# Conjugated Macrocycles Related to the Porphyrins. Part 16.[1] Synthesis of Hexa- and Heptaalkyl-Substituted Inverted or N-Confused Porphyrins by the "3 + 1" Methodology

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Pyrrole-2,4-dicarboxaldehydes **13a**−**c** were condensed with a tripyrrane dicarboxylic acid **12** in 1% TFA−$CH_2Cl_2$ to give, following oxidation with 0.1% $FeCl_3$, a series of "etio-type" N-confused porphyrins **14a**−**c**. Excellent yields were obtained when the diformylpyrrole possessed a 5-alkyl substituent, although the products were most easily isolated in the form of their hydrochloride salts. Addition of TFA to the free base inverted porphyrins led to initial protonation onto the external nitrogen atom to produce monocations **19** and further acidification afforded a dications **21**. UV−vis spectroscopy showed strong Soret bands for **14**, **19**, and **21**, features that are associated with fully aromatic porphyrinoid systems, and proton NMR spectroscopy confirmed the presence of powerful diamagnetic ring current where the *meso*-protons resonated near 10 ppm while the interior CH was strongly shielded to −6 ppm for the free base structures and −4 ppm for the dications **21**. Taking into account the effect of the introduction of delocalized positive charges within the protonated species, the diatropic character of the macrocyclic system appeared to be slightly decreased upon protonation. Proton NMR spectroscopy demonstrated that a single tautomer was favored for the free base porphyrinoids **14** and furthermore NH exchange was slow on the NMR time scale even at room temperature. While this is not a factor for the dications, deuterium exchange was noted by NMR spectroscopy for the interior CH upon addition of TFA-*d*, indicating that C-protonated species are present in equilibrium with **21** and/or **19**. Addition of a series of mineral acids (HF, HCl, HBr, HI, and $HNO_3$) to solutions of **14** produced dications with significantly different UV−vis and NMR spectra, and these data indicate that strong ion pairing is occurring at the external NH. Reaction of **14** with nickel(II) acetate in DMF at 145 °C afforded a relatively unstable nickel complex **25**. Proton NMR spectra for **25** indicated that the macrocyclic ring current was considerably reduced, as would be expected for a cross-conjugated structure of this type. However, addition of TFA resulted in an unprecedented C-protonation that produced a new nickel(II)-containing aromatic species **29** that slowly demetalated to form the dication **21**. The new results demonstrate that the alkyl-substituted inverted porphyrin series has many unique properties and the improved synthetic procedures will facilitate future investigations.

## Introduction

In 1935, Rothemund reported that aldehydes reacted with pyrrole in the presence of pyridine at elevated temperatures in a sealed tube to produce porphyrin products (Scheme 1).[2] Over the years, many modifications of the "Rothemund reaction" have been developed including the Adler−Longo conditions (refluxing propionic acid)[3] and the Lindsey protocols (catalytic $BF_3$ or TFA under equilibrium conditions, followed by oxidation with an electron-deficient quinone)[4] in order to generate symmetrically substituted porphyrins such as *meso*-tetraphenylporphyrin (**1**, Ar = Ph; TPP).[5,6] It is perhaps surprising that this approach should produce the porphyrin system at all, and indeed the cyclic oligomers with five or six pyrrolic units (pentaphyrins and hexaphyrins) are virtually never observed in these reactions.[7] The large number of individual steps required (eight carbon−carbon bonds must be generated) and the number of possible intermediates involved has led to this type of chemistry being described as a "kinetic and thermodynamic nightmare".[8] In fact, additional products were discerned in Rothemund's early work, and the possibility

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(1) Part 15: Lash, T. D.; Romanic, J. L.; Hayes, M. J.; Spence, J. D. *Chem. Commun.* **1999**, 819.

(2) Rothemund, P. *J. Am. Chem. Soc.* **1935**, *57*, 2010. Rothemund, P. *J. Am. Chem. Soc.* **1936**, *58*, 625. Rothemund, P.; Menotti, A. R. *J. Am. Chem. Soc.* **1941**, *63*, 267.

(3) Adler, A. D.; Longo, F. R.; Shergalis, W. *J. Am. Chem. Soc.* **1964**, *86*, 3145. Adler, A. D.; Sklar, L.; Longo, F. R.; Finarelli, J. D.; Finarelli, M. G. *J. Heterocycl. Chem.* **1968**, *5*, 669.

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(5) Both the Alder−Longo and Lindsey conditions have been adapted for the synthesis of sterically crowded porphyrin systems: Dolphin, D. *J. Heterocycl. Chem.* **1970**, *7*, 275. Evans, B.; Smith, K. M.; Fuhrhop, J.-H. *Tetrahedron Lett.* **1977**, 443. Barkigia, K. M.; Berber, M. D.; Fajer, J.; Medforth, C. J.; Renner, M. W.; Smith, K. M. *J. Am. Chem. Soc.* **1990**, *112*, 8851. Lash, T. D.; Chandrasekar, P. *J. Am. Chem. Soc.* **1996**, *118*, 8767.

(6) For other recent syntheses of *meso*-tetrasubstituted porphyrins, see: Gonsalves, A. M. d'A. R.; Peira, M. M. *J. Heterocycl. Chem.* **1985**, *22*, 931. Gonsalves, A. M. d'A. R.; Varejao, J. M. T. B.; Peira, M. M. *J. Heterocycl. Chem.* **1991**, *28*, 635. Kuroda, Y.; Murase, H.; Suzuki, Y.; Ogoshi, H. *Tetrahedron Lett.* **1989**, *30*, 2411. Onaka, M.; Shinoda, T.; Izumi, Y.; Nolen, E. *Chem. Lett.* **1993**, 117. Laszlo, P.; Luchetti, J. *Chem. Lett.* **1993**, 449. Gradillas, A.; Campo, C. del; Sinisterra, J. V.; Llama, E. F. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2611.

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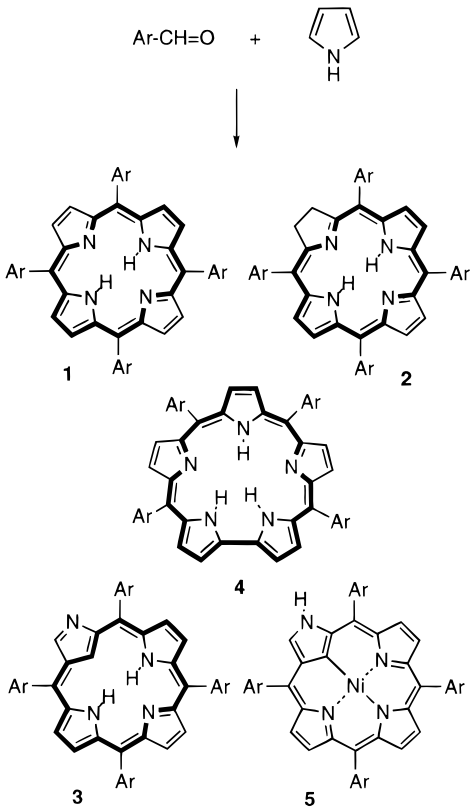
**Scheme 1**




