Porphyrin Isomers

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Neo-Confused Porphyrins, a New Class of Porphyrin Isomers**

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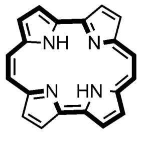
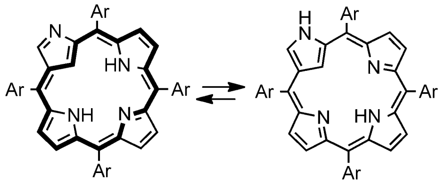
In memory of Emanuel Vogel (1927–2011)

In 1986, Vogel reported the first synthesis of a porphyrin isomer **1** which was named porphycene due to its structural relationship to the acenes.[1] Porphycene differs from regular porphyrins by having the bridging carbon atoms arranged so that there are two C_2 bridges and two direct linkages between the pyrrolic subunits. Porphycene retains highly aromatic characteristics and while the macrocyclic core is elongated compared to the symmetrical cavity in true porphyrins, the system retains the ability to form numerous coordination complexes.[2] Constitutional isomers with other arrangements of the linking carbon atoms were subsequently reported,[3–6] specifically hemiporphycene,[4] corrphycene,[5] and isoporphycene.[6] In all of these analogues, the pyrrolic nitrogens are orientated into the central macrocyclic cavity. A different type of porphyrin isomer **2** with an inverted pyrrole ring was reported by two groups in 1994.[7] This system, named N-confused porphyrin (NCP) by Furuta and co-workers,[7a] has a CH unit within the macrocyclic interior and an external nitrogen. NCPs have been widely investigated due to their ability to afford unusual derivatives such as N-fused porphyrins and because they can form diverse coordination complexes including organometallic derivatives and supramolecular species.[8] NCPs were originally obtained as minor by-products from Rothemund or Lindsey-type reactions between pyrrole and aromatic aldehydes,[7] although a relatively high yielding method was subsequently reported by Geier et al.[9] Syntheses of *meso*-unsubstituted NCPs were also developed.[10]

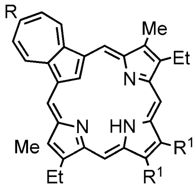
We have investigated the synthesis of closely related carbaporphyrinoid systems including azuliporphyrins (**3**),[11] benzocarbaporphyrins (**4**),[12] tropiporphyrins,[13] oxybenziporphyrins,[14] oxynaphthiporphyrins,[14c] and pyrazoloporphyrins (**5**).[15] These systems also readily form organometallic derivatives and undergo unusual reactions.[16] In relation to these studies, we speculated that another type of porphyrin isomer **6** should be possible where a pyrrole nitrogen is connected to a *meso*-carbon. This system can be formally named as 1-aza-21-carba-1*H*,23*H*-porphyrin and could retain aromatic characteristics by virtue of the 17-atom 18π-electron delocalization pathway highlighted in bold. Very recently, Furuta et al. obtained a related corrole isomer **7** as a minor by-product from the oxidative ring closure of an N-confused bilane.[17] This group named compound **7** "norrole" and considered the system to be "neo-confused".[17] Although our investigations have been completely independent and make use of a very different synthetic approach, we have elected to name the analogous porphyrin isomer **6** as neo-confused porphyrin. The first examples of this novel carbaporphyrinoid system are described below.



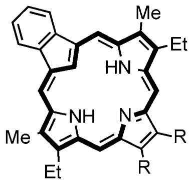
1 (Porphycene)



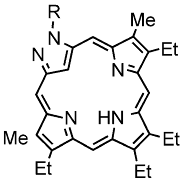
2a (N-Confused porphyrins) **2b**



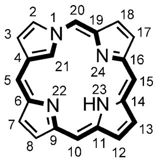
3 (Azuliporphyrins)



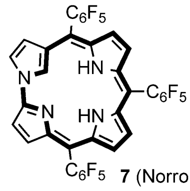
4 (Benzocarbaporphyrins)
a. R = Et; b. R = Ph



5 (Pyrazoloporphyrins)



6 Neo-confused porphyrin



7 (Norrole)

The present study describes the synthesis of benzo-fused neo-confused porphyrins **8**. The synthesis of this system requires the formation of a dipyrrolic intermediate **9** that incorporates the crucial methylene linkage to a pyrrole-type nitrogen (Scheme 1). This was accomplished by reacting 3-indolecarbaldehyde with acetoxymethylpyrrole **10** and sodium hydride in refluxing THF. Following recrystallization from ethanol, the neo-confused intermediate was isolated in 85% yield. This method allows the introduction of an aldehyde unit on the indole ring, but a second formyl moiety is also required on the pyrrole ring. Treatment of **9** with TFA at room temperature for 10 min cleaved the *tert*-butyl ester to form **11**, and subsequent reaction with trimethyl orthoformate afforded the required dialdehyde **12**. MacDonald "2+2" condensation[18] of **12** with dipyrrylmethanes **13a**

