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PAPER

Pyrazole analogues of porphyrins and oxophlorins†‡

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A series of porphyrin analogues with pyrazole rings replacing one of the usual pyrrole subunits have been synthesized. This was accomplished by reacting 1-phenyl, 1-methyl and 1-ethyl pyrazole-1,3-dicarbaldehydes with a tripyrrane in the presence of TFA, followed by an oxidation step. The initially formed phlorin product was sufficiently stable for the *N*-phenyl system to be isolated and characterized, although the related *N*-alkyl phlorin analogues were less stable. Attempts to dehydrogenate the intermediary phlorins with DDQ resulted in decomposition, but the *N*-alkylphlorins could be oxidized with 0.2% aqueous ferric chloride solutions. Although the phenyl-substituted phlorin could not be oxidized under these conditions, it did afford the pyrazoloporphyrin upon treatment with silver acetate under acidic conditions. Oxidations with silver acetate also afforded oxophlorin analogues where the oxo-linkage was selectively formed at the 5-position. The pyrazole-containing porphyrin analogues are cross-conjugated and exhibit only a small degree of diatropic character. The internal CH resonances were observed between 5.27 and 5.87 ppm, while the external *meso*-protons fell into a range of 6.84–7.88 ppm. The borderline overall aromatic character was attributed to dipolar resonance contributors. Protonation considerably increased the diatropicity and the diprotonated dications formed from these porphyrin analogues gave the internal CH resonance at upfield values of 2.65–3.20 ppm. The aromatic character was enhanced by the presence of an electron-donating alkyl substituent on the nitrogen compared to the phenyl-substituted species. The pyrazoloporphyrins reacted with nickel(II) acetate in DMF, or palladium(II) acetate in acetonitrile, to give the corresponding organometallic derivatives. The metal complexes showed increased diatropic character but protonation afforded nonaromatic cations. The oxophlorin analogues were also nonaromatic in the free base and protonated forms. This work extends our understanding of carbaporphyrinoid systems and provides the first detailed studies on pyrazole-containing porphyrin analogues.

Introduction

Although porphyrin analogues were first investigated in the 1960s,[1,2] it was not until 1986 that the first example of a porphyrin isomer **1** was reported by Vogel and coworkers.[3,4] This system, named porphycene due to its structural relationship to the acenes, proved to be a stable aromatic system that readily forms metalated derivatives.[5,6] In the mid to late 1990s, further examples of porphyrin isomers, specifically corrphycene,[7,8] hemicorphycene[9,10] and isoporphycene,[11] were synthesized. In these systems, all four nitrogens are orientated into the macrocyclic cavity. However, another type of porphyrin isomer **2** with an inverted pyrrole ring was also discovered around this time.[12,13] This type of porphyrin isomer was named N-confused porphyrin (NCP) by Furuta,[12] and was obtained as a by-product from Rothemund or Lindsey-type tetraarylporphyrin syntheses.[14] NCPs attracted considerable interest due to their unusual properties.[15] They have relatively long wavelength absorptions compared to porphyrins and this could lead to applications as photosensitizers in photodynamic therapy.[16] NCPs readily form organometallic derivatives and can act as dianionic and trianionic ligands.[17] In addition, coordination can occur on the external nitrogen and this can lead to the formation of supramolecular systems.[18] These investigations have been facilitated by the development of high yielding conditions for the synthesis of NCPs.[19] NCPs are generally isolated as the fully aromatic tautomer **2**, but this species is only slightly more stable than the less aromatic cross-conjugated form **3** which is favored in polar aprotic solvents.[20] Alkylation of the external nitrogen can also be used to trap the less aromatic form,[21] and a rational synthesis of *N*-methyl and *N*-phenyl NCPs **4** has been developed.[22]

NCPs have a core arrangement of three nitrogens and one carbon atom, and may be considered to be carbaporphyrinoids. Contemporaneously with the initial studies on NCPs, other examples of carbaporphyrinoids were also synthesized in the 1990s.[23,24] These included benzocarbaporphyrins **5**,[25] carbachlorins **6**,[26] azuliporphyrins **7**,[27] tropiporphyrins **8**,[28] benziporphyrins

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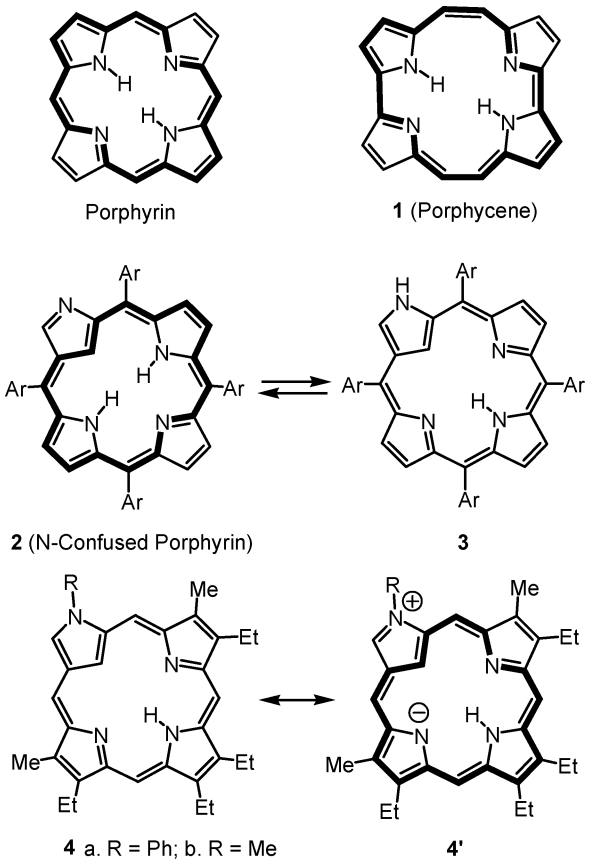
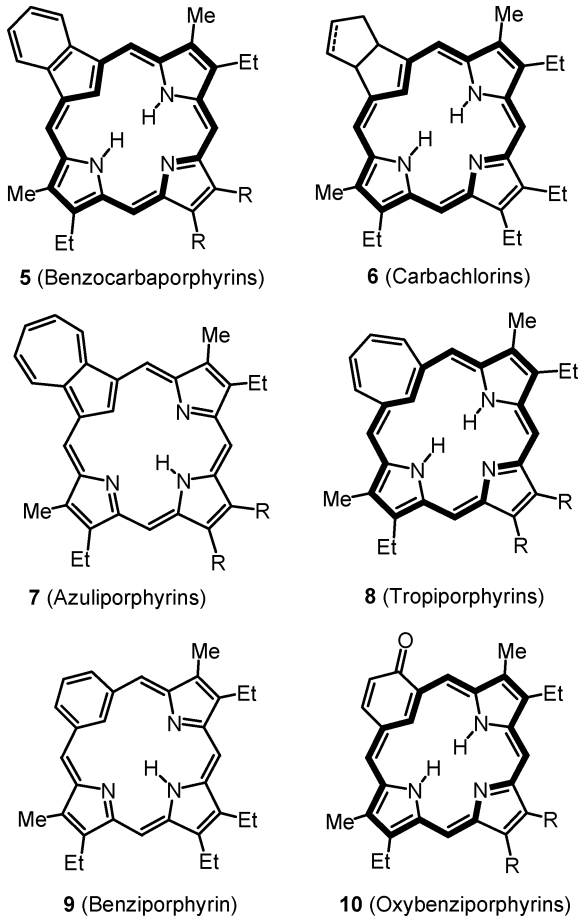
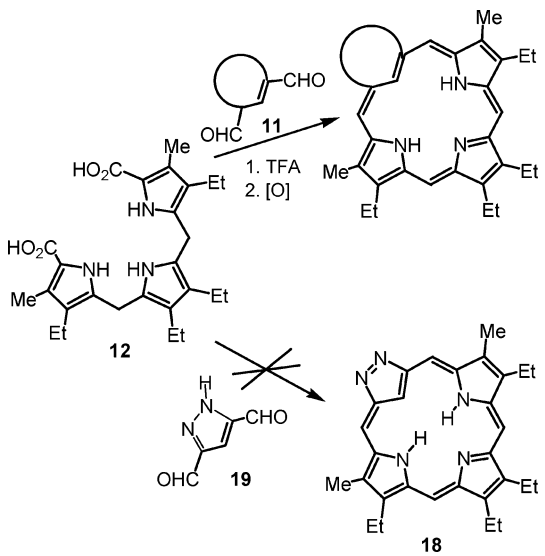
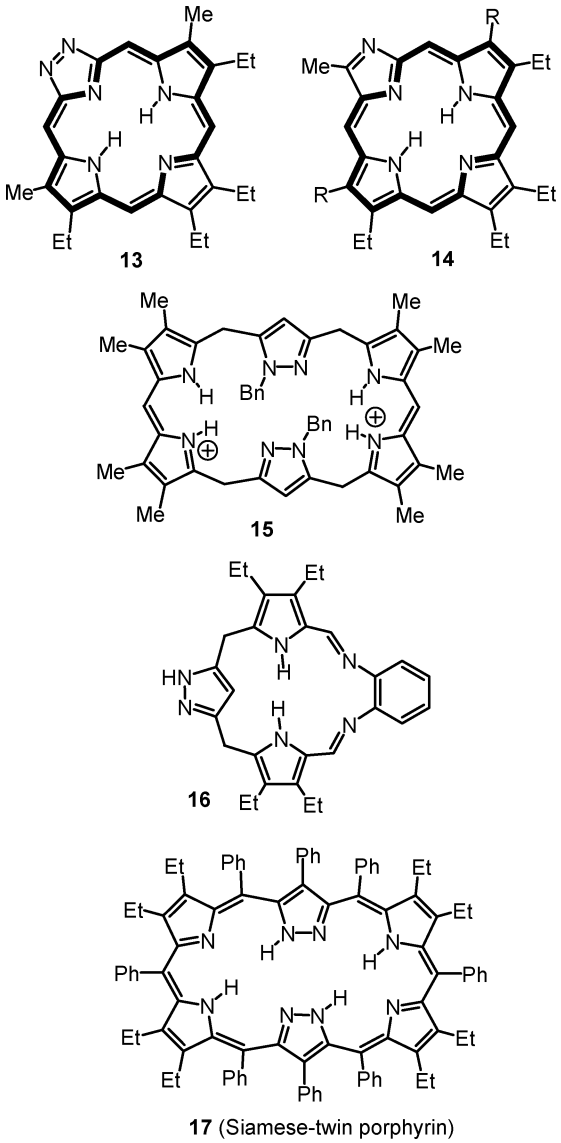