of porphyrin isomer formation (the proposed structure would now be considered to be a disfavored porphyrin tautomer) was considered.[9] A major biproduct in TPP synthesis was later identified as the corresponding 2,3-dihydroporphyrin or chlorin **2**.[10] While the Rothemund reaction became a mainstay for porphyrin synthesis, no further examples of macrocyclic systems arising from this chemistry were characterized over the following 60 years. This situation was to change abruptly in 1994 when two different groups independently described the isolation of porphyrin isomer **3** with an inverted pyrrole ring,[11,12] while a *meso*-tetraphenylsapphyrin **4** was subsequently isolated and characterized by Latos−Grazynski and coworkers (Scheme 1).[13] The inverted porphyrin system **3**, for which the designation "N-confused porphyrin" has been coined by Furuta et al.,[12] immediately captured the imagination of porphyrin chemists for a variety of reasons. The formation of this system involves electrophilic attack at seven α- and one *β*- positions on the four pyrrolic units that give rise to the porphyrinoid structure. In this respect, the origin of **3** is perhaps not so very surprising as the electrophilic substitution chemistry of pyrrole commonly gives rise to some *β*-substitution products in addition to the more favored α-products.[14] On the other hand, given the widespread use of the Rothemund chemistry over such a long period of time it is astounding that this system was not observed earlier. The inverted porphyrin system represented a new type of porphyrin isomer, an area of study that has attracted widespread attention.[15] Further, the N-confused porphyrins show longer wavelength absorptions than regular porphyrins, a feature that is much sought after for applications in material science[16] and medicine.[17] Still more intriguingly, porphyrin isomer **3** (Ar = *p*-$MeC_6H_4$) was found to react under mild conditions with nickel(II) acetate to generate the stable organometallic species **5**.[11] The ease of carbon−metal bond formation makes this chemistry quite remarkable, and a theoretical study has made a case for stabilized carbenoid characteristics being responsible for the observed reactivity.[18] Some additional, highly unusual chemistry has been reported for the N-confused porphyrins,[19−22] including substitutions onto the internal carbon atom,[20,21] and these observations suggest that this system will produce a rich and unique chemistry that will most likely lead to novel applications.

Shortly after the first reports on the N-confused porphyrins appeared in the literature, a series of carbaporphyrinoid structures (e.g., **6**−**10**) were synthesized using a stepwise "3 + 1" methodology.[23−32] These por-

(7) For a discussion on the preferential formation of porphyrins, rather than oligopyrrolic expanded systems, in a slightly different context, see: Bringmann, G.; Franck, B. *Liebigs Ann. Chem.* **1982**, 1261 and 1272. The selectivity for tetrameric species does not hold true; however, in the synthesis of thiophene-containing analogues of the porphyrins where tetra- and pentathiophene cyclocondensation products are formed by reacting 3,4-diethyl-2-(hydroxymethyl)thiophene with *p*-toluenesulfonic acid in nitromethane: Vogel, E.; Pohl, M.; Herrmann, A.; Wiss, T.; König, C.; Lex, J.; Gross, M.; Gisselbrecht, J. P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1520. For syntheses of pentaphyrins and hexaphyrins, see: Rexhausen, H.; Gossauer, A. *J. Chem. Soc., Chem. Commun.* **1983**, 275. Gossauer, A. *Bull. Soc. Chim. Belg.* **1983**, *92*, 793. Burrell, A. K.; Hemmi, G.; Lynch, V.; Sessler, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 4690. Charriere, R.; Jenny, T. A.; Rexhausen, H.; Gossauer, A. *Heterocycles* **1993**, *36*, 1561. Very recently, the formation of hexakis(pentafluorophenyl)hexaphyrin from the reaction of pyrrole and pentafluorobenzaldehyde under modified Rothemund conditions ($AcOH-PhNO_2$) has been noted: Neves, M. G. P. M. S.; Martins, R. M.; Tomé, A.; Silvestre, A. J. D.; Silva, A. M. S.; Félix, V.; Drew, M. G. B.; Cavaleiro, J. A. S. *Chem. Commun.* **1999**, 385. In unrelated studies, corroles have also been isolated under Rothemund-type conditions: Gross, Z.; Galili, N.; Saltsman, I. *Angew. Chemie, Int. Ed.* **1999**, *38*, 1427. Paolesse, R.; Jaquinod, L.; Nurco, D. J.; Mini, S.; Sagone, F.; Boschi, T.; Smith, K. M. *Chem. Commun.* **1999**, 1307.

(8) LeGoff, E.; Cheng, D. O. In *Porphyrin Chemistry Advances*; Longo, F. R., Ed.; Ann Arbor Science Publishers: Ann Arbor, MI, 1979; p 153.

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(10) Ball, R. H.; Dorough, G. D.; Calvin, M. *J. Am. Chem. Soc.* **1946**, *68*, 2278.

(11) Chmielewski, P. J.; Latos-Grazynski, L.; Rachlewicz, K.; Glowiak, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 779.

(12) Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767. See also: Geier, G. R., III; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1596. Narayanan, S. J.; Sridevi, B.; Srinivasan, A.; Chandrashekar, T. K.; Roy, R. *Tetrahedron Lett.* **1998**, *39*, 7389.

(13) Chmielewski, P. J.; Latos-Grazynski, L.; Rachlewicz, K. *Chem. Eur. J.* **1995**, *1*, 68. For syntheses of other *meso*-substituted sapphyrins, see: Sessler, J. L.; Lisowski, J.; Boudreaux, K. A.; Lynch, V.; Barry, J.; Kodadek, T. J. *J. Org. Chem.* **1995**, *60*, 5975. Rachlewicz, K.; Sprutta, N.; Latos-Grazynski, L.; Chmielewski, P. J.; Szterenberg, L. *J. Chem. Soc., Perkin Trans. 2* **1998**, 959. Rachlewicz, K.; Sprutta, N.; Chmielewski, P. J.; Latos-Grazynski, L. *J. Chem. Soc., Perkin Trans. 2* **1998**, 969. Brückner, C.; Sternberg, E. D.; Boyle, R. W.; Dolphin, D. *Chem. Commun.* **1997**, 1689. Narayan, S. J.; Sridevi, B.; Chandrashekar, T. K.; Vij, A.; Roy, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 3394. For a review on expanded porphyrins, see: Ayub, J.; Dolphin, D. *Chem. Rev.* **1997**, *97*, 2267.

(14) Gilchrist, T. L. *Heterocyclic Chemistry*, 3rd ed.; Longman: Birmingham, AL, 1997; pp 198−202.

(15) Vogel, E. *J. Heterocycl. Chem.* **1996**, *33*, 1461.

(16) Fabian, J.; Nakazumi, H.; Matsuoka, M. *Chem. Rev.* **1992**, *92*, 1197.

(17) Bonnett, R. *Chem. Soc. Rev.* **1995**, *24*, 19. Milgrom, L. R.; MacRobert, S. *Chem. Br.* **1998**, *34* (35), 45.

(18) Ghosh, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1028.

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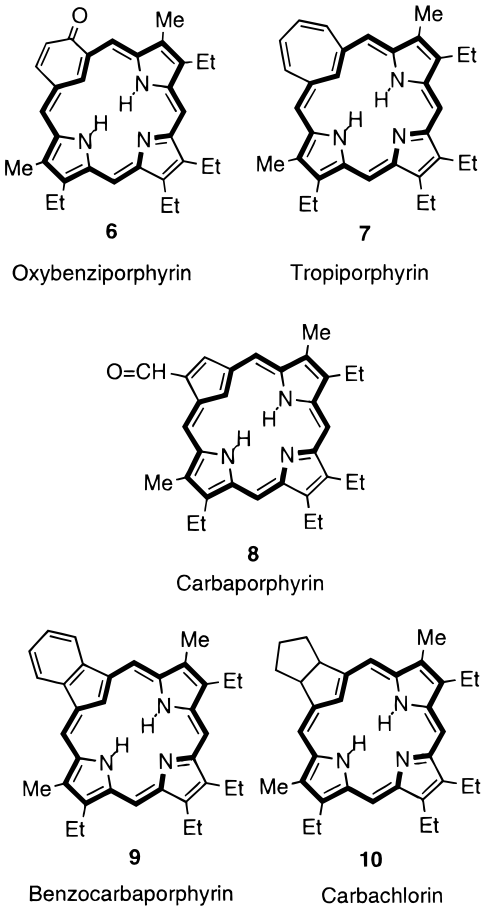
(20) Chmielewski, P. J.; Latos-Grazynski, L.; Glowiak, T. *J. Am. Chem. Soc.* **1996**, *118*, 5690.