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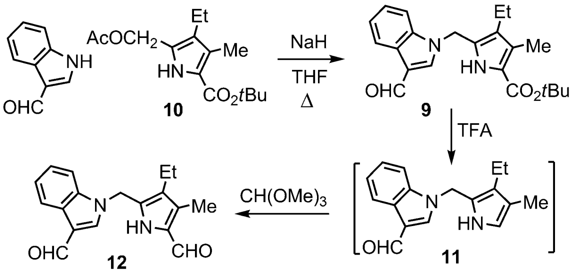
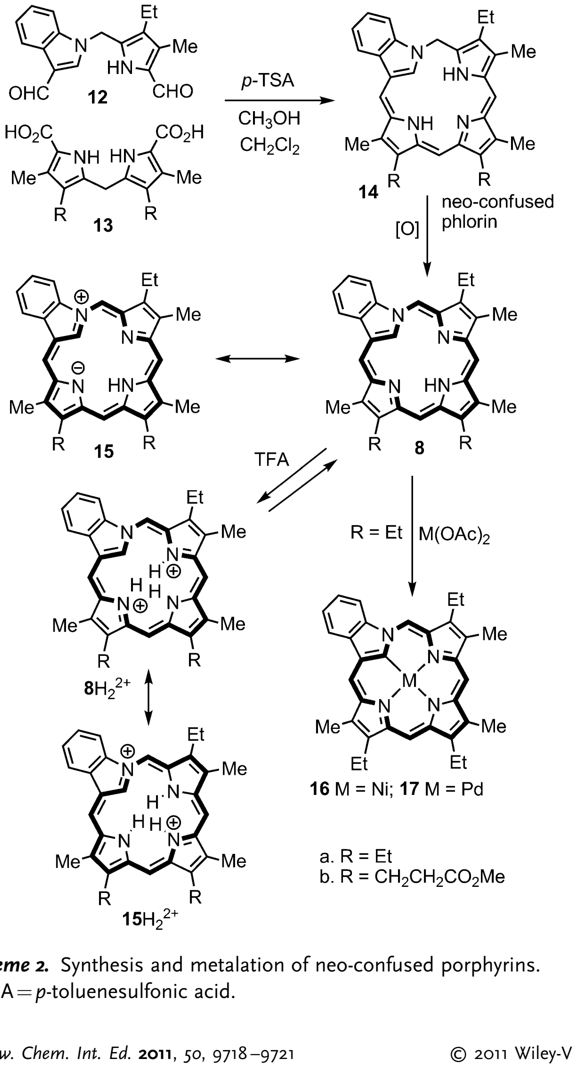


Scheme 1. Synthesis of the dialdehyde intermediate. TFA = trifluoroacetic acid.

and **13b**[19] was carried out in the presence of *p*-toluenesulfonic acid in methanol/dichloromethane (Scheme 2). In the initial studies, the crude reaction mixture was shaken with a 0.1% aqueous ferric chloride solution to oxidize the dihydroporphyrin intermediates to the fully conjugated neo-confused porphyrins. Column chromatography gave two major fractions, an unstable pink fraction and a dark purple band corresponding to the neo-confused porphyrin. When the oxidation step was omitted, a dark blue fraction was isolated instead. Again this compound proved to be unstable and could not be fully purified, but the nOe difference proton NMR spectra for this species demonstrated that a phlorin **14** had been formed. These results parallel those obtained in the synthesis of pyrazoloporphyrins **5**.[15] However, in this series oxidation of the phlorin intermediates with DDQ (DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) gave much better results and the benzoporphyrin isomers **8** could be isolated following chromatography and recrystallization from chloroform-methanol in 24–25% yield.



Scheme 2. Synthesis and metalation of neo-confused porphyrins. *p*-TSA = *p*-toluenesulfonic acid.