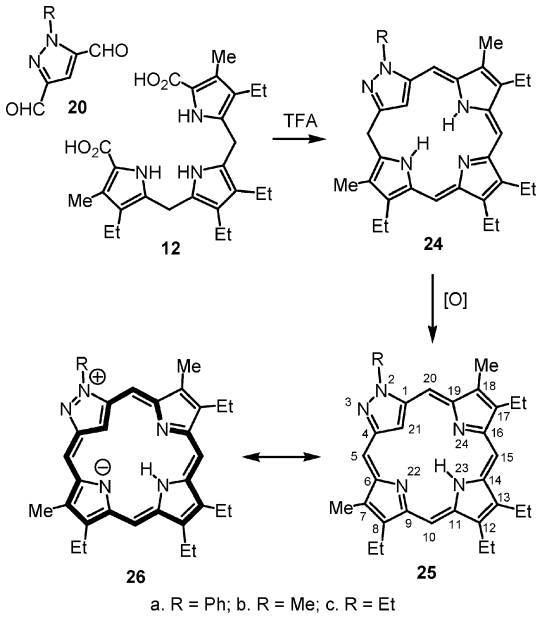


9[29,30] and oxybenziporphyrins **10**.[30] Carbaporphyrinoids **5–10** were all synthesized by using a '3 + 1' version of the MacDonald condensation.[31,32] In this methodology, a dialdehyde **11** is reacted with a tripyrrane **12** in the presence of an acid catalyst, usually TFA, and following oxidation, fully conjugated carbaporphyrinoids can be generated (Scheme 1).[31] This approach is quite versatile and can also be used to prepare NCPs.[22,33,34] More recently, tetraaryl substituted benziporphyrins[35] and azuliporphyrins[36] have been prepared using Lindsey–Rothemund type conditions. Triazole analogues of the porphyrins **13** have also been prepared using the MacDonald '3 + 1' approach[37,38] and an alternative procedure was used to prepare imidazole-containing porphyrinoids **14**.[39,40] However, pyrazole analogues of the porphyrins were not known. Non-conjugated hexaphyrin analogues with two pyrazole subunits (*e.g.* **15**) were investigated some time ago,[41] but attempts to convert this system into a fully aromatic macrocycle were unsuccessful. More recently, Schiff base macrocycles **16** containing a pyrazole subunit were reported by Brückner and coworkers, but again this system could not be oxidized to the related fully conjugated texaphyrin analogue.[42] However, very recently a fully conjugated octaphenyl hexaphyrin analogue with two pyrazole rings was reported.[43] This "Siamese-twin" porphyrin is not aromatic but allows the formation of bimetallic complexes.[43] Our earlier attempts to prepare a pyrazole-containing porphyrinoid system **18** by the '3 + 1' condensation of 1,3-pyrazoledicarbaldehyde (**19**) with a tripyrrane were unsuccessful (Scheme 1).[44] Nevertheless, pyrazole analogues of the porphyrins are of interest because they extend the "confused" aspect of these porphyrinoid macrocycles while retaining the carbaporphyrinoid arrangement of core atoms. In this paper, the synthesis of pyrazole-containing porphyrin analogues and related oxophlorins is presented.[45,46] These porphyrin analogues proved to have very different properties from regular porphyrins or N-confused porphyrins.

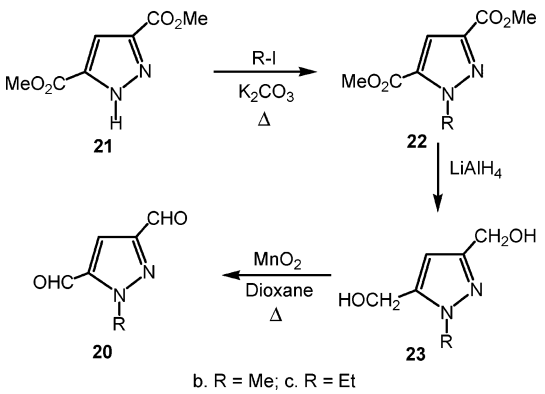


Scheme 1





Scheme 2



Scheme 3

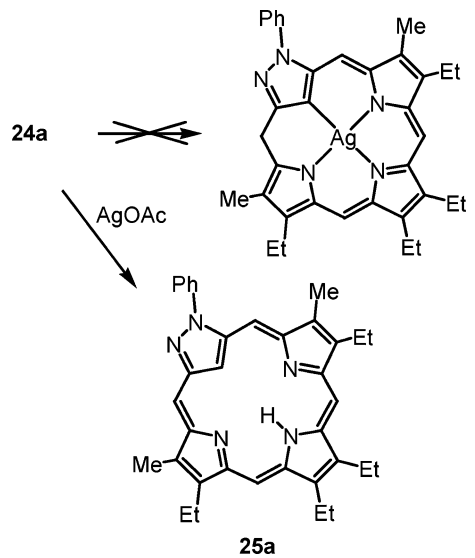
Results and discussion

The presence of substituents often aids in the formation of porphyrin systems, and for this reason the synthesis of pyrazole-containing porphyrin analogues from *N*-substituted pyrazole dialdehydes **20** was investigated (Scheme 2). 1-Phenyl-3,5-pyrazoledicarbaldehyde (**20a**) was prepared by a literature method from the osazone of D-xylose.[47] The corresponding *N*-methyl and *N*-ethyl dialdehydes, **20b** and **20c**, were generated from dimethyl pyrazole-1,3-dicarboxylate[48] (**21**, Scheme 3). Alkylation of pyrazole **21** with methyl or ethyl iodide affords *N*-alkylpyrazoles **22** and subsequent reduction with lithium aluminum hydride gave the related dicarbinols **23**. Subsequent oxidation with freshly activated manganese dioxide in refluxing dioxane then gave the required diformyl pyrazoles **20b** and **20c** in good yields. The methyl substituted dialdehyde **20b** has been reported previously[48a] but the ethyl version **20c** has been synthesized for the first time.

Phenylpyrazole dialdehyde **20a** was reacted with tripyrrane **12** in the presence of TFA in dichloromethane for 16 h (Scheme 2). This affords a phlorin **24** that must then be oxidized to afford the fully conjugated pyrazoloporphyrin **25**. However, attempts to oxidize the crude product with DDQ led to complete decomposition. In related work, it was found that dilute aqueous solutions of ferric chloride could be used as a mild oxidant and may give superior yields of conjugated porphyrinoid macrocycles.[33,49] This transformation is usually carried out by vigorously shaking the reaction solution in a separatory funnel with 0.1% aqueous ferric chloride solution. Prolonged shaking (*ca*. 10 min) again led to decomposition, but shorter exposure times failed to oxidize the intermediate. Extraction and column chromatography on grade 3 basic alumina, eluting with dichloromethane, gave a blue fraction that corresponded to the phlorin analogue **24a**. This species was moderately stable and could be recrystallized from chloroform–methanol to give the macrocyclic product in 40% yield. The position of the methylene bridge was confirmed by nOe difference proton NMR spectroscopy. Reactions of dialdehydes **20b** and **20c** were also carried out, and unstable phlorin products **24b** and **24c** were observed by proton NMR spectroscopy prior to oxidation. However, in these cases oxidation with 0.2% aqueous ferric chloride solution gave the fully conjugated pyrazole-containing porphyrin analogues **25b** and **25c** (Scheme 2). The reaction

mixtures were shaken for 7–8 min with the ferric chloride solution, and porphyrin analogues **25b** and **25c** were isolated as blue–green crystals in 16–21% yield following column chromatography on grade 3 basic alumina and recrystallization from chloroform–ligroin.

Metalation studies were performed on phlorin **24a** and pyrazole-porphyrins **25b** and **25c** (see later). Silver(I) acetate has been shown to react with tetraphenyl NCP **2**,[50] benzocarbaporphyrins **5**,[51] oxybenziporphyrins **10**,[52] oxynaphthiporphyrins[52] and tropiporphyrins **8**[28b] to give silver(III) derivatives. With this in mind, *N*-phenylphlorin analogue **21a** was reacted with silver(I) acetate in an attempt to generate the corresponding silver(III) complex (Scheme 4). Although these conditions failed to form any metallo-derivative, the conjugated macrocyclic product **25a** was unexpectedly formed instead. Based on these observations, a modified '3 + 1' procedure was carried out to prepare **25a** (Scheme 2) where tripyrrane **12** was reacted with pyrazole dialdehyde **20a** for 4 h, followed by treatment with silver acetate for 16 h. The alternative oxidation conditions gave the phenyl substituted porphyrin analogue **25a** in 18% yield, and thereby provided us with a third member of the pyrazoloporphyrin series.



Scheme 4

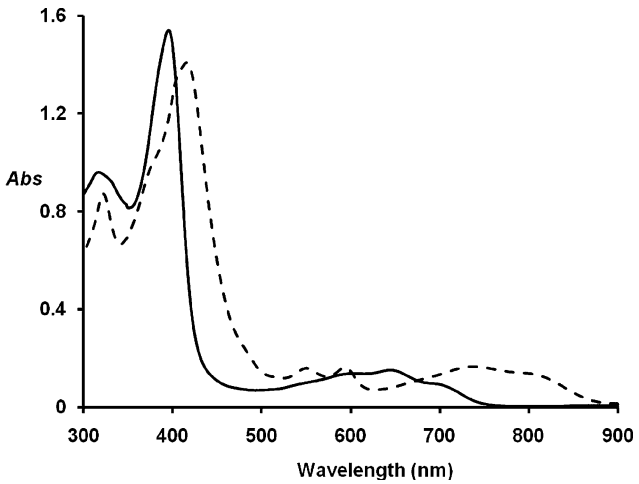
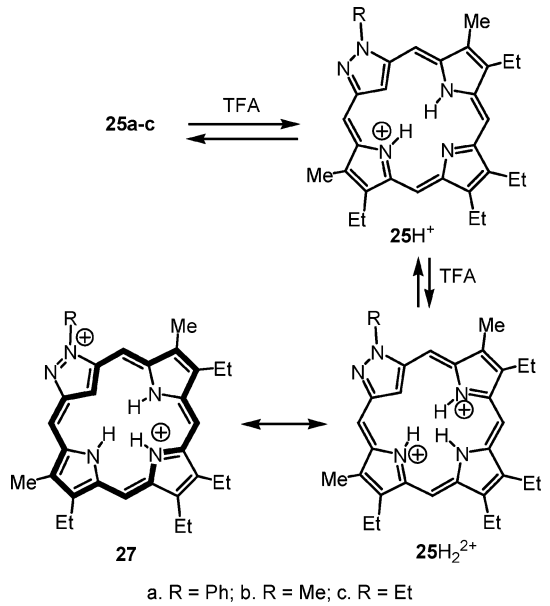


Fig. 1 UV-vis spectra of pyrazoloporphyrin **25a** in 1% Et_3N–chloroform (free base, solid line) and 1% TFA–chloroform (dication **25a**H_2^{2+}, dashed line).



Scheme 5

The phenyl substituted pyrazole porphyrin analogue gave a UV-visible spectrum in 1% triethylamine–chloroform with a Soret-like band at 395 nm and broad absorptions through the visible region (Fig. 1). Titration of this species in chloroform with TFA showed the formation of a new species with 5–10 equiv TFA which was assigned as the monoprotonated cation **25a**H^+ (Scheme 5). In the presence of a larger excess of TFA, a bathochromically shifted Soret-like band was observed at 403 nm (Fig. 1) and this new species was attributed to the dication **25a**H_2^{2+} (Scheme 5). The UV-vis absorption spectra for **25b** and **25c** in 1% Et_3N–$CHCl_3$ gave similar results showing Soret-like bands at 393 and 392 nm, respectively, and broad absorptions at higher wavelengths. In the presence of excess TFA, a stronger Soret band was observed near 410 nm.