(21) Ishikawa, Y.; Yoshida, I.; Akaiwa, K.; Koguchi, E.; Sasaki, T.; Furuta, H. *Chem. Lett.* **1997**, 453.

(22) Nilsen, H. J.; Ghosh, A. *Acta Chem. Scand.* **1998**, *52*, 827. Ghosh, A.; Wondimagegn, T.; Nilsen, H. J. *J. Phys. Chem. B* **1998**, *102*, 10459.

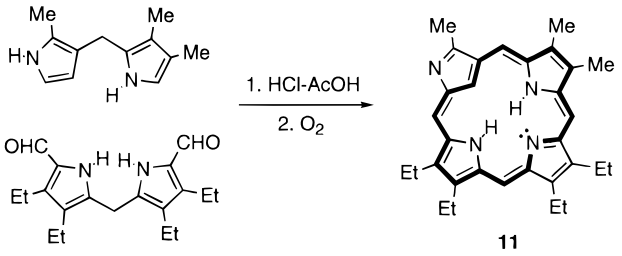
(23) Lash, T. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2533.

**Chart 1**

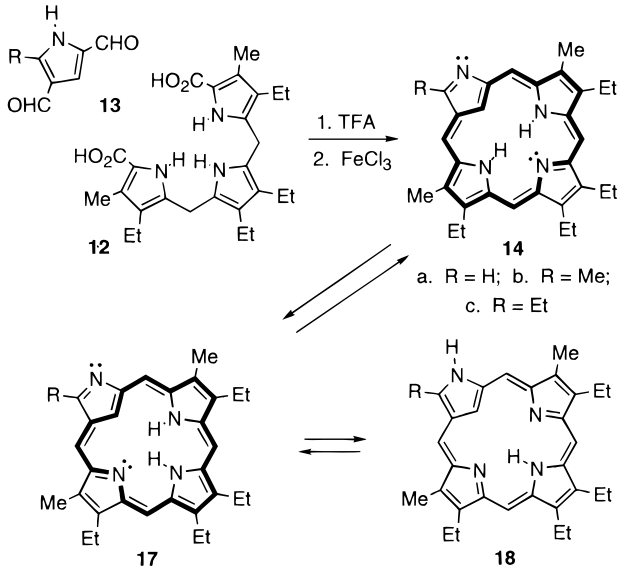



phyrinoids resemble porphyrin isomer **3** as they possess an internal carbon atom in place of the usual nitrogen, but they are further modified in that the heterocyclic subunit has now been completely replaced by a carbocyclic ring. These systems are also demonstrating some fascinating new chemistry,[27,29] although no stable organometallic derivatives of **6**−**10** have been reported at the present time.[27] Given the highly topical nature of the *meso*-tetraaryl N-confused porphyrins **3**, it was desirable to design rational ring syntheses to the related *β*-alkyl-substituted porphyrinoids (e.g., **11**). This was initially accomplished in 1996 by Liu et al.[33] using the MacDonald "2 + 2" synthesis (Scheme 2), although good yields were only obtainable for small scale reactions.[33,34] In our ongoing research, we have found the "3 + 1" variant on the MacDonald synthesis to be a superior methodology

**Scheme 2**




**Scheme 3**




for synthesizing porphyrin analogues[23−26,29−32,35,36] and anticipated that this approach would allow much more convenient access to "etio" N-confused porphyrins. Under suitably modified conditions, we demonstrate that this approach is highly successful, and the availability of more substantial quantities of material allows the properties of the "etio" series to be assessed.

## Results and Discussion

The success of the "3 + 1" route in porphyrinoid synthesis derives in part from the ready availability of the required tripyrrane intermediates (e.g., structure **12**, Scheme 3)[35,37] and aromatic dialdehydes.[35] In the present study, 2,4-diformylpyrroles were needed to introduce the required inverted pyrrolic unit into the N-confused macrocycle. A convenient one-pot synthesis of 2,4-pyrroledicarboxaldehyde (**13a**) from pyrrole had been reported by Anderson et al. using a Vilsmeier formylation, followed by electrophilic substitution onto the resulting imine salt with dichloromethyl methyl ether and aluminum chloride−nitromethane (Scheme 4).[38] Dialdehyde **13a** was reacted with tripyrrane **12** under the standard "3 + 1" conditions (5% TFA−$CH_2Cl_2$)[35] and subsequently oxidized with DDQ with the expectation that the hexaalkyl N-confused porphyrin **14a** would be produced in worthwhile yields. Unfortunately, despite the success of this methodology in the synthesis of diverse porphyrinoid structures, none of the required macrocyclic product could be isolated in these studies. Attempts to modify the reaction conditions using different acid catalysts similarly produced negative results.

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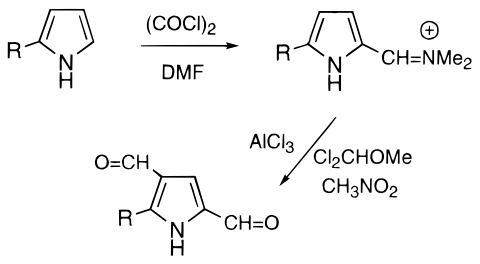
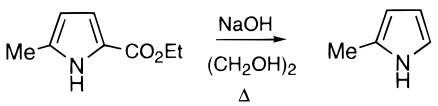
(25) Lash, T. D.; Chaney, S. T *Tetrahedron Lett.* **1996**, *37*, 8825.
(26) Lash, T. D.; Hayes, M. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 840.
(27) Hayes, M. J.; Spence, J. D.; Lash, T. D. *Chem. Commun.* **1998**, 2409.
(28) Hayes, M. J. M.S. Thesis, Illinois State University, 1997.
(29) Lash, T. D.; Chaney, S. T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 839. Lash, T. D. *Chem. Commun.* **1998**, 1683.
(30) Berlin, K. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1820.
(31) Hayes, M. J.; Lash, T. D. *Chem. Eur. J.* **1998**, *4*, 508.
(32) See also: (a) Lash, T. D.; Chaney, S. T. *Chem. Eur. J.* **1996**, *2*, 944. (b) Lash, T. D.; Richter, D. T. *J. Am. Chem. Soc.* **1998**, *120*, 9965. (c) Kozyrev, A. N.; Alderfer, J. L.; Dougherty, T. J.; Pandey, R. K. *Angew. Chem., Int. Ed.* **1999**, *38*, 126.
(33) Liu, B. Y.; Brückner, C.; Dolphin, D. *Chem. Commun.* **1996**, 2141. See also: Pandey, R. K.; Leung, S. H.; Forsyth, T. P.; Smith, K. M. *Tetrahedron Lett.* **1994**, *35*, 8995.
(34) Brückner, C. Personal communication to C.M.S., 1998.