For the most part, neo-confused porphyrins **8a** and **8b** gave similar spectroscopic results and only the data for **8a** will be discussed in detail. The UV/Vis spectrum for **8a** was surprisingly porphyrin-like showing a strong Soret band at 407 nm and a series of Q bands at 503, 537, 567, and 615 nm (Figure 1). Addition of TFA afforded a diprotonated species **8a**-H_2^{2+} which gave a split Soret band at 402 and 428 nm and a series of Q bands extending to > 700 nm. Titration of the neo-confused porphyrin with TFA showed no intermediary monocationic species but a gradual conversion of the free base to the dication. Porphyrins also generally go directly to the diprotonated form and a similar result was also recently noted for a dideazaporphyrin.[20] Further addition of TFA led to minor spectroscopic shifts but did not indicate that any further protonation had occurred. Unexpectedly, the diprotonated form for the dipropionate ester **8b**-H_2^{2+} gave a significantly different UV/Vis spectrum with a single Soret band. This difference may be due to hydrogen bonding between the protonated porphyrinoid core and the ester side chains. The proton NMR spectrum of **8a** confirmed that the neo-confused porphyrin system is highly diatropic (Figure 2), although the shifts are somewhat reduced compared to regular porphyrins. In the proton NMR spectra for *meso*-unsubstituted porphyrins, the *meso*-proton resonances generally show up near $\delta = +10$ ppm, while methyl substituents give singlets near $\delta = 3.6$ ppm and the internal NH protons appear upfield close to $\delta = -4$ ppm. For **8a**, the *meso*-protons

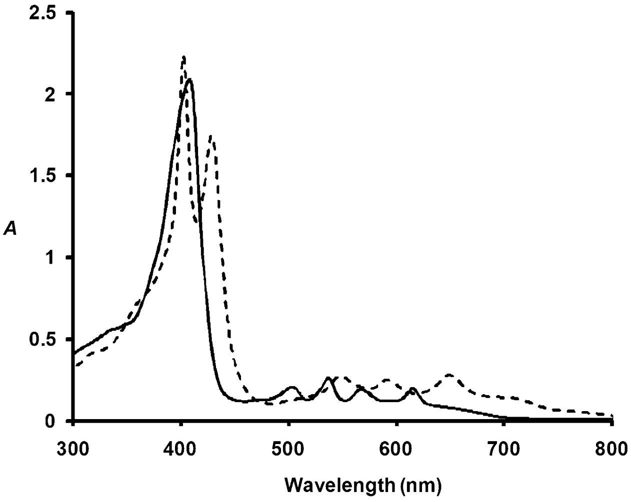


Figure 1. UV/Vis spectra of neo-confused porphyrin **8a** in chloroform (free base, bold line) and in 1% TFA/chloroform (dication **8a**-H_2^{2+}, dotted line).

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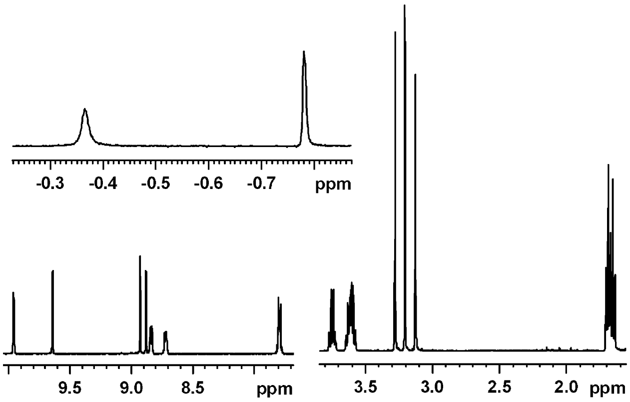

Figure 2. 500 MHz proton NMR spectrum of neo-confused porphyrin **8a** in $CDCl_3$.

were observed as four ^1H singlets at $\delta = 8.91$, 8.96, 9.68 and 9.99 ppm, while the methyl substituents gave rise to three 3H singlets at $\delta = 3.16$, 3.24 and 3.32 ppm. The internal CH proton gave a singlet at $\delta = -0.74$ ppm and the NH produced a broadened resonance at $\delta = -0.33$ ppm, confirming the presence of a diatropic ring current. The aromatic properties of neo-confused porphyrins **8** could be due to dipolar resonance contributors like **15** that provide carbaporphyrin-like 18π-electron pathways. This type of interaction has been used to explain the aromatic properties of azuliporphyrins[11] and cross-conjugated N-confused porphyrins **2b**.[10c] However, porphyrinoids **8** are nonpolar compounds and possess a higher degree of aromatic character than these systems, and our results indicate that canonical forms like **15** do not significantly contribute to the properties of neo-confused porphyrins **8**. In the ^{13}C NMR spectrum, the *meso*-protons gave rise to four resonances at $\delta = 93.6$, 94.1, 107.7 and 108.9 ppm, values that are consistent with the equivalent carbon resonances in porphyrins and aromatic porphyrin analogues like **4**, and the interior CH appeared at $\delta = 124.4$ ppm. Addition of TFA to the $CDCl_3$ solution produced the dication **8a**-H_2^{2+} and this species showed enhanced diatropicity. The *meso*-protons were shifted downfield to give four ^1H singlets at $\delta = 9.77$, 9.80, 10.52 and 10.92 ppm and the methyl substituents also show up further downfield at $\delta = 3.42$, 3.44 and 3.51 ppm. These shifts may be due in part to the delocalized positive charges, so it is notable that the internal CH moves upfield to $\delta = -3.85$ ppm. The enhanced diatropicity may well be due in part to resonance contributors like **15**-H_2^{2+} which now aid in charge delocalization.