The proton NMR spectra of **25a**, **25b** and **25c** in $CDCl_3$ were very insightful, showing a series of 1H singlets for the *meso*-protons between 6.8 and 7.9 ppm (Fig. 2). These values are nowhere near as far downfield as those seen for true porphyrins (*ca.* 10 ppm),[53] but the shifts are consistent with a system that has a degree of diatropic character. This interpretation is reinforced by the presence of relatively upfield NH resonances for **25b** and **25c** around 6.7 ppm, and the presence of a 1H singlet for the internal CH near 5.3 ppm. The aliphatic region shows the methyl resonances at 2.5 ppm, which is slightly downfield from values seen for nonaromatic porphyrinoids, but again much less deshielded than the values for fully aromatic porphyrinoid systems (*ca.* 3.5 ppm).[53] The proton NMR spectrum of **25a** in $CDCl_3$ gave four 1H singlets for the *meso*-protons at 6.84, 6.89, 7.39 and 7.87 ppm, a broadened peak for the NH at 7.19 ppm and the internal CH singlet showing up near 5.9 ppm (Table 1). Again, the internal protons show a small but significant upfield shift demonstrating that the system has some diatropic character, and the external *meso*-protons are slightly downfield compared to nonaromatic porphyrinoids like benziporphyrin **9**.[30b] However, the

Table 1 ^{1}H NMR shifts (ppm) for free base *N*-substituted pyrazole porphyrins **25a–c** in $CDCl_3$

	5-CH	20-CH	10,15-CH	21-CH	NH
25a (R = Ph)	7.87	7.39	6.84, 6.89	5.87	7.19
25b (R = Me)	7.82	7.45	6.89, 6.95	5.34	6.75
25c (R = Et)	7.88	7.47	6.92, 6.98	5.27	6.70

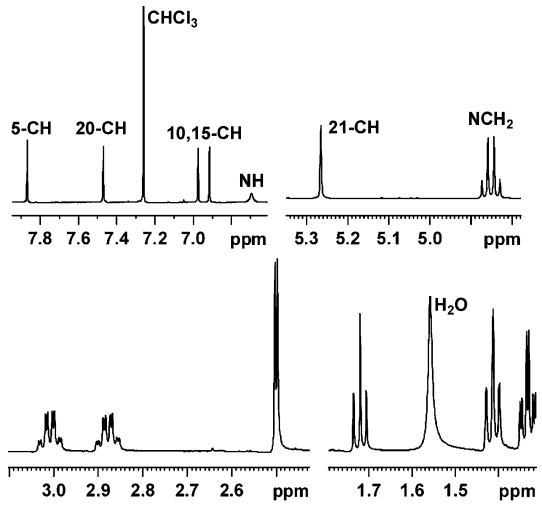


Fig. 2 500 MHz proton NMR spectrum of pyrazole porphyrin **25c** in $CDCl_3$.

proton NMR spectra of **25b** and **25c** in $CDCl_3$ showed the *meso*-protons a little further downfield between 6.8 and 7.9 ppm (*e.g.*, Fig. 2), and the internal protons are also more upfield than the resonances for **25a**. Even so, the latter values are nowhere near as far upfield as those seen in cross-conjugated azuliporphyrins **7**[27] or 2-substututed NCPs **4**.[22] For instance, 2-methyl NCP **4a** shows the internal CH and NH resonances at 1.50 and 2.75 ppm, respectively, while the external *meso*-protons give rise to four 1H singlets between 8.00 and 8.47 ppm.[22] Even the methyl resonances for **4a** are further downfield than in **25a–c**, giving rise to two 3H singlets at 2.83 and 2.84 ppm.[22] The aromatic character of these cross-conjugated porphyrinoids is attributed to dipolar resonance contributors like **26** (Scheme 2). The comparative favorability of this type of canonical form (*i.e.*, structure **4′**) for 21-substituted NCPs **4** is most likely because the positive charge is not placed next to a nitrogen atom as is the case for **25a–c**. If this hypothesis is correct, an electron-donating alkyl group would stabilize this form and lead to increased diatropicity compared to the poorly electron-donating characteristics of a phenyl substituent. Hence, the lesser diatropic character of phenyl-substituted pyrazole porphyrin **25a** is consistent with this proposal (Table 1). It is also worth noting that an ethyl group is a more effective electron-donating substituent than methyl, and the slightly increased downfield shifts for the external protons and upfield shifts to the internal protons for **25c** also supports this interpretation.

Although the aromatic character of **25a–c** can be attributed to the presence of dipolar canonical forms like **26** (Scheme 2), this contributor is not likely to be very favorable due to the requirement for charge separation, as well as the placement of a positive charge next to a nitrogen atom. Protonation studies were also carried out (Scheme 5). Addition of TFA to solutions of **25** may lead to the formation of monocations **25**H$^+$ and dications **25**H$_2^{2+}$. Addition of trace amounts of TFA (1–10 eq.) to NMR solutions of **25b** or **25c** gave poor quality spectra but a species could be observed, for both methyl and ethyl substituted versions, where the *meso*-protons were shifted downfield to between 7.6 and 8.8 ppm. The internal CH was likely overlapped by the upfield multiplet at 1.5 ppm for the methyl version, as this integrated for an extra proton. This spectrum also showed two broad peaks at 1.25 and 1.34 ppm that may correspond to shielded internal NHs. The ethyl version, however, showed messy broad peaks upfield and was less clearly identifiable. Nonetheless, these observations are consistent with the formation of a monoprotonated species **25**H$^+$ that has a slightly increased diatropic ring current compared to the free base forms **25**. Addition of one drop of TFA to an NMR solution of **25** in $CDCl_3$ changed the dark green colored solutions to brown and gave a new species, attributed to dication **25**H$_2^{2+}$, where the *meso*-protons were shifted downfield to values between 6.9 and 8.8 ppm (Table 2, Fig. 3). The resonances for the two exterior pyrrole methyl groups were also shifted downfield to between 2.6 and 3.2 ppm. Although the shifts for the external protons may be attributable in part to the positive charges, these results suggest that the diprotonated species has significantly increased diatropic characteristics compared to the free base. The presence of the internal CH resonances near 3 ppm provides the best evidence for the presence of an enhanced diatropic ring current (Table 2, Fig. 3). The observed increase in diatropicity is likely due to resonance forms like **27** (Scheme 5) that aid in generating an 18 π electron delocalization pathway. This type of contributor is more favorable for the protonated form as charge separation is no longer a factor and indeed this electronic interaction will aid in charge delocalization. The pyrazole-substituents play a similar role in stabilizing this canonical form, as the ethyl substituted version

Table 2 ^{1}H NMR shifts (ppm) for protonated pyrazole porphyrins **25a–c**H$_2^{2+}$ in TFA–$CDCl_3$

	5-CH	20-CH	10,15-CH	21-CH	NH
25a (R = Ph)	8.83	7.94	7.45, 7.49	3.20	Not observed
25b (R = Me)	8.72	8.27	7.47, 7.52	2.77	Not observed
25c (R = Et)	8.82	8.31	7.51, 7.56	2.64	Not observed

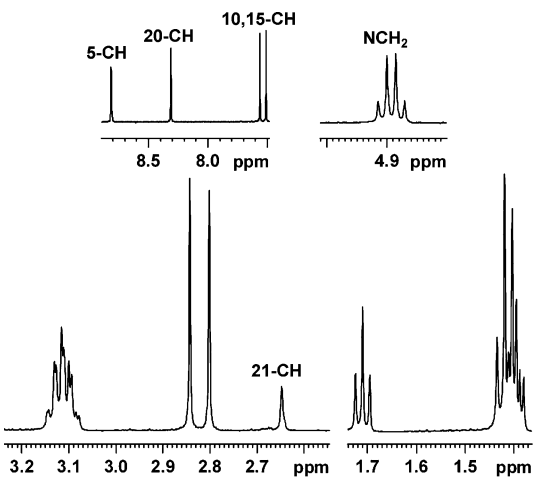
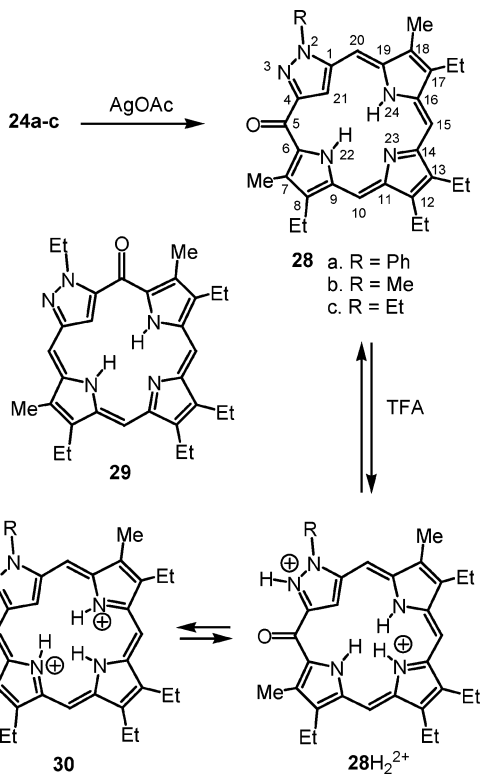


Fig. 3 500 MHz proton NMR spectrum of pyrazole porphyrin dication **25c** in TFA–$CDCl_3$.

shows the largest shifts and the phenyl version the smallest shifts. The porphyrin analogues were also characterized by carbon-13 NMR spectroscopy and mass spectrometry.

A new and unexpected oxidation product **28a** was also observed when phlorin **24a** was oxidized using silver acetate (Scheme 6). This oxophlorin product was first noted as a brightly colored blue band that eluted after the turquoise porphyrin analogue **25a** during product purification by column chromatography. Following re-crystallization from chloroform–ligroin, the oxophlorin analogue **28a** was isolated as dark blue crystals in 9% yield. This type of oxidation product could also be generated for the methyl and ethyl-substituted systems, and a minor regioisomeric product **29** could also be identified for the ethyl series. The yield of oxophlorin product was low for the methyl version (approximately 3%) but the major oxophlorin analogue for the ethyl version was isolated in 14% yield. Proton NMR spectroscopy for the major blue oxidation products gave very different spectra from the porphyrin analogues **25a–c**. For example, oxophlorin **28a** gave four singlets between 5.8 and 7.0 ppm, as well as two broad resonances for the NHs near 9.2 ppm (Fig. 4). As expected, these new macrocycles appear to have no overall diatropic character based on the downfield resonances for the internal NHs and the relatively upfield positions of the *meso*-protons.