**Scheme 4**




**13** a. R = H; b. R = Me; c. R = Et

**Scheme 5**




**16** **15**

The presence of substituents on the condensing fragments is known to be a major factor in the success of porphyrin syntheses, because these result in steric interactions that favor helical geometries for the conformations of the partially condensed intermediates and thereby facilitate the cyclization process.[39] This consideration suggested that alkyl-substituted pyrroledialdehydes might be better suited for these studies. 2-Methylpyrrole (**15**) was prepared by treating ethyl 5-methylpyrrole-2-carboxylate (**16**)[40] with sodium hydroxide in ethylene glycol at 180 °C for 6 h (Scheme 5). Subsequent sequential reaction of **15** with oxalyl chloride−DMF and $MeOCHCl_2$−$AlCl_3$−$MeNO_2$ afforded the required diformylpyrrole **13b** in good overall yields (Scheme 4). Similarly, bis-formylation of commercially available 2-ethylpyrrole generated the related dialdehyde **13c**. When pyrrole **13b** was reacted with tripyrrane **12** in the presence of TFA−$CH_2Cl_2$ and further oxidized with DDQ, the required inverted porphyrin **14b** was easily detected by TLC. However, attempts to purify **14b** were plagued with difficulties, and while the methyl substituent clearly had produced the anticipated positive influence, the reaction and workup conditions remained problematic. Column chromatography provided partially purified fractions of **14b**, but attempts to isolate pure samples by further chromatography or crystallization were not successful. During the course of these studies, alternative methods for oxidation were considered. Condensation of **12** and **13b** would be expected to give a dihydro derivative of **14b**, and the aromatic porphyrinoid will only be generated following a dehydrogenation step. Ferric chloride proved to be an effective oxidant for this chemistry, and this gave the best results when the crude reaction mixture was washed with a 0.1% aqueous solution of $FeCl_3$. Using this innovation, chromatography produced clean fractions of the desired porphyrinoid **14b**. Crystallization from chloroform−methanol gave **14b** as a dull purple powder, but there were significant losses due to the solubility of the N-confused porphyrin. Far better results were obtained by washing the solution of **14b** with 10% HCl and recrystallizing the protonated species from chloroform−petroleum ether. In this fashion, the inverted porphyrin could be isolated in surprisingly high yields (53−61%). This species was initially formulated as the bis-hydrochloride salt, although NMR data subsequently suggested that the isolated material was not fully protonated (see below). Condensation of **13c** with **12** also gave the related heptaalkyl-substituted porphyrinoid **14c** in good yields. Under the improved reaction conditions, the α-unsubstituted diformylpyrrole **13a** also reacted with **12** to give the hexaalkyl N-confused porphyrin **14a**, although, as expected, the yield (16%) was far poorer in this case.

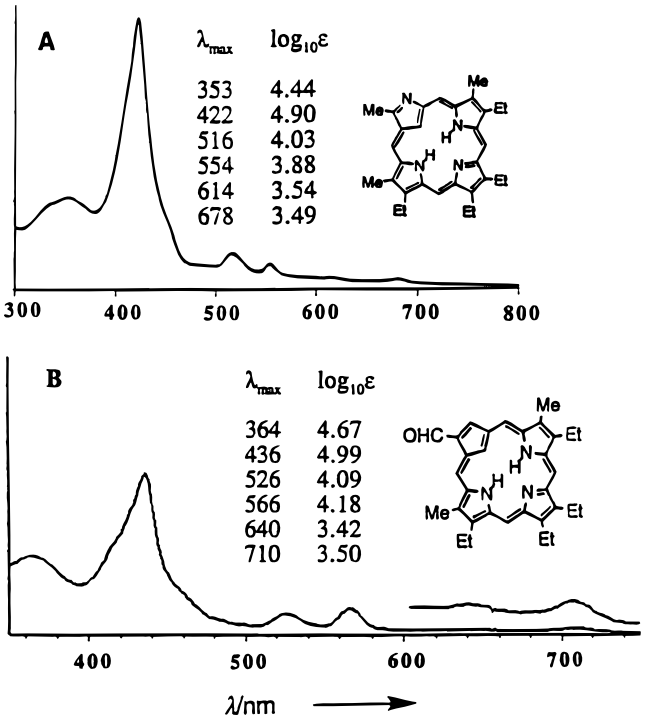



**Figure 1.** (A) UV−vis spectrum of N-confused porphyrin **14b** in chloroform. (B) UV−vis spectrum of formylcarbaporphyrin **8** in chloroform.[28]

The structures of N-confused porphyrins **14a**−**c** were confirmed by MS, UV−vis, and NMR spectroscopy. The EI MS showed strong molecular ions with some benzylic fragmentation and moderate doubly charged ions. The UV−vis spectra for porphyrinoids **14** were porphyrin-like (Figure 1A) and closely resembled the spectra previously reported by Liu et al.,[33] although the molar absorptivities for our samples were somewhat higher. The free base spectrum for **14b** (Figure 1A) shows a strong Soret band at 422 nm that is somewhat broadened compared to most porphyrins, and a secondary broad absorption band is evident near 350 nm. In addition, a typical series of Q-bands is noted between 500 and 700 nm and while

(35) Lash, T. D. *Chem. Eur. J.* **1996**, *2*, 1197. Lin, Y.; Lash, T. D. *Tetrahedron Lett.* **1995**, *36*, 9441. Lash, T. D. *J. Porphyrins Phthalocyanines* **1997**, *1*, 29.

(36) In addition, furan- and thiophene-containing *meso*-tetraphenylporphyrinoids with inverted pyrrole units have been prepared by a very different type of "3 + 1" methodology: Heo, P.-Y.; Shin, K.; Lee, C.-H. *Tetrahedron Lett.* **1996**, *37*, 197. Lee, C.-H.; Kim, H.-J. *Tetrahedron Lett.* **1997**, *38*, 3935. A synthesis of imidazole-containing porphyrin analogues using Smith's alternative "3 + 1" approach[37c] has also been noted recently: Kai, S.; Suzuki, M.; Masaki, Y. *Tetrahedron Lett.* **1998**, *39*, 4063.

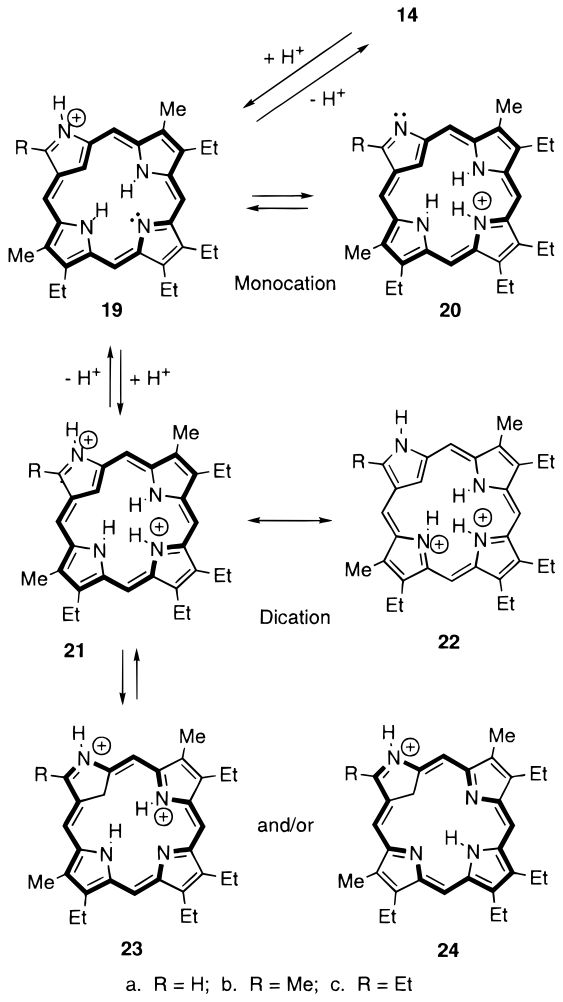
(37) (a) Sessler, J. L.; Johnson, M. R.; Lynch, V. *J. Org. Chem.* **1987**, *52*, 4394. (b) Boudif, A.; Momenteau, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1235. (c) Nguyen, L. T.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1996**, *61*, 998.