When neo-confused porphyrin **8a** was heated with nickel(II) acetate in acetonitrile, the corresponding nickel(II) complex **16** was generated in > 90 % yield. Nickel(II) neo-confused porphyrin **16** was isolated as stable dark green crystals and gave a very different UV/Vis spectrum from **8a** showing a Soret band at 390 nm with a pronounced shoulder at 425 nm. In the proton NMR spectum for **16** in $CDCl_3$, the *meso*-protons showed comparable downfield shifts to **8a** giving four ^1H singlets at $\delta = 8.98$, 9.22, 9.71 and 9.85 ppm, and the methyl substituents produced three 3H singlets at $\delta = 3.09$, 3.19 and 3.27 ppm. The *meso*-carbons also gave similar values to **8a** in the ^{13}C NMR spectrum, showing up as four separate resonances at $\delta = 95.2$, 97.1, 107.2 and 108.2 ppm. We also attempted to prepare the corresponding palladium(II) complex **17**, but the pure complex could not be isolated in this case. Reaction of **8a** with palladium(II) acetate in refluxing acetonitrile or pyridine generated this metalated species but relatively poor yields were obtained and contaminants could not be completely removed by column chromatography. Nevertheless, neo-confused porphyrins show promise in the generation of novel organometallic derivatives.

The X-ray crystal structure of nickel complex **16** has also been obtained (Figure 3), and this confirms the presence of a neo-confused moiety. The asymmetry provided by the ethyl substituents provided a well ordered structure where the neo-confused nitrogen atom was easily identified in the initial crystallographic solution. In addition to the well behaved displacement parameters, the structure also demonstrates that the macrocycle is remarkably planar as evidenced by the 0.056 Å rms distance the framework atoms lie from the plane defined by Ni, C21, N22, N23, and N24. The largest deviations from the plane are C5 (0.111(4) Å), C15 (0.093(4) Å), and C20 (−0.111(4) Å). Of the 24 framework atoms, only these three deviate more than 0.07 Å from the aforementioned plane. The structure exhibits framework bond distances consistent with a generally localized π-bonding model. The metal coordination environment of **16** is essentially a 4-coordinate square planar geometry about the Ni^{II} metal center. The planarity and coordination sphere metrics are similar to related NCP complexes,[7b,21] although disorder in the NCP complexes precludes differentiation between N-confused and regular pyrrolic orientation. In **16**, the 1.907(3) Å Ni−C21 distance is significantly shorter than the 1.970(3) Å Ni−N23 distance, consistent with the greater basicity of the carbanion ligand.

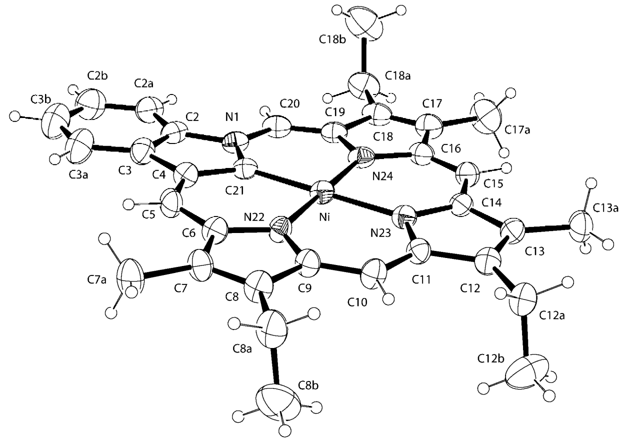

Figure 3. ORTEP III drawing (30 % probability level, hydrogen atoms drawn arbitrarily small) of compound **16**. Selected bond lengths [Å]: Ni–N(24) 1.929(3), Ni–N(23) 1.970(3), Ni–N(22) 1.951(3), Ni–C(21) 1.907(3). Selected bond angels [°]: C(21)-Ni-N(24) 90.6(1), C(21)-Ni-N(22) 89.5(1), N(24)-Ni-N(22) 179.6(1), C(21)-Ni-N(23) 179.5(1), N(24)-Ni-N(23) 89.8(1), N(22)-Ni-N(23) 90.2(1).

In conclusion, the first examples of neo-confused porphyrins have been prepared and these have proven to be diatropic compounds with global aromatic properties. The formation of a stable nickel(II) complex also demonstrates

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that this new type of porphyrin isomer has potential as an organometallic ligand.

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