Scheme 6

NOE difference proton NMR spectroscopy was used to confirm the identity of the oxophlorins and to assign the *meso*-proton resonances. Irradiation of the peak near 5.5 ppm for **28c** enhanced both of the broad downfield NH peaks, indicating that this singlet was due to the internal pyrazole CH. The other three singlets between 6.0 and 7.0 ppm enhanced the methyl and ethyl peaks around the exterior of the macrocycle confirming

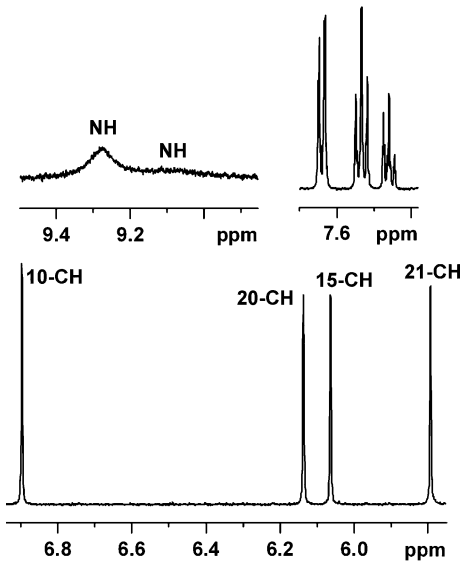


Fig. 4 Partial 500 MHz proton NMR spectrum showing the downfield region for **28a** in $CDCl_3$.

Table 3 ^{1}H NMR shifts (ppm) for pyrazole oxophlorins **28a–c** in TFA–$CDCl_3$

	10-CH	15-CH	20-CH	21-CH	NHs
28a (R = Ph)	6.90	6.07	6.14	5.79	9.08, 9.28
28b (R = Me)	6.89	6.05	6.13	5.56	8.94, 9.17
28c (R = Et)	6.90	6.06	6.15	5.50	8.91, 9.13

that these corresponded to three of the four possible *meso*-protons (Table 3). The absence of the fourth *meso*-proton from the spectra indicated that an oxidation had occurred at one of these positions (identified as carbon 5). A carbonyl stretch was present in the IR spectrum at 1625 cm^{-1}, and the proposed structures **28** were supported by carbon-13 NMR spectroscopy and high resolution mass spectrometry. The UV-visible spectra for **28** gave weak Soret-like bands near 380 nm and a broad lower intensity band that stretched between 600 and 700 nm, confirming that these compounds are not porphyrin-like and suggesting the absence of an aromatic delocalization pathway. These results fit the anticipated properties for compounds with a carbonyl at a *meso*-position that interrupts any fully conjugated pathway. As noted above, a second oxophlorin analogue **29** was also isolated from oxidations of the ethyl substituted phlorin. This less favored oxidation product was seen as a faint blue band that eluted in front of the other oxidation products during column chromatography. Proton NMR spectroscopy and NOE difference proton NMR data for this compound indicate that the oxidation occurred at the other *meso*-position flanking the pyrazole moiety. It is reasonable to assume that the steric interactions between the *N*-substituent and the carbonyl group leads to this product being less favored.

Addition of TFA to oxophlorins **28** gave rise to a color change from dark blue to a bright green. The internal CHs shifted from 5.5–5.8 ppm to 6.69–6.94 ppm, which is farther downfield than two of the *meso*-protons in this protonated form. These results are likely due to the positive charges on the macrocycle resulting from protonation, and the new species were attributed to dications **28**H_2^{2+}. There is no evidence for these species having an aromatic

Table 4 ^{1}H NMR shifts (ppm) for pyrazole oxophlorins **28a–c**H_2^{2+} in TFA–$CDCl_3$

	10-CH	15-CH	20-CH	21-CH	NHs
28a (R = Ph)	7.07	6.32	6.37	6.69	8.53, 9.11, 9.85
28b (R = Me)	6.97	6.21	6.72	6.90	9.25, 9.63, 10.57
28c (R = Et)	6.96	6.19	6.68	6.94	9.28, 9.71, 10.62

delocalization pathway and the *meso*-protons are too far upfield to be affected by any significant diamagnetic ring current (Table 4). The color change observed may be due to tautomerization to a cross-conjugated hydroxyporphyrin species **30** (Scheme 6). The UV-vis spectra also showed the transformation to this species, where the Soret-like band is slightly red shifted towards 400 nm and a broad intense band appears between 700 and 800 nm (Fig. 5). Further changes in the UV-vis spectrum were noted at higher concentration of TFA (see ESI section).

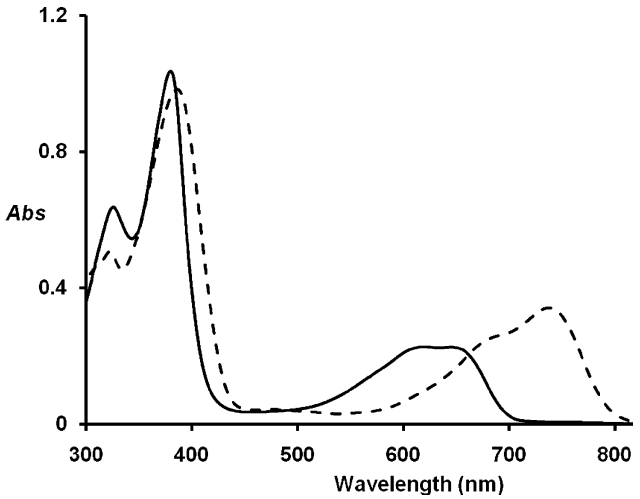
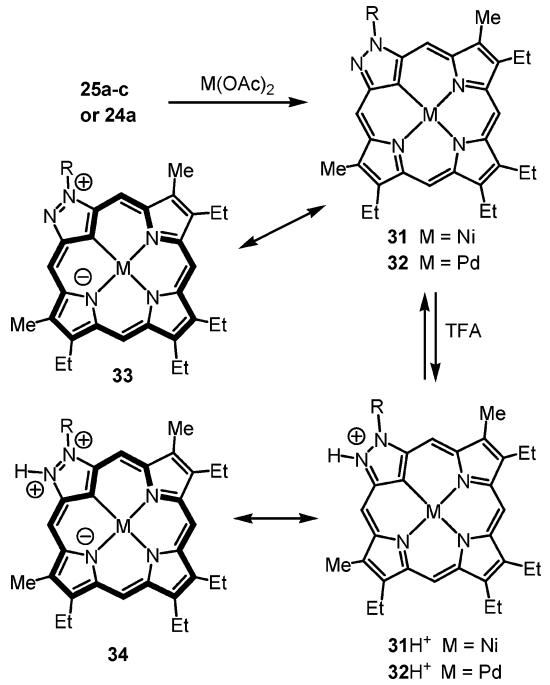


Fig. 5 UV-vis spectra of ethyl pyrazole oxophlorin **28c** in chloroform (free base, solid line) and 1% TFA–chloroform (**28c**H_2^{2+}, dashed line).

The pyrazole-containing porphyrin analogues **25** were all reacted with nickel(II) acetate in refluxing DMF to give the fully conjugated nickel(II) derivatives **31** in 41–45% yield (Scheme 7); the nickel complex for the phenyl version could also be prepared directly from the unoxidized phlorin **24a**. Similarly, porphyrin analogues **25** or phlorin **24a** could be reacted with palladium(II) acetate in refluxing acetonitrile to give the corresponding palladium(II) organometallic complexes **32** in 54–61% yield (Scheme 7). The nickel(II) complexes gave green colored solutions that produced very different UV-vis spectra from the red–brown solutions of the palladium(II) derivatives (Fig. 6 and 7). The nickel complexes showed two strong bands near 340 and 390 nm, and a series of weaker bands between 500 and 700 nm (Fig. 6). The palladium complexes gave one major Soret-like band at 414–416 nm and a series of broad absorptions extending into the far red region (Fig. 7). The proton NMR data for these Pd(II) and Ni(II) derivatives all showed similar downfield shifts for the external protons, with singlets showing up between 7.38 and 8.02 ppm corresponding to the *meso*-resonances. These derivatives showed significant downfield shifts compared to the parent porphyrinoid, possibly due to dipolar resonance contributors like **33**. However, it is somewhat surprising that there is so little difference between



Scheme 7

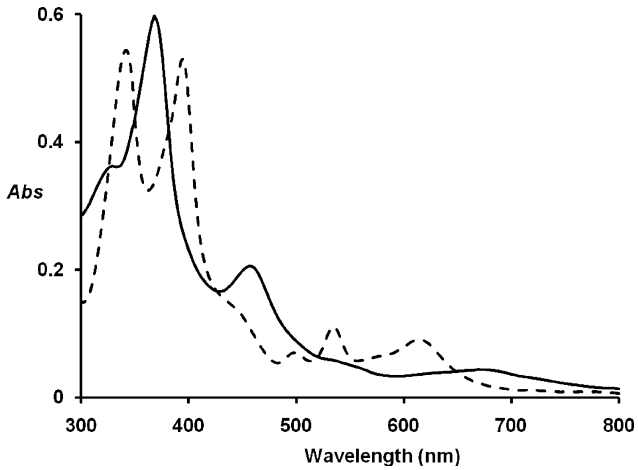


Fig. 6 UV-vis spectra of nickel(II) complex **31c** in chloroform (dashed line) and in chloroform with 500 equiv TFA (**31c**H^+, solid line).

the diatropic character as palladium(II) is a better fit for the macrocyclic core and the palladium derivatives would be expected to be more planar than the nickel complexes.[54] The substituent on the pyrazole nitrogen also had little effect on these shifts for the metal chelates, unlike the free base pyrazole porphyrins and their diprotonated dications. An X-ray crystal structure for palladium complex **32a** was obtained and this demonstrated that the macrocycle is quite planar. The structure exhibits framework bond distances that are consistent with a localized π-bonding system and the planarity was attributed to the requirements for metal binding.[55] Addition of TFA to solutions of nickel or palladium complexes **31** and **32** gave rise to simplified UV-vis absorptions with a Soret-like band at 368–377 nm for **31a–c** and 387–396 nm for the palladium derivatives **32a–c** (Fig. 6 and 7). Both series also showed a broad band running through most of the visible region. The new species were attributed to monocations

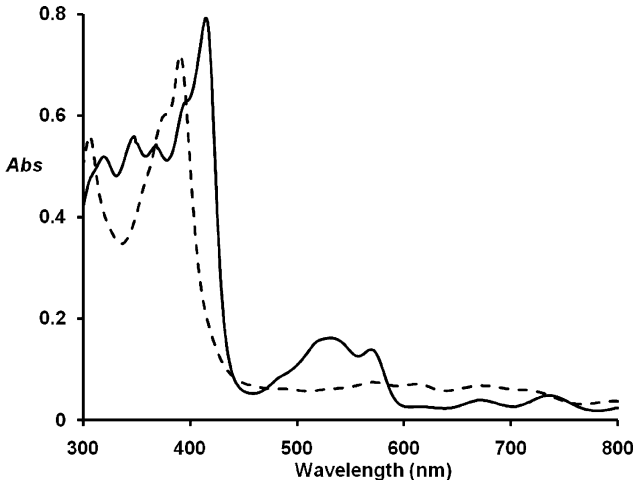


Fig. 7 UV-vis spectra of palladium(II) complex **32c** in chloroform (solid line) and in chloroform with 500 equiv TFA (**32c**H^+, dashed line).