(38) Anderson, H. J.; Loader, C. E.; Foster, A. *Can. J. Chem.* **1980**, *58*, 2527.

(39) E.g.: Clezy, P. S.; Diakiw, V. *Aust. J. Chem.* **1971**, *24*, 2665. Franck, B.; Nonn, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1795.

(40) Fischer, H.; Beller, H.; Storm, A. *Chem. Ber.* **1928**, *61*, 1B, 1074. Lash, T. D.; Hoehner, M. C. *J. Heterocycl. Chem.* **1991**, *28*, 1671. Curran, T. P.; Keany, M. T. *J. Org. Chem.* **1996**, *61*, 9068.

**Scheme 6**




Q-band I is present at a longer than typical wavelength for porphyrins with this type of substitution pattern, this region is unexceptional. In many respects, the spectra for **14a**−**c** resemble those for true carbaporphyrins such as **8** (Chart 1; Figure 1B). In the free base electronic spectrum for **8**, the Soret band is similarly broadened and diminished in intensity, and a second broad band is present at 364 nm (Figure 1B). Four Q-bands are present in both cases, although Q-band I is still further red-shifted for porphyrinoid **8**. It is worth noting that a number of tautomeric forms are possible for the N-confused porphyrins including aromatic species such as **17** and cross-conjugated structures with external NH's such as **18** (Scheme 3), although the UV-vis data does not support the latter possibility. The proton NMR spectra (see below) also strongly support the aromatic nature of these N-confused porphyrins.

Addition of 1 equiv of TFA to **14b** resulted in the formation of a new species that presumably corresponds to a monoprotonated porphyrinoid structure such as **19b** or **20b** (Scheme 6). The UV−vis spectrum for this species shows the retention of a strong Soret band at 421 nm, and this suggests that the monocation retains an aromatic electronic structure. Although external or internal protonation is possible (structures **19b** and **20b**, respectively), data for the tetraaryl system indicates that protonation initially occurs at the macrocyclic periphery. Further addition of TFA produced the corresponding dication, and while it was evident that a new species had been formed, the presence of a strong Soret band at 425 nm supported an aromatic formulation **21b** for this species (Scheme 6). This observation, along with the NMR data for the dication, shows that resonance contributors with cross-conjugated pyrrole units (e.g., **22b**) are not significant for the N-confused dications. Similar observations were made for porphyrinoids **14a** and **14c**.

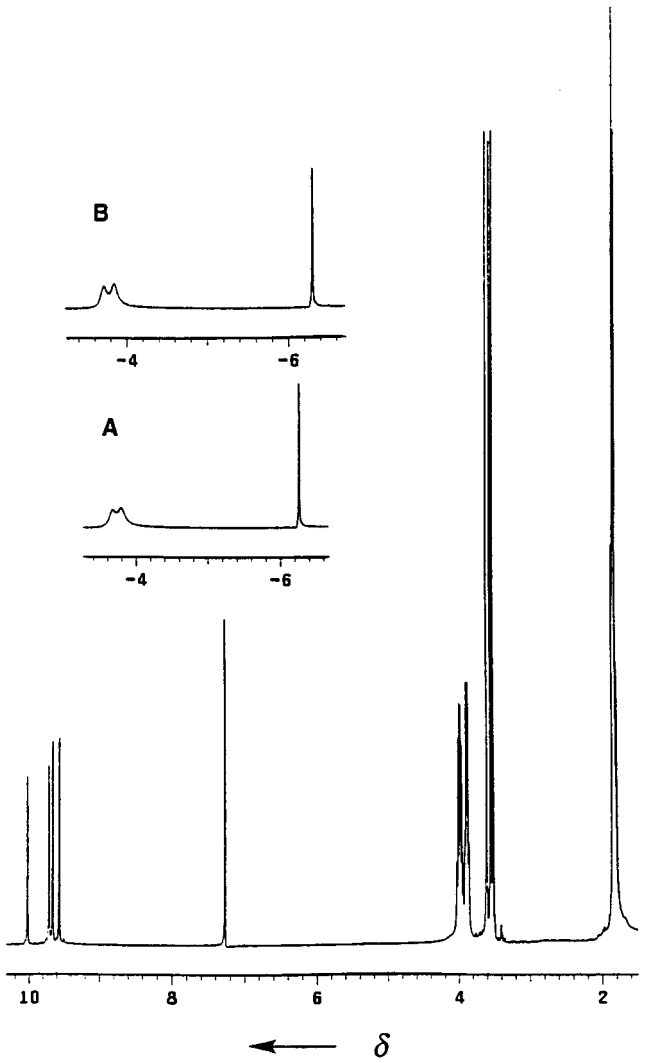



**Figure 2.** 400 MHz Proton NMR spectrum of N-confused porphyrin **14b** in $CDCl_3$. Inset: (A) Upfield region at 30 °C. (B) Upfield region for the same sample at 20 °C. The resolution of the NH resonances suggests that a single dominant tautomer is present and NH exchange must be slow even above room temperature.

The proton NMR spectra for N-confused porphyrins **14a**−**c** confirmed their aromatic character. In the initial spectra for **14b**, the strong diamagnetic ring current produced a series of four 1H singlets near 10 ppm for the *meso*-protons, while the interior CH appeared upfield beyond −6 ppm while the NHs gave a broad resonance near −4 ppm. However, when cleaner samples of **14b** became available the proton NMR spectra showed that the NH protons had resolved into two separate resonances (Figure 2). Similar results were also obtained for porphyrinoids **14a** and **14c**. In a variable temperature study on **14b** in $CDCl_3$ at 400 MHz, the NH resonances were completely resolved at −40 °C, but full coalescence was not observed until the temperature had reached +45 °C. At 40 °C, a degree of resolution between the two

resonances was evident, and this was further enhanced at 30 °C (Figure 2A) and 20 °C (Figure 2B). The NMR data are consistent with the presence of a single tautomeric species, and the slow exchange of the NH protons suggests a high barrier for this process. The favored tautomer is probably **14**, rather than **17**, due to the ability of both NHs to participate in hydrogen bonding interactions.[22] In the earlier studies for the *meso*-tetraaryl N-confused porphyrin series **3**,[11] the NH protons appeared as a single broad singlet at 25 °C, although two well-resolved singlets were observed at −50 °C, and this presumably implies that these porphyrinoids have a much lower energy barrier for NH exchange. Liu et al. also noted that the NH protons of N-confused "etioporphyrin" **11** (Scheme 2) only resolved at lower temperatures (−50 °C), but in this case only very limited amounts of material were available for study.[33,34] As we were only able to observe this phenomenon in rigorously purified material, the lowered coalescence temperature is presumably an artifact in this case. Carbon-13 NMR spectra for **14a**−**c** were also in accord with the presence of single porphyrinoid species. The *meso*-carbons for **14b** appeared at 94.3, 95.9, 101.6, and 106.6 ppm, values that are comparable to those observed for true porphyrins,[35] while the internal methine showed up in the same region at 102.9 ppm.

