HSQC NMR spectrum of oxyquinolizinoporphyrin 84b in CDCl$_3$
Figure A-39. 500 MHz $^1$H NMR spectrum of oxyquinolizinoporphyrin 84b in CDCl$_3$-TFA
Figure A-40. $^1$H-$^1$H COSY NMR spectrum of oxyquinoliniporphyrin 84b in CDCl$_3$-TFA
Figure A-41. 125 MHz $^{13}$C NMR spectrum of oxyquinolizinoporphyrin $84b$ in CDCl$_3$-TFA
Figure A-42. DEPT-135 NMR spectrum of oxyquinolizinoporphyrrin 84b in CDCl₃-TFA
Figure A-43. HSQC NMR spectrum of oxyquinolizinoporphyrin 84b in CDCl₃-TFA
Figure A-44. ESI Mass Spectrum of oxyquinoliziniporphyrin \textbf{84b} porph CHCl$_3$

Figure A-45. UV-Vis spectrum of oxyquinoliziniporphyrin \textbf{84b} in 1\%TEA-CH$_2$Cl$_2$
Figure A-46. UV-Vis spectrum of oxyquinolizinoporphyrin 84b in 5 eq TFA-CH$_2$Cl$_2$

Figure A-47. UV-Vis spectrum of oxyquinolizinoporphyrin 84b in 10% TFA-CH$_2$Cl$_2$
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Figure A-49. $^1$H-$^1$H COSY NMR spectrum of palladium(II) complex 106b in CDCl$_3$
Figure A-50. 125 MHz $^{13}$C NMR spectrum of palladium(II) complex 106b in CDCl$_3$. 
Figure A-51. DEPT 135 NMR spectrum of palladium(II) complex 106b in CDCl₃
Figure A-52. HSQC NMR spectrum of palladium(II) complex 106b in CDCl₃
Figure A-53. ESI Mass spectrum of palladium(II) complex $106b$ in CHCl$_3$.

Figure A-54. UV-Vis spectrum of palladium(II) complex $106b$ in CH$_2$Cl$_2$. 

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Figure A-55. 500 MHz $^1$HNMR spectrum of nickel(II) complex 107b in CDCl$_3$. 
Figure A-56. $^1$H-$^1$H COSY NMR spectrum of nickel(II) complex 107b in CDCl$_3$
Figure A-57. 125 MHz $^{13}$C NMR spectrum of nickel(II) complex 107b in CDCl$_3$
Figure A-58. DEPT 135 NMR spectrum of nickel(II) complex 107\textbf{b} in CDCl$_3$
Figure A-59. HSQC NMR spectrum of nickel(II) complex 107b in CDCl₃

Figure A-60. UV-Vis spectrum of nickel(II) complex 107b in CH₂Cl₂
Figure A-61. ESI Mass spectrum of nickel(II) complex 107b
Figure B-1. 500 MHz $^1$H NMR spectrum of tert-butyl ethyl 4H-quinolizin-4-ylidenemalonate (115) in CDCl$_3$. 
Figure B-2. $^1$H-$^1$H COSY NMR spectrum of tert-butyl ethyl 4H-quinolizin-4-ylidenemalonate (115) in CDCl$_3$
Figure B-3. 125 MHz $^{13}$C NMR spectrum of tert-butyl ethyl 4H-quinolizin-4-ylidenemalonate (115) in CDCl$_3$
Figure B-4. HSQC NMR spectrum of tert-butyl ethyl 4H-quinolizin-4-ylidenemalonate (115) in CDCl₃
Figure B-5. 500 MHz $^1$H NMR spectrum of ethyl 4H-quinolizin-4-ylidenemalonate (116) in CDCl$_3$
Figure B-6. $^1$H-$^1$H COSY NMR spectrum of ethyl 4H-quinolizin-4-ylidenemalonate (116) in CDCl$_3$
Figure B-7. HSQC NMR spectrum of ethyl 4H-quinolizin-4-ylidenemalonate (116) in CDCl₃.
Figure B-8. 500 MHz $^1$H NMR spectrum of diethyl pyrido[2,1,6-de]quinolizine-1,3-dicarboxylate (117) in CDCl$_3$. 