31H^+ and **32**H^+, where protonation has taken place on the external nitrogen. The protonated species showed no signs of macrocyclic aromaticity by proton NMR spectroscopy. The *meso*-proton resonances in the nickel series **31**H^+ were shifted upfield and showed up between 6.47–6.86 ppm, while the protonated palladium complexes **32**H^+ gave these resonances slightly further upfield between 6.33—6.86 ppm. The pyrrolic methyls were also shifted upfield in all of the metalated species by 0.4–0.6 ppm, which is consistent with the formation of a nonaromatic species. These results are to be expected if the aromatic characteristics of the nonprotonated metallo-derivatives are drawn from 18π electron delocalized contributors like **33** because the protonated species would have to place two positive charges directly next to one another (structure **34**) in order to obtain this type of interaction.

Conclusion

The first fully conjugated porphyrinoid systems with pyrazole subunits have been synthesized and the nature of the *N*-substituent has been shown to be a crucial factor for the stabilization of this species. Interesting and unexpected oxidation side products were also isolated and these results provide some insights into the reactivity of this system. In addition, these diazacarbaporphyrins readily form stable organometallic derivatives and in this respect parallel the properties of the *N*-confused porphyrins.

Experimental

Dimethyl 1-ethyl-3,5-pyrazoledicarboxylate (22c)

Iodoethane (6.8 g, 43.6 mmol) was added dropwise to a stirred mixture of dimethyl 3,5-pyrazoledicarboxylate[48b] (4.00 g, 21.7 mmol) and potassium carbonate (3.0 g) in 80 mL of methyl ethyl ketone. The mixture was stirred under reflux overnight, suction filtered, and evaporated under reduced pressure. The residue was dissolved in dichloromethane, washed with water and dried over sodium sulfate. Recrystallization from hexanes gave dimethyl 1-ethyl-3,5-pyrazoledicarboxylate (4.04 g, 19.0 mmol, 88%) as white crystals, mp 48–49 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (3H, t, J = 7.2 Hz), 3.90 (3H, s), 3.93 (3H, s), 4.67 (2H, q, J = 7.2 Hz), 7.34 (1H, s); ^{13}C NMR ($CDCl_3$): δ 15.9, 48.4, 52.40, 52.42, 114.4, 133.0, 142.0, 159.7, 162.2. Anal. calcd for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found: C, 51.06; H, 5.59; N, 12.91%.

1-Ethyl-3,5-bis(hydroxymethyl)pyrazole (23c)

A solution of diethyl 1-ethyl-3,5-pyrazoledicarboxylate (4.00 g, 18.9 mmol) in sodium dried ether (100 mL) was added dropwise to a suspension of lithium aluminum hydride (3.1 g, 80 mmol) in sodium dried ether (100 mL), and the resulting mixture was stirred under reflux overnight. The excess $LiAlH_4$ was then hydrolyzed by the slow dropwise addition of methanol (25 mL), followed by the addition of saturated aqueous ammonium chloride solution (100 mL). Insoluble inorganic materials were removed by suction filtration and these were washed with ether, ethyl acetate and water. The combined filtrates were evaporated to give a solid, and traces of water were removed azeotropically with ethanol. The solid residue was then extracted using a Soxhlet apparatus with ethyl acetate to give 1-ethyl-3,5-bis(hydroxymethyl)pyrazole as a pale yellow oil (2.91 g, 19 mmol, quantitative).^{1}H NMR (D_2O): δ 1.38 (3H, t, J = 7.3 Hz), 4.16 (2H, q, J = 7.3 Hz), 4.58 (2H, s), 4.68 (2H, s), 6.35 (1H, s); ^{13}C NMR (D_2O): δ 14.9, 44.0, 53.8, 57.0, 104.6, 142.6, 150.7; HR MS (EI): Calc. for $C_7H_{12}N_2O_2$: 156.0898. Found: 156.0904.

1-Ethylpyrazole-3,5-dicarboxaldehyde (20c)

Activated MnO_2 (3.20 g, 36.8 mmol) was added to refluxing 1-ethyl-3,5-bis(hydroxymethyl)pyrazole (500 mg, 3.20 mmol) in freshly distilled 1,4-dioxane (45 mL). The mixture was stirred under reflux overnight, after which the insoluble material was removed by filtration through Celite and the residues washed with ether and dichloromethane. The filtrate was evaporated under reduced pressure and the residue further purified on a silica column eluting with dichloromethane. Upon evaporation of the solvent, the dialdehyde (287 mg, 1.89 mmol, 59%) was obtained as a white solid, mp 40–41 °C; ^{1}H NMR ($CDCl_3$) δ 1.48 (3H, t, J = 7.2 Hz), 4.65 (2H, q, J = 7.2 Hz), 7.39 (1H, s), 9.89 (1H, s), 9.99 (1H, s); ^{13}C NMR ($CDCl_3$) δ 15.4, 48.6, 114.7, 140.0, 150.4, 179.8, 185.7. Anal. calcd for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.29; H, 5.18; N, 18.01%.

8,12,13,17-Tetraethyl-2,7,18-trimethyl-2,3-diaza-21-carbaporphyrin (25b)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) was stirred for 1 min in TFA (1 mL) under N_2, then diluted with dichloromethane (99 mL) and 1-methylpyrazole-3,5-dicarbaldehyde[48a] (31 mg, 0.22 mmol) was immediately added. The reaction mixture was stirred under nitrogen in the dark for 16 h. The reaction solution was then shaken vigorously with 0.2% w/v aqueous ferric chloride solution (100 mL) for 7–8 min. The two layers were separated, the aqueous solution was extracted with chloroform, and the combined organic solutions were washed with water (100 mL) and saturated sodium bicarbonate solution (100 mL). The solvent was evaporated under reduced pressure and the dark colored residue was run through a grade 3 basic alumina column, eluting with dichloromethane. A dark fraction was collected and rechromatographed on grade 3 basic alumina, eluting initially with 50% dichloromethane–hexanes and then with

70% dichloromethane–hexanes. Green and blue colored fractions eluted initially, followed by a turquoise fraction that corresponded to the pyrazole-containing porphyrin analogue. Evaporation of the solvent gave the title compound (21.6 mg, 0.0465 mmol, 21%) as blue–green crystals, mp >300 °C. A sample was recrystallized from chloroform–ligroin to give dark blue–green crystals, mp > 300 °C; UV-vis (1% Et_3N-$CHCl_3$): λ_{max} (log ε) 323 (4.65), 393 (4.77), 639 nm (3.82); UV-vis (5 eq TFA–$CHCl_3$): λ_{max} (log ε) 403 (4.67), 526 (3.65), 567 (3.85), 711 (4.22), 787 nm (3.97); UV-vis (5% TFA–$CHCl_3$): λ_{max} (log ε) 348 (4.60), 408 (4.80), 546 (3.58), 588 (3.62), 735 nm (3.84); ^{1}H NMR ($CDCl_3$): δ 1.31–1.35 (6H, 2 overlapping triplets), 1.39–1.43 (6H, 2 overlapping triplets), 2.49 (6H, s), 2.84–2.90 (2H, 2 overlapping quartets), 2.97–3.03 (4H, 2 overlapping quartets), 4.50 (3H, s), 5.34 (1H, s), 6.75 (1H, br s), 6.89 (1H, s), 6.95 (1H, s), 7.45 (1H, s), 7.82 (1H, s); ^{1}H NMR (trace TFA–$CDCl_3$): δ 1.46–1.51 (13H, m), 2.92 (6H, 2 overlapping singlets), 3.13–3.18 (4H, 2 overlapping quartets), 3.20–3.26 (4H, 2 overlapping quartets), 4.73 (3H, s), 7.69 (1H, s), 7.73 (1H, s), 8.65 (1H, s), 8.76 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.37–1.43 (12H, s), 2.77 (1H, s), 2.79 (3H, s), 2.83 (3H, s), 3.06–3.14 (8H, m), 4.56 (3H, s), 7.47 (1H, s), 7.52 (1H, s), 8.27 (1H, s), 8.72 (1H, s); ^{13}C NMR ($CDCl_3$): δ 10.17, 10.23, 15.6, 16.4, 18.45, 18.47, 18.6, 37.7, 92.7, 94.3, 104.3, 109.0, 114.9, 138.4, 139.4, 140.05, 140.52, 141.1, 141.6, 142.8, 146.2, 146.7, 147.5, 157.5, 157.9, 166.5, 167.5; ^{13}C NMR (TFA–$CDCl_3$): δ 10.7, 10.9, 14.62, 14.66, 15.4, 15.5, 18.46, 18.50, 18.80, 18.86, 39.9, 93.6, 94.9, 95.9, 109.2, 120.9, 137.5, 142.9, 143.9, 144.3, 145.2, 145.5, 146.8, 147.3, 147.7, 147.9, 153.3, 154.8, 159.1, 159.9; HR MS (EI): Calc. for $C_{30}H_{35}N_5$: 465.2893. Found: 465.2893.

2,8,12,13,17-Pentaethyl-7,18-dimethyl-2,3-diaza-21-carbaporphyrin (25c)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) and 1-ethylpyrazole-3,5-dicarbaldehyde (36.5 mg, 0.24 mmol) were reacted under the foregoing conditions. The crude product was run through a grade 3 basic alumina column eluting with dichloromethane. A dark fraction was collected and rechromatographed on grade 3 basic alumina, eluting first with 50% dichloromethane–hexanes and then with 70% dichloromethane–hexanes. Blue colored fractions eluted initially, followed by a turquoise fraction that corresponded to the pyrazole-containing porphyrin analogue. Evaporation of the solvent and recrystallization from chloroform–ligroin gave **25c** (16 mg, 0.035 mmol, 16%) as dark blue–green crystals, mp > 300 °C. UV-vis (1% Et_3N–$CHCl_3$): λ_{max} (log ε) 324 (4.64), 393 (4.78), 594 (sh, 3.57), 643 (3.77), 694 nm (sh, 3.57); UV-vis (20 equiv TFA–$CHCl_3$): λ_{max} (log ε) 293 (4.46), 320 (4.33), 364 (4.64), 406 (4.81), 489 (3.49), 526 (3.78), 566 (3.95), 720 (4.00), 789 nm (4.27); UV-vis (1% TFA–$CHCl_3$): λ_{max} (log ε) 277 (4.25), 304 (4.34), 348 (4.59), 411 (4.81), 547 (3.38), 590 (3.42), 740 (3.83), 794 nm (sh, 3.77); ^{1}H NMR ($CDCl_3$): δ 1.32–1.36 (6H, 2 overlapping triplets), 1.42 (6H, t, J = 7.7 Hz), 1.72 (3H, t, J = 7.3 Hz), 2.505 (3H, s), 2.507 (3H, s), 2.89 (4H, q, J = 7.7 Hz), 2.98–3.04 (4H, 2 overlapping quartets), 4.85 (2H, q, J = 7.3 Hz), 5.27 (1H, s), 6.70 (1H, br s), 6.92 (1H, s), 6.98 (1H, s), 7.47 (1H, s), 7.88 (1H, s); ^{1}H NMR (trace TFA–$CDCl_3$): δ 1.43–1.47 (12H, m), 1.74 (3H, t, J = 7.3 Hz), 1.96 (1H, br s), 2.87 (3H, s), 2.88 (3H, s), 3.10–3.21 (8H, m), 4.98 (2H, q, J = 7.3 Hz), 7.60 (1H, s), 7.64 (1H, s), 8.43 (1H, s), 8.75 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.38–1.43 (12H, m), 1.71 (3H, t, J = 7.3 Hz), 2.65 (1H, s), 2.80 (3H, s), 2.84 (3H, s), 3.08–3.15 (8H, 4 overlapping quartets), 4.89 (2H, q, J = 7.3 Hz), 7.51 (1H, s), 7.56 (1H, s), 8.31 (1H, s), 8.82 (1H, s); ^{13}C NMR ($CDCl_3$): δ 10.17, 10.26, 15.7, 16.38, 16.45, 17.1, 18.44, 18.47, 18.61, 18.66, 45.7, 92.7, 94.2, 104.1, 108.9, 115.0, 137.4, 139.5, 140.0, 140.5, 141.1, 141.6, 142.8, 146.1, 146.7, 147.3, 157.4, 157.9, 166.4, 167.3; HR MS (ESI): Calc. for $C_{31}H_{37}N_5$ + H: 480.3127. Found: 480.3122.