It was anticipated that the addition of one drop of TFA to the free base NMR solutions of **14b** would result in the formation of dication **21b**. However, while a degree of protonation was evident in the resulting spectra, it was initially unclear whether the monocation **19b** or the dication **21b** predominated in solution. The spectra for this species retained the large aromatic ring current effects, and showed the *meso*-protons as four singlets between 9.4 and 10.1 ppm together with an external NH at 13.8 ppm, while the inner CH afforded an upfield singlet at −4.3 ppm. However, the internal NH protons produced only two broad 1H singlets near −0.4 ppm, as might be expected for the monocation **19b**, whereas three interior NH's should be observed for dications **21b**. However, the presence of two distinct resonances for the interior NH's at room-temperature implies that NH exchange within the macrocyclic cavity of **19b** is relatively slow, and given the presence of protic acid within these solutions such an interpetation seemed unlikely. Further addition of TFA-induced minor shifts to the positions of the *meso*-protons and the exterior NH resonance, but more importantly the upfield region showed the presence of three internal NH's, two of which were relatively sharp peaks resonating near −1.0 ppm, while the third absorbance was very broad signal at −1.7 ppm, together with a sharp singlet at −4.0 ppm for the interior CH (Figure 3A). Although it is possible that the dication is only produced at higher concentrations of TFA, this is not consistent with the UV−vis data. Furthermore, when the temperature of the original solution containing one drop of TFA was lowered, the third upfield NH resonance emerged and became progressively sharper as the temperature was decreased. These data can be interpreted to indicate that the dication is the predominant species in all of these spectra, but at lower concentrations one of the NHs undergoes rapid exchange, presumably due to equilibation with the monocation. Higher concentrations of TFA disfavor this exchange due to the lower concentration of monocation, and indeed stronger acids such as HCl do not exhibit this phenomenon at all (see below). Similar observations were made for N-confused porphyrins **14a** and **14c**.

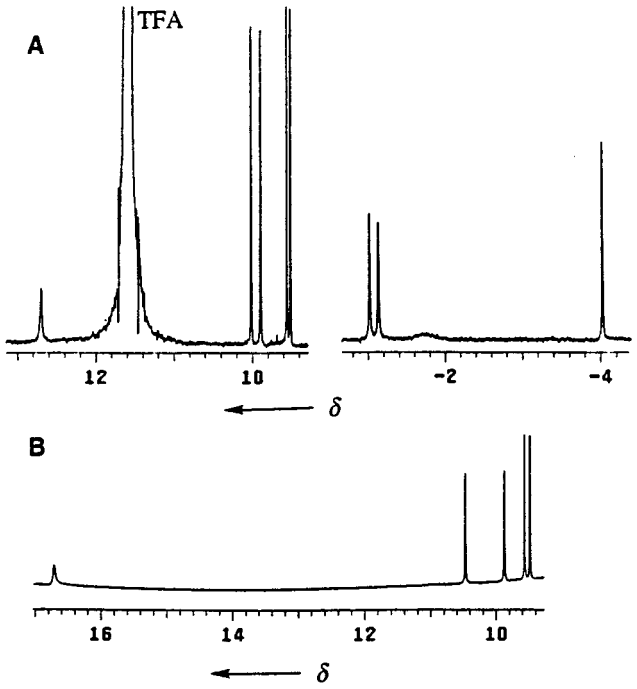



**Figure 3.** (A) Upfield and downfield regions for the 400 MHz proton NMR spectrum of N-confused porphyrin **14b** with 7 drops of TFA in $CDCl_3$. The external NH for the resulting dication **21b** appears downfield from the TFA absorption at 12.7 ppm while the three internal NH's produce two sharp 1H singlets near −1 ppm and a broad 1H resonance at −1.7 ppm. The 1H singlet at −4 ppm corresponds to the interior CH. (B) Downfield region for the 400 MHz proton NMR spectrum of N-confused porphyrin **14b** with 1 drop of concentrated hydrochloric acid in $CDCl_3$. The dication **21b** generated under these circumstances shows deshielding to a far greater extent for the external NH (broad singlet at 16.7 ppm), while one of the *meso*-protons is also shifted further downfield to 10.5 ppm. These changes are consistent with a high degree of ion association with the chloride anions at the porphyrinoid dication periphery.

The proton NMR spectra for dications **21** showed a decrease in the upfield shift of the interior CH proton, and this can be partially attributed to the delocalization of one or two positive charges over the porphyrinoid macrocycle. However, there is no increase in the downfield shift for the *meso*-protons, and this observation suggests that protonation leads to a slight decrease in macrocyclic ring current. When TFA-*d* was added to solutions of **14b**, the internal CH resonance was lost in addition to the NH signals. This exchange must arise due to the presence of a tautomeric C-protonated species such as **23**, or possibly the related monocation **24** (more than one tautomeric species can be considered for both of these possibilities), in equilibrium with the major species **21** (Scheme 6). Similar observations have been made for the carbaporphyrins **8** and **9**,[26,28] and *meso*-tetraaryl N-confused porphyrins have also been reported to undergo CH exchange upon heating with deuterated acetic acid.[11] In the carbon-13 NMR spectrum of **14b** in TFA−$CDCl_3$, the *meso*-carbons appeared at 94.7, 96.3, 110.2, and 112.6 ppm, while the interior carbon resonated at 105.8 ppm.

In most cases, porphyrinoids **14a**−**c** were isolated as the hydrochloride salts, but the NMR spectra showed some broadening particularly for the *meso*-protons, the

**Table 1. Electronic Spectra of N-Confused Porphyrin 14b in the Presence of Various Acids**

| acid[a] | $\lambda_{max}$ (nm) (log $\epsilon$) | Soret bands | | | Q bands | | |
|---|---|---|---|---|---|---|---|
| TFA | 337 | 425 | 456 | | 578 | 620 | 706 |
| | (4.48) | (4.88) | (3.94) | | (3.87) | (3.87) | (3.97) |
| $HNO_3$ | 338 | 429 | 458 | | 548 | 594 | 710 |
| | (4.44) | (4.79) | (4.57) | | (3.91) | (3.82) | (3.71) |
| HF | 335 | 428 | 457 | | 549 | 596 | 714 |
| | (4.75) | (4.97) | (4.78) | | (4.29) | (4.23) | (4.16) |
| HCl | 344 | 432 | 461 | 513 | 549 | 596 | 717 |
| | (4.51) | (4.86) | (4.59) | (3.93) | (4.00) | (3.92) | (3.88) |
| HBr | 332 368 | 436 | 465 | | 551 | 597 | 717 |
| | (4.48) (4.45) | (4.94) | (4.58) | | (4.04) | (3.92) | (3.86) |
| HI | 338 | 442 | | | 558 | 602 | 725 |
| | (4.67) | (4.86) | | | (4.08) | (3.97) | (3.85) |

[a] 1% concentrated acid by volume.

interior CH, and the NH resonances. Addition of a drop of concentrated HCl to the NMR solution produced a marked improvement and considerably sharpened up these resonances. This suggests that the crystallized material was not completely converted to the dihydrochloride, and additional HCl was required to obtain clean spectroscopic data for this species. The chemical shifts for the dication differed considerably from those for the same species generated by addition of TFA. In particular, the external NH proton was shifted to nearly 17 ppm, and one of the *meso*-protons was significantly deshielded to 10.5 ppm (Figure 3B). These observations implied that the chloride anion was influencing the chemical shifts through ion pair interactions and this supposition was supported by observation of significant differences in the UV−vis spectra (Table 1). The Soret band for **14b** in the presence of HCl was noted at 432 nm, compared to 425 nm for the TFA generated dication, while the longest wavelength band also underwent a bathochromic shift to 717 nm (Table 1). A series of acids were investigated (HF, HBr, HI, and $HNO_3$), and each one gave somewhat different results implying that the spectra were modulated by ion pairing effects (Table 1). The HI UV−vis spectrum was particularly modified, showing a broadened Soret band at 442 nm and the longest wavelength band at 725 nm. The proton NMR spectra for HBr and HI also showed some differences. In particular, the external NH for the former appeared at 16.5 ppm, while the latter gave this resonance at 14.8 ppm. Although selective iodide binding by the *meso*-tetraphenyl N-confused porphyrin **3** at the air−water interface has been reported,[41] this appears to be due to a totally different phenomenon where iodide induces the formation of a "J-like" aggregate of monoprotonated N-confused porphyrins within a surfactant monolayer.[41] Our observations suggest that the "etio" N-confused porphyrins may have value in the development of selective anion binding reagents. On the other hand, the proton NMR data clearly indicate that these interactions must be taking place at the exterior of the macrocycle.

The formation of the nickel(II) chelate for **14b** was also investigated. This study was far from straightforward and the conditions utilized to prepare the nickel complex of the *meso*-tetraaryl N-confused porphyrin[11] were not successful. Refluxing **14b** and nickel(II) acetate in DMF under nitrogen also gave poor results and primarily led

**Scheme 7**

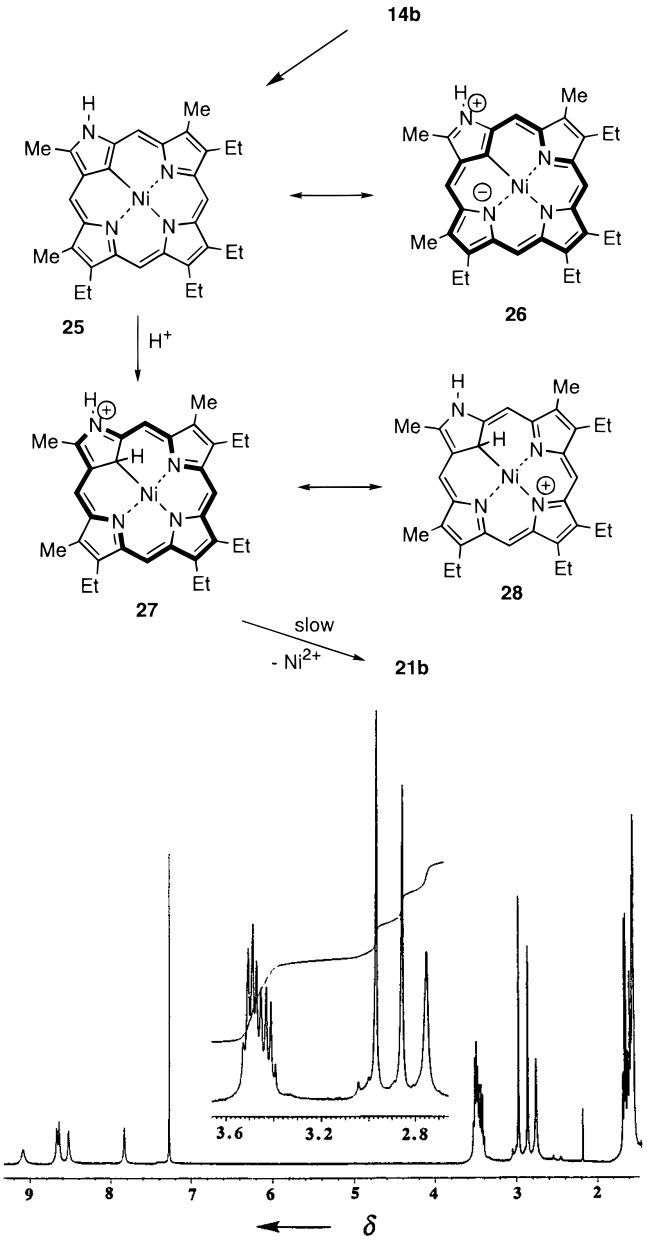



**Figure 4.** 400 MHz proton NMR spectrum of nickel(II) complex **25** in $CDCl_3$. The *meso*-protons between 7.8 and 8.8 ppm are broadened by aggregation effects. The much reduced downfield shifts to the peripheral protons are consistent with a cross-conjugated species that has lost most of the diatropic character associated with **14b**.

to decomposition. However, if the temperature was maintained at 145 °C for 30 min the nickel(II) complex **25** could be isolated in 45% yield (Scheme 7). This organometallic derivative proved to be rather unstable, unlike the tetraaryl complexes **5**, and great care was required when handling this species. As was the case for the precursory structure **14**, the nickel complex was robust toward 70 eV EI MS showing a strong molecular ion together with a small amount of benzylic fragmentation. However, the proton NMR spectrum for **25** in $CDCl_3$ showed a considerable loss of diatropic character (Figure 4). The *meso*-protons appeared as four somewhat broadened singlets between 7.8 and 8.7 ppm while the external NH resonated near 9 ppm. The three pyrrole methyl units appeared as 3 singlets between 2.7 and 3.0 ppm,

(41) Ariga, K.; Kunitake, T.; Furuta, H. *J. Chem. Soc., Perkin Trans. 2* **1996**, 667.

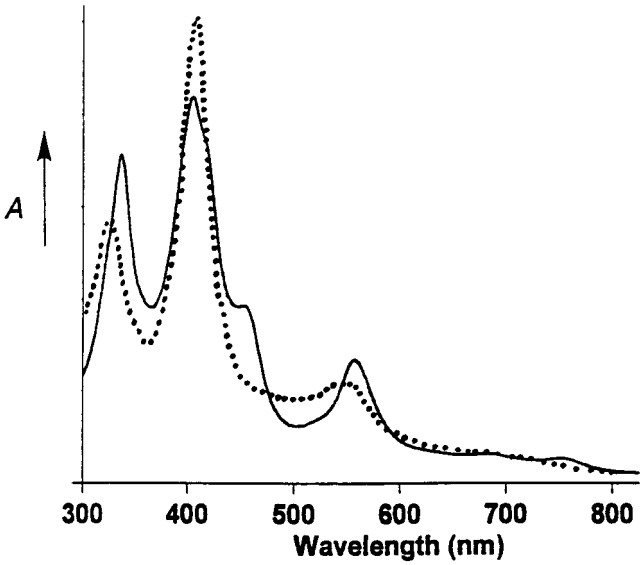



**Figure 5.** UV−vis spectra of nickel(II) complex **25** in chloroform (solid line) and 1% TFA−chloroform (dotted line). The latter spectrum shows an intensified Soret band which indicates that some porphyrinoid aromatic characteristics have been regained.

compared to 3.7−3.8 ppm for the aromatic free base **14b**. The insertion of $Ni^{2+}$ into the macrocyclic cavity of **14b** results in the displacement of 3 protons, one of which is relocated on the outer nitrogen atom. This necessitates the generation of a cross-conjugated species **25** and while dipolar contributors such as **26** probably contribute to the structure of the nickel complex, it is to be expected that the macrocyclic aromaticity of **25** will have been compromised. This is also manifest by the broadened Soret absorption in the UV-vis spectrum of **25** (Figure 5). The nickel complex was not very soluble in chloroform, and some of the proton NMR resonances for **25** were broadened possibly due to aggregation. However, DMSO proved to be a much better solvent for this species and gave significantly improved resolution. However, the data for **25** in DMSO-$d_6$ suggested that the compound had regained some of its diatropic characteristics. The NH proton was shifted downfield to 13.8 ppm, presumably due to hydrogen bonding with the solvent, but the *meso*-protons were also shifted downfield to 8.7−9.2 ppm and the porphyrin-methyls resonated at 3.02, 3.07, and 3.45 ppm. These shifts may be attributed to the stabilization of dipolar canonical forms such as **26** by hydrogen bonding interactions. The UV−vis spectrum of **25** in DMSO is better resolved, and the Soret bands are slightly intensified, but the overall appearance was not significantly altered.