8,12,13,17-Tetraethyl-5,22-dihydro-7,18-dimethyl-2-phenyl-2,3-diaza-21-carbaporphyrin (pyrazolophlorin 24a)

Tripyrrane dicarboxylic acid **12**[32,56] (100 mg, 0.220 mmol) was stirred with TFA (1 mL) under nitrogen for 2 min. The mixture was diluted with dichloromethane (99 mL) and 1-phenylpyrazole-3,5-dicarbaldehyde[47] (48.0 mg, 0.24 mmol) was immediately added in a single portion. The resulting solution was stirred overnight under nitrogen and then washed with water, 0.1% ferric chloride solution, water, and saturated sodium bicarbonate (the aqueous solutions were back-extracted with chloroform at each stage in the extractions). The solvent was removed under reduced pressure and the residue chromatographed on grade 3 basic alumina, eluting with dichloromethane. The solvent was removed under reduced pressure and recrystallized from chloroform–methanol to yield the pyrazole phlorin analogue (47.5 mg, 0.090 mmol, 41%) as dark blue crystals, mp >300 °C; UV-vis (1% Et_3N-$CHCl_3$): λ_{max} (log ε) 377 (4.67), 528 (sh, 4.08), 578 (4.27), 627 (4.28); ^{1}H NMR ($CDCl_3$): δ 1.16–1.25 (12H, m), 2.09 (3H, s), 2.15 (3H, s), 2.56–2.63 (4H, m), 2.64–2.74 (4H, m), 4.17 (2H, s), 5.84 (1H, s), 5.90 (1H, s), 6.34 (1H, s), 6.84 (1H, s), 7.35 (1H, t, J = 7.0 Hz), 7.44 (2H, t, J = 7.8 Hz), 7.51 (2H, d, J = 8.0 Hz), 9.17 (2H, br s); ^{13}C NMR ($CDCl_3$): δ 9.1, 9.5, 14.8, 16.0, 16.5, 17.3, 17.8, 18.27, 18.29, 18.4, 26.1, 87.2, 89.4, 104.7, 111.8, 116.7, 124.7, 127.6, 129.0, 129.2, 129.3, 132.1, 133.5, 136.2, 137.5, 140.5, 141.4, 146.0, 147.3, 147.8, 148.1, 165.1; HR MS (FAB): Calc. for $C_{35}H_{39}N_5$: 529.3205. Found: 529.3206. Anal. calcd for $C_{35}H_{39}N_5 \cdot 0.6CHCl_3$: C, 71.10; H, 6.30; N, 11.64. Found: C, 70.79; H, 6.70; N, 11.22%.

8,12,13,17-Tetraethyl-7,18-dimethyl-2-phenyl-2,3-diaza-21-carbaporphyrin (25a)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) was stirred with TFA (1 mL) under nitrogen for 2 min. The mixture was diluted with dichloromethane (99 mL) and dialdehyde **20a**[47] (48.0 mg, 0.24 mmol) was immediately added in a single portion. The resulting solution was stirred for 4 h under nitrogen and then oxidized overnight with silver acetate (77 mg, 0.46 mmol). The mixture was then washed with water, followed by saturated sodium bicarbonate (the aqueous solutions were back-extracted with chloroform at each stage in the extractions). The solvent was removed under reduced pressure and the residue chromatographed on grade 3 basic alumina, eluting with dichloromethane, to give an early turquoise fraction. The solvent was removed under reduced pressure and the residue was recrystallized from chloroform–methanol to yield the pyrazoloporphyrin (20 mg, 18%) as dark blue–green crystals, mp >300 °C; UV-vis (1% Et_3N–$CHCl_3$): λ_{max} (log ε) 318 (4.49), 395 (4.70), 595 (sh, 3.65), 643 (3.70), 695 nm (sh, 3.51); UV-vis (10 equiv TFA–$CHCl_3$): λ_{max} (log ε) 292 (sh, 4.38), 302 (4.39), 372 (sh, 4.55), 408 (4.64), 489 (sh, 3.63), 529 (3.77), 570

(3.91), 727 (3.87), 798 nm (4.05); UV-vis (1% TFA–$CHCl_3$): λ_{max} (log ε) 322 (4.45), 416 (4.66), 550 (3.72), 594 (3.72), 738 (3.73), 804 nm (sh, 3.65); ^{1}H-NMR ($CDCl_3$): δ 1.30–1.35 (6H, 2 overlapping triplets), 1.39–1.43 (6H, 2 overlapping triplets), 2.37 (3H, s), 2.49 (3H, s), 2.82–2.88 (4H, 2 overlapping quartets), 2.96–3.01 (4H, 2 overlapping quartets), 5.87 (1H, s), 6.84 (1H, s), 6.89 (1H, s), 7.19 (1H, br s), 7.39 (1H, s), 7.54 (1H, t, J = 7.7 Hz), 7.65 (2H, t, J = 7.7 Hz), 7.79 (2H, d, J = 7.3 Hz), 7.87 (1H, s); ^{1}H NMR (trace TFA–$CDCl_3$): δ 1.37–1.42 (13H, m), 2.63 (3H, s), 2.75 (3H, s), 3.02–3.12 (8H, m), 7.44 (1H, s), 7.48 (1H, s), 7.60 (1H, t, J = 7.4 Hz), 7.67 (2H, t, J = 7.4 Hz), 7.74 (2H, d, J = 7.4 Hz), 7.89 (1H, s), 8.51 (1H, s);^{1}H NMR (TFA–$CDCl_3$): δ 1.37–1.43 (12H, 4 overlapping triplets), 2.68 (3H, s), 2.84 (3H, s), 3.04–3.13 (8H, 4 overlapping quartets), 3.20 (1H, s), 7.45 (1H, s), 7.49 (1H, s), 7.63–7.76 (5H, m), 7.94 (1H, s), 8.83 (1H, s); ^{13}C NMR ($CDCl_3$): δ 10.2, 15.6, 16.32, 16.39, 18.40, 18.43, 18.58, 18.60, 92.9, 94.1, 106.1, 109.5, 114.7, 127.0, 128.3, 129.6, 138.2, 139.7, 140.1, 140.6, 141.1, 141.8, 142.7, 146.6, 147.7, 148.2, 157.9, 158.8, 167.2, 167.8; HR MS (EI): Calc. for $C_{35}H_{37}N_5$: 527.3049. Found: 527.3044.

[8,12,13,17-Tetraethyl-2,7,18-trimethyl-2,3-diaza-21-carbaporphyrinato]nickel(II) (31b)

Porphyrin analogue **25b** (34 mg, 0.0731 mmol) and nickel(II) acetate tetrahydrate (36 mg; 0.145 mmol; 2 equiv) were reacted in DMF (37 mL) and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, and washed with water. The organic layer was separated, evaporated to dryness and chromatographed on grade 3 basic alumina, eluting with chloroform, to give a dark green band. Recrystallization from chloroform–methanol gave the nickel complex (17.0 mg, 0.0326 mmol, 45%) as dark green crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 340 (4.64), 393 (4.62), 497 (3.72), 533 (3.91), 614 (3.85), 731 (2.86), 870 nm (2.83); UV-vis (1% TFA–$CHCl_3$): λ_{max} (log ε) 325 (4.44), 370 (4.70), 683 (3.69), 842 nm (3.08); ^{1}H NMR ($CDCl_3$): δ 1.34–1.39 (6H, 2 overlapping triplets), 1.42–1.47 (6H, 2 overlapping triplets), 2.54 (3H, s), 2.56 (3H, s), 2.93–3.07 (8H, m), 4.53 (3H, s), 7.43 (1H, s), 7.47 (1H, s), 7.56 (1H, s), 7.96 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.16–1.21 (6H, 2 overlapping triplets), 1.27 (6H, t, J = 7.5 Hz), 2.13 (3H, s), 2.15 (3H, s), 2.53–2.58 (4H, 2 overlapping quartets), 2.63–2.67 (4H, 2 overlapping quartets), 4.31 (3H, s), 6.47 (2H, s), 6.52 (1H, s), 6.78 (1H, s); ^{13}C NMR ($CDCl_3$): δ 10.46, 10.54, 15.6, 15.7, 16.70, 16.75, 18.65, 18.70, 18.8, 37.7, 95.3, 96.2, 102.0, 109.6, 113.6, 137.7, 138.9, 139.8, 140.7, 141.4, 144.61, 144.62, 146.7, 149.2, 149.8, 153.4, 154.1, 158.5, 159.2; HR MS (EI): Calc. for $C_{30}H_{33}N_5Ni$: 521.2089. Found: 521.2093.

[2,8,12,13,17-Pentaethyl-7,18-dimethyl-2,3-diaza-21-carbaporphyrinato]nickel(II) (31c)

Porphyrin analogue **25c** (9.0 mg, 0.017 mmol) and nickel(II) acetate tetrahydrate (12 mg, 0.047 mmol) were reacted in DMF (10 mL) and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, and washed with water. The organic layer was separated, evaporated to dryness and chromatographed on grade 3 basic alumina, eluting with chloroform, to give a dark green band. Recrystallization from chloroform–methanol gave the nickel complex (4.3 mg, 0.0073 mmol, 41%) as dark green crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 342 (4.61), 394 (4.60), 499 (3.73), 535 (3.92), 613 nm (3.83); UV-vis (500 eq TFA–$CHCl_3$): λ_{max} (log ε) 368 (4.65), 458 (4.19), 670 nm (3.52); ^{1}H NMR ($CDCl_3$): δ 1.35–1.39 (6H, 2 overlapping triplets), 1.44–1.47 (6H, 2 overlapping triplets), 1.81 (3H, t, J = 7.3 Hz), 2.57 (3H, s), 2.58 (3H, s), 2.95–3.08 (8H, 4 overlapping quartets), 4.90 (2H, q, J = 7.4 Hz), 7.46 (1H, s), 7.50 (1H, s), 7.62 (1H, s), 8.02 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.18–1.23 (6H, 2 overlapping triplets), 1.26–1.30 (6H, 2 overlapping triplets), 1.64 (3H, t, J = 7.3 Hz), 2.17 (3H, s), 2.22 (3H, s), 2.58–2.62 (4H, 2 overlapping quartets), 2.66–2.70 (4H, 2 overlapping quartets), 4.73 (2H, quartet, J = 7.3 Hz), 6.54 (3H, br s), 6.86 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.5, 10.6, 15.6, 15.7, 16.74, 16.76, 16.9, 18.67, 18.72, 18.8, 45.6, 53.6, 95.3, 96.2, 101.8, 109.6, 113.7, 136.7, 138.9, 139.9, 140.7, 141.5, 144.60, 144.63, 146.7, 149.1, 149.8, 153.3, 154.0, 158.4, 159.1; HR MS (EI): Calc. for $C_{31}H_{35}N_5Ni$ 535.2246. Found: 535.2232.

[8,12,13,17-Tetraethyl-7,18-dimethyl-2-phenyl-2,3-diaza-21-carbaporphyrinato]nickel(II) (31a)

Two equivalents of nickel(II) acetate tetrahydrate (12.0 mg, 0.048 mmol) were added to a solution of 2,3-diaza-21-carbaporphyrin **25a** (12.7 mg, 0.024 mmol) in DMF (13 mL), and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, and washed with water. The organic layer was separated, evaporated to dryness and chromatographed on grade 3 basic alumina, eluting with chloroform, to give a dark green band. The solvent was removed under reduced pressure and the residue recrystallized from chloroform–methanol to yield the nickel(II) complex (6.0 mg, 43%) as dark purple crystals, mp >300 °C; (UV-vis $CHCl_3$): λ_{max} (log ε) 343 (4.66), 394 (4.67), 498 (4.08), 535 (4.18), 624 (4.06), 883 nm (3.84); (UV-vis TFA–$CHCl_3$): λ_{max} (log ε) 377 (4.71), 529 (3.98), 632 (4.01), 883 nm (3.83); ^{1}H-NMR ($CDCl_3$): δ 1.33–1.39 (6H, m), 1.43–1.47 (6H, m), 2.53 (3H, s), 2.62 (3H, s), 2.92–3.06 (8H, 2 overlapping quartets), 7.38 (1H, s), 7.45 (1H, s), 7.54 (1H, t, J = 8.0 Hz), 7.58 (1H, s), 7.68 (2H, t, J = 7.8 Hz), 7.86 (2H, d, J = 7.6 Hz), 8.02 (1H, s); ^{1}H-NMR (TFA–CDCl3): δ 1.18–1.22 (6H, m), 1.26–1.31 (6H, m), 2.06 (3H, s), 2.17 (3H, s), 2.58–2.68 (8H, m), 6.50 (3H, br s), 6.83 (1H, br s), 7.57 (2H, m), 7.66–7.71 (3H, m); ^{13}C NMR ($CDCl_3$): δ 10.4, 10.5, 15.4, 15.5, 15.6, 16.6, 18.66, 18.71, 18.8, 29.9, 95.5, 96.1, 104.1, 108.6, 110.8, 113.6, 126.5, 128.3, 129.6, 137.3, 139.3, 140.0, 140.4, 141.1, 141.5, 144.6, 144.9, 145.7, 148.3, 149.7, 151.1, 154.3, 154.4, 158.9, 160.0; HR MS (EI): Calc. for $C_{35}H_{35}N_5Ni$: 583.2246. Found: 583.2248. Anal. calcd for $C_{35}H_{35}N_5Ni{\cdot}0.5H_2O$: C, 70.84; H, 6.11; N, 11.79. Found: C, 70.56; H, 6.11; N, 11.33%.

[8,12,13,17-Tetraethyl-2,7,18-trimethyl-2,3-diaza-21-carbaporphyrinato]palladium(II) (32b)

Pyrazole porphyrin analogue **25b** (21.0 mg, 0.045 mmol) was reacted with palladium(II) acetate (10.0 mg; 0.045 mmol) in acetonitrile (65 mL) and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, washed with water, and the organic layer separated and then evaporated to dryness. Following chromatography on grade 3 basic alumina, eluting with chloroform, the product was recrystallized from chloroform–methanol to give the palladium complex (15.7 mg,

0.0276 mmol, 61%) as dark purplish brown crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 320 (4.45), 347 (4.48), 368 (4.47), 414 (4.63), 533 (3.93), 570 (3.87), 674 (3.35), 738 (3.44), 816 nm (3.24); UV-vis (1% TFA–$CHCl_3$): λ_{max} (log ε) 304 (4.52), 370 (sh, 4.63), 387 (4.96), 576 (3.64), 817 nm (3.47); ^{1}H NMR ($CDCl_3$): δ 1.38–1.42 (6H, 2 overlapping triplets), 1.44–1.48 (6H, 2 overlapping triplets), 2.62 (3H, s), 2.64 (3H, s), 2.94–3.06 (8H, m), 4.59 (3H, s), 7.41 (1H, s), 7.45 (1H, s), 7.63 (1H, s), 7.97 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.19–1.29 (12H, m), 2.22 (3H, s), 2.23 (3H, s), 2.56–2.67 (8H, m), 4.34 (3H, s), 6.41 (2H, s), 6.49 (1H, s), 6.86 (1H, s); ^{13}C NMR ($CDCl_3$): δ 10.37, 10.45, 15.5, 15.6, 16.7, 16.8, 18.62, 18.64, 18.8, 18.9, 37.7, 95.6, 96.8, 104.3, 115.7, 119.6, 135.7, 137.8, 138.6, 140.1, 140.7, 143.85, 143.92, 144.2, 146.6, 147.4, 152.1, 152.5, 155.5, 156.2; HR MS (EI): Calc. for $C_{30}H_{33}N_5Pd$: 569.1771. Found: 569.1767.

[2,8,12,13,17-Pentaethyl-7,18-dimethyl-2,3-diaza-21-carbaporphyrinato]palladium(II) (32c)

Pyrazole porphyrin analogue **25c** (9.0 mg, 0.017 mmol) was reacted with palladium(II) acetate (6.0 mg, 0.026 mmol) in acetonitrile (40 mL) and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, washed with water, and the organic layer separated and then evaporated to dryness. Following chromatography on grade 3 basic alumina, eluting with chloroform, the product was recrystallized from chloroform–methanol to give the palladium complex (5.3 mg, 0.0089 mmol, 54%) as dark purplish brown crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 319 (4.49), 347 (4.52), 368 (4.51), 415 (4.68), 532 (3.98), 569 (3.91), 669 (3.35), 736 nm (3.45); UV-vis (500 eq TFA–$CHCl_3$): λ_{max} (log ε) 306 (4.54), 391 (4.65), 571 (3.67), 669 nm (3.63); ^{1}H NMR ($CDCl_3$): δ 1.38–1.42 (6H, 2 overlapping triplets), 1.45–1.48 (6H, 2 overlapping triplets), 1.83 (3H, t, J = 7.3 Hz), 2.63 (3H, s), 2.64 (3H, s), 2.99–3.07 (8H, 4 overlapping quartets), 4.91 (2H, q, J = 7.3 Hz), 7.42 (1H, s), 7.45 (1H, s), 7.62 (1H, s), 8.02 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.19–1.24 (6H, 2 overlapping triplets), 1.27 (6H, t, J = 7.7 Hz), 1.63 (3H, t, J = 7.3 Hz), 2.16 (3H, s), 2.21 (3H, s), 2.54–2.64 (8H, 4 overlapping quartets), 4.66 (2H, q, J = 7.3 Hz), 6.33 (2H, br s), 6.41 (1H, br s), 6.57 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.4, 10.5, 15.5, 15.7, 16.7, 16.8, 17.0, 18.6, 18.86, 18.95, 45.7, 95.5, 96.8, 104.1, 115.7, 119.6, 134.7, 137.8, 138.6, 140.0, 140.7, 143.84, 143.89, 144.3, 146.5, 147.4, 152.0, 152.5, 155.3, 156.1; HR MS (EI): Calc. for $C_{31}H_{35}N_5Pd$: 583.1927. Found: 583.1912.

[8,12,13,17-Tetraethyl-7,18-dimethyl-2-phenyl-2,3-diaza-21-carbaporphyrinato]palladium(II) (32a)

Palladium(II) acetate (5.4 mg, 0.024 mmol) was added to a solution of 2,3-diaza-21-carbaporphyrin **25a** (12.7 mg, 0.024 mmol) in acetonitrile (40 mL), and the solution was stirred under reflux for 30 min. The solution was cooled, diluted with chloroform, washed with water, and the organic layer separated and then evaporated to dryness. The residue was chromatographed with grade 3 basic alumina, eluting with chloroform, and the product was collected as a reddish/brown band. The solvent was evaporated to dryness and the residue recrystallized from chloroform–methanol to yield the palladium(II) complex (8.9 mg, 59%) as dark purple crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 416 (4.68), 523 (4.18), 575 (4.11), 672 (3.86), 731 (3.87), 817 (3.78), 883 nm (3.84); UV-vis (TFA–$CHCl_3$): λ_{max} (log ε) 396 (4.66), 483 (4.09), 522 (4.16), 544 (4.15), 678 (3.88), 742 (3.88), 883 nm (3.85); ^{1}H-NMR (CDCl3): δ 1.34–1.48 (12H, 4 overlapping triplets), 2.53 (3H, s), 2.62 (3H, s), 2.96–3.05 (8H, m), 7.35 (1H, s), 7.40 (1H, s), 7.57 (1H, t, J = 7.6 Hz), 7.61 (1H, s), 7.69 (2H, t, J = 7.8 Hz), 7.90 (2H, d, J = 7.6 Hz), 8.02 (1H, s); ^{1}H-NMR (TFA–$CDCl_3$): δ 1.18–1.23 (6H, 2 overlapping triplets), 1.25–1.29 (6H, 2 overlapping triplets), 2.09 (3H, s), 2.20 (3H, s), 2.54–2.64 (8H, 4 overlapping quartets), 6.33 (3H, br s), 6.79 (1H, br s), 7.58–7.60 (2H, m), 7.66–7.68 (3H, m); ^{13}C NMR ($CDCl_3$): δ 10.9, 16.3, 16.4, 16.6, 16.8, 17.4, 19.17, 19.22, 19.5, 30.0, 96.0, 96.6, 106.7, 113.3, 119.4, 121.7, 127.2, 128.8, 130.0, 131.2, 135.5, 136.2, 136.9, 138.3, 139.3, 140.0, 140.5, 142.2, 143.4, 143.8, 144.7, 145.3, 146.0, 147.3, 149.3, 150.5; HR MS (EI): Calc. for $C_{35}H_{35}N_5Pd$: 631.1927. Found: 631.1930.

8,12,13,17-Tetraethyl-5,22-dihydro-2,7,18-trimethyl-5-oxo-2,3-diaza-21-carbaporphyrin (pyrazolo-oxophlorin 28b)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) was stirred for 1 min in TFA (1 mL) under N_2, then diluted with dichloromethane (99 mL) and 1-methylpyrazole-3,5-dicarbaldehyde[48a] (33 mg, 0.24 mmol) was immediately added. The reaction mixture was stirred under nitrogen in the dark for 4 h and then was oxidized overnight by continued stirring with silver acetate (77 mg, 0.46 mmol). The solution was then washed with water (150 mL) and saturated sodium bicarbonate solution (150 mL), back extracting at each stage with chloroform. The solvent was evaporated under reduced pressure and the dark colored residue was run through a grade 3 basic alumina column eluting with dichloromethane. A dark fraction was collected and rechromatographed on grade 3 basic alumina eluting with 50% dichloromethane–hexanes. Unidentified green and blue colored fractions eluted initially followed by a turquoise fraction that corresponded to the pyrazole-containing porphyrin analogue, and finally a dark blue fraction containing the oxophlorin product. Evaporation of the solvent and recrystallization from chloroform–ligroin gave **28b** (3.4 mg, 0.0071 mmol, 3.2%) as dark blue crystals, mp >300 °C; UV-vis (0.5% Et_3N-$CHCl_3$): λ_{max} (log ε) 326 (4.52), 380 (4.72), 62o (4.06), 651 nm (sh, 4.05); UV-vis (1% TFA–$CHCl_3$): λ_{max} (log ε) 322 (4.42), 386 (4.71), 681 (sh, 4.10), 734 nm (4.22); ^{1}H NMR ($CDCl_3$): δ 1.21–1.28 (12H, 4 overlapping triplets), 2.27 (3H, s), 2.63 (3H, s), 2.62–2.74 (6H, 3 overlapping quartets), 2.80 (2H, q, J = 7.7 Hz), 4.10 (3H, s), 5.56 (1H, s), 6.05 (1H, s), 6.13 (1H, s), 6.89 (1H, s), 8.94 (1H, br s), 9.17 (1H br s); ^{1}H NMR (trace TFA–$CDCl_3$): δ 1.19–1.33 (12H, m), 2.36 (3H, s), 2.55 (3H, s), 2.68–2.83 (8H, m), 4.16 (3H, s), 6.03 (1H, br s), 6.14 (1H, s), 6.71 (1H, br s), 6.97 (1H, s), 10.12 (1H, br s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.22–1.34 (12H, 4 overlapping triplets), 2.37 (3H, s), 2.58 (3H, s), 2.70–2.84 (8H, m), 4.28 (3H, s), 6.21 (1H, s), 6.72 (1H, s), 6.90 (1H, s), 6.97 (1H, s), 9.25 (1H, br s), 9.63 (1H, br s), 10.57 (1H br s);^{13}C NMR ($CDCl_3$): δ 9.7, 11.5, 15.0, 15.9, 16.5, 17.1, 17.6, 17.9, 18.37, 18.44, 87.3, 89.4, 93.5, 108.7, 130.6, 131.3 132.5, 134.0, 134.2, 140.0, 140.44, 140.47, 146.1, 146.9, 148.7, 149.6, 153.0, 168.7, 176.2; HR MS (ESI): Calc. for $C_{30}H_{35}N_5O$ + H: 482.2920. Found: 482.2915.

2,8,12,13,17-Pentaethyl-5,22-dihydro-7,18-dimethyl-5-oxo-2,3-diaza-21-carbaporphyrin (pyrazolo-oxophlorin 28c)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) was stirred for 1 min in TFA (1 mL) under nitrogen, then diluted with dichloromethane (99 mL) and dialdehyde **20c** (36.5 mg, 0.24 mmol) was immediately added. The reaction mixture was stirred under nitrogen in the dark for 4 h, silver acetate (77 mg, 0.46 mmol) was added, and stirring was continued overnight. The solution was then washed with water (150 mL) and saturated sodium bicarbonate solution (150 mL), back extracting with chloroform each time. The solvent was evaporated under reduced pressure and the dark colored residue was run through a grade 3 basic alumina column eluting with dichloromethane. A dark fraction was collected and rechromatographed on grade 3 basic alumina eluting with 50% dichloromethane–hexanes. Green and blue colored fractions eluted initially, followed by a turquoise fraction that corresponded to the pyrazole-containing porphyrin analogue, and finally a dark blue fraction containing the oxophlorin product. Evaporation of the solvent and recrystallization from chloroform–ligroin gave **28c** (15 mg, 0.030 mmol, 14%) as dark blue crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 325 (4.52), 380 (4.72), 618 nm (4.06); UV-vis (10% TFA–$CHCl_3$): λ_{max} (log ε) 388 (4.69), 734 nm (4.12); ^{1}H NMR ($CDCl_3$): δ 1.21–1.28 (12H, 4 overlapping triplets), 1.51 (3H, t, J = 7.3 Hz), 2.27 (3H, s), 2.64 (3H, s), 2.62–2.75 (6H, 3 overlapping quartets), 2.80 (2H, q, J = 7.6 Hz), 4.45 (2H, q, J = 7.3 Hz), 5.50 (1H, s), 6.06 (1H, s), 6.15 (1H, s), 6.90 (1H, s), 8.91 (1H, br s), 9.13 (1H, br s); ^{1}H NMR (trace TFA–$CDCl_3$): δ 1.19–1.27 (9H, 3 overlapping triplets), 1.31 (3H, t, J = 7.7 Hz), 1.52 (3H, t, J = 7.3 Hz), 2.37 (3H, s), 2.56 (3H, s), 2.68–2.83 (8H, 4 overlapping quartets), 4.46 (2H, q, J = 7.3 Hz), 5.84 (1H, s), 6.11 (1H, s), 6.67 (1H, s), 6.98 (1H, s), 9.73 (1H, br s), 10.15 (1H, br s); ^{1}H NMR (TFA–$CDCl_3$): δ 1.21–1.27 (9H, 3 overlapping triplets), 1.31 (3H, t, J = 7.7 Hz), 1.58 (3H, t, J = 6.8 Hz), 2.36 (3H, s), 2.57 (3H, s), 2.69–2.83 (8H, m), 4.62 (2H, q, J = 7.3 Hz), 6.19 (1H, s), 6.68 (1H, s), 6.94 (1H, br s), 6.96 (1H, s), 9.28 (1H, br s), 9.71 (1H, s), 10.62 (1H, s); ^{13}C NMR ($CDCl_3$): δ 9.7, 11.5, 15.0, 15.89, 15.90, 16.5, 17.1, 17.6, 17.9, 18.37, 18.44, 45.9, 87.4, 89.3, 93.4, 108.6, 130.6, 131.2, 132.5, 134.0, 134.2, 139.0, 140.35, 140.44, 145.9, 146.9, 148.9, 149.7, 153.0, 168.6, 176.3; IR: ν_{CO} 1625 cm^{-1}; HR MS (ESI): Calc. for $C_{31}H_{37}N_5O$ + H: 496.3076. Found: 496.3067.

2,8,12,13,17-Pentaethyl-20,22-dihydro-7,18-dimethyl-20-oxo-2,3-diaza-21-carbaporphyrin (pyrazolo-oxophlorin 29)

An early blue colored fraction from the previous experiment corresponded to the less favored pyrazole-containing oxophlorin analogue. Evaporation of the solvent gave the oxophlorin product **29** (1.0 mg, 0.002 mmol, 1%) as dark blue crystals that were somewhat unstable in solution. UV-vis ($CHCl_3$): λ_{max} (relative intensity) 326 (0.81), 381 (1.00), 637 (0.23), 669 nm (0.23); ^{1}H NMR ($CDCl_3$): δ 1.22–1.28 (12H, 4 overlapping triplets), 1.56 (3H, t, J = 7.3 Hz), 2.29 (3H, s), 2.65 (3H, s), 2.65–2.76 (6H, 3 overlapping quartets), 2.82 (2H, q, J = 7.6 Hz), 4.74 (2H, q, J = 7.3 Hz), 5.36 (1H, s), 6.05 (1H, s), 6.69 (1H, s), 6.86 (1H, s), 8.83 (1H, br s); HR MS (EI): Calc. for: $C_{31}H_{37}N_5O$: 495.2998. Found: 495.2991.

8,12,13,17-Tetraethyl-5,22-dihydro-7,18-dimethyl-5-oxo-2-phenyl-2,3-diaza-21-carbaporphyrin (pyrazolo-oxophlorin 28a)

Tripyrrane dicarboxylic acid **12**[32d,56] (100 mg, 0.22 mmol) was stirred with TFA (1 mL) under nitrogen for 2 min. The mixture was diluted with dichloromethane (99 mL) and dialdehyde **20a**[47] (48.0 mg, 0.24 mmol) was immediately added in a single portion. The resulting solution was stirred for 4 h under nitrogen and then oxidized overnight with silver acetate (77 mg, 0.46 mmol). The mixture was then washed with water followed by saturated sodium bicarbonate (the aqueous solutions were back-extracted with chloroform at each stage in the extractions). The solvent was removed under reduced pressure and the residue chromatographed on grade 3 basic alumina, eluting with dichloromethane, to give the oxophlorin as a late dark blue fraction. The solvent was removed under reduced pressure and recrystallized from chloroform–ligroin to yield the pyrazole oxophlorin analogue (10.7 mg, 0.0020 mmol, 9%) as dark blue crystals, mp >300 °C; UV-vis ($CHCl_3$): λ_{max} (log ε) 324 (4.59), 381 (4.77), 623 (4.10); (20% TFA–$CHCl_3$): λ_{max} (log ε) 324 (4.50), 394 (4.70), 737 (4.11); ^{1}H-NMR ($CDCl_3$): δ 1.22–1.28 (12H, 4 overlapping triplets), 2.16 (3H, s), 2.65 (3H, s), 2.66 (4H, q, J = 7.7 Hz), 2.73 (2H, q, J = 7.7 Hz), 2.81 (2H, q, J = 7.7 Hz), 5.79 (1H, s), 6.07 (1H, s), 6.14 (1H, s), 6.90 (1H, s), 7.46 (1H, t, J = 7.7 Hz), 7.53 (2H, t, J = 7.7 Hz), 7.64 (2H, d, J = 7.3 Hz), 9.08 (1H, br s), 9.28 (1H, br s); ^{1}H-NMR (trace TFA–$CDCl_3$): δ 1.20–1.28 (9H, m), 1.32 (3H, t, J = 7.7 Hz), 2.27 (3H, s), 2.59 (3H, s), 2.68–2.74 (4H, 2 overlapping quartets), 2.78–2.83 (4H, 2 overlapping quartets), 6.09 (1H, s), 6.17 (1H, s), 6.55 (1H, s), 7.00 (1H, s), 7.53–7.61 (5H, m), 9.69 (1H, br s), 10.11 (1H, br s); ^{1}H-NMR (TFA–$CDCl_3$): δ 1.24–1.30 (9H, m), 1.33 (3H, t, J = 7.7 Hz), 2.32 (3H, s), 2.66 (3H, s), 2.71–2.90 (8H, m), 6.32 (1H, s), 6.37 (1H, s), 6.69 (1H, s), 7.07 (1H, s), 7.49–7.56 (3H, m), 7.63–7.68 (2H, m), 8.53 (1H, br s), 9.11 (1H, br s), 9.85 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.7, 11.6, 14.9, 15.9, 16.5, 17.1, 17.6, 17.9, 18.37, 18.45, 89.0, 89.4, 93.9, 108.5, 126.5, 128.6, 129.4, 130.9, 131.5, 132.4, 134.3, 139.7, 140.2, 140.4, 140.5, 146.0, 147.0, 149.9, 150.1, 153.1, 168.9, 176.0; HR MS (ESI): Calc. for $C_{35}H_{37}N_5O$ + H: 544.3076. Found: 544.3073.

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