Addition of a drop of TFA to a chloroform solution of nickel complex **25** turned the red solution to a green color, and the proton NMR spectrum showed the presence of a strong diamagnetic ring current (Figure 6). A poorly resolved doublet was noted upfield at −4.7 ppm, while the *meso*-protons appeared as four separate singlets between 9.7 and 10.1 ppm, and the NH resonance was further deshielded to beyond 14 ppm. These data are consistent with the formation of a C-protonated species **27**, which allows for both the stabilization of the positive charge and 18-$\pi$ electron delocalization pathways to promote macrocyclic aromaticity. While nonaromatic canonical forms such as **28** can be envisaged, it is clear

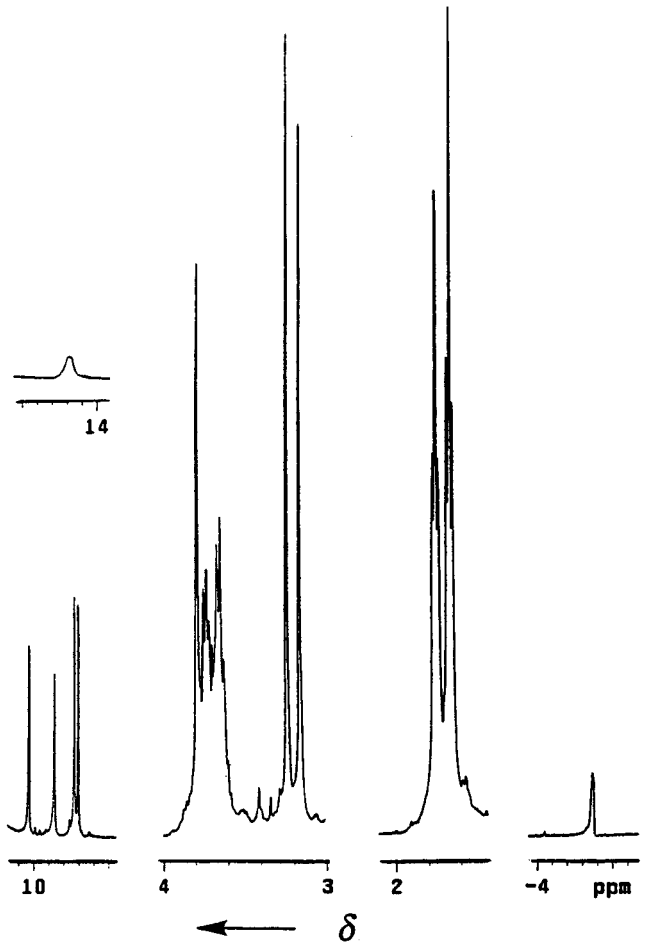
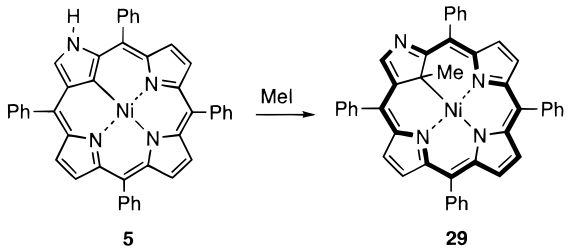



**Figure 6.** 400 MHz proton NMR spectrum of protonated nickel(II) complex **29** in TFA−$CDCl_3$. The external NH is deshielded to 14.2 ppm, while the interior $sp^3$ C−H appears upfield as an unresolved doublet at −4.8 ppm. This spectrum confirms the presence of a powerful macrocyclic ring current, although after several hours at room temperature demetalation leads to the dication **21b**.

**Scheme 8**




that the species is best described by contributing species such as **27**. The UV−vis spectra also support this structure as the Soret band is strengthened in the acidic solution (Figure 5). Protonation of the nickel(II) complex **5** has not been reported, but the tetraphenyl complex has been shown to react with methyl iodide at the same carbon atom to produce a similar species **29** with an $sp^3$ carbon−nickel bond (Scheme 8).[20] C-Protonation in this case acts as an unusual "molecular switch" that restores the aromaticity of the inverted porphyrinoid. However, solutions of the protonated nickel complex **27** are not stable as they slowly demetalate to form the dication **21b**. This demetalation goes to completion on standing at room-temperature overnight.

## Conclusions

The "3 + 1" methodology provides an excellent high-yielding route to heptaalkyl-substituted N-confused porphyrins, although it was necessary to develop suitable reaction conditions to facilitate this chemistry. In particular, brief treatment with ferric chloride provided a superior method for dehydrogenating the dihydro intermediate to the aromatic porphyrinoid. NH exhange in the macrocyclic cavity for these N-confused porphyrins is slow on the NMR time scale even at room temperature, and the data implies that there is a strong preference for a single tautomeric species. Addition of acid results in the formation of mono- and diprotonated structures that retain aromatic character, but the dications of these "etio" N-confused porphyrins show indications of strong anion pairing in solution. The nickel(II) organometallic complex of trimethyl N-confused porphyrin **14b** was generated and this rather unstable species was shown to have lost most of its aromatic character. However, addition of acid resulted in C-protonation to generate a new aromatic cation that slowly demetalated over the period of several hours. Clearly, the "etio" series of N-confused porphyrins have somewhat different spectroscopic and chemical properties than their better known *meso*-tetraaryl cousins and the improved synthetic procedures to these porphyrinoids will allow their chemistry to be fully explored.

## Experimental Section

2-Ethylpyrrole, oxalyl chloride, DMF, nitromethane, dichloromethyl methyl ether, and TFA were purchased from Aldrich Chemical Co. and used without further purification. Chromatography was performed using Grade 3 neutral alumina or 70−230 mesh silica gel. EI and FAB mass spectral determinations were made at the Mass Spectral Laboratory, School of Chemical Sciences, University of Illinois at Urbana-Champaign, supported in part by a grant from the National Institute of General Medical Sciences (GM 27029). Elemental analyses were obtained from the School of Chemical Sciences Microanalysis Laboratory at the University of Illinois.

**2-Methylpyrrole (15).** Ethyl 5-methylpyrrole-2-carboxylate (**16**; 12.50 g),[40] sodium hydroxide (10.0 g), and ethylene glycol (100 mL) were stirred in a 250 mL round-bottomed flask under an atmosphere of nitrogen and heated on an oil bath at 180−185 °C for 6 h. The mixture was cooled, diluted with water, and extracted with dichloromethane. The organic extracts were dried over sodium sulfate, the solvent was removed on a rotary evaporator, and the residue was distilled to give the title pyrrole (5.35 g; 81%) as a colorless oil: bp 154 °C; IR (neat): $\nu$ 3381 $cm^{-1}$ (NH str); $^1H$ NMR ($CDCl_3$): $\delta$ 2.35 (3H, s), 5.98 (1H, br m), 6.19−6.22 (1H, m), 6.70−6.72 (1H, m), 7.90 (1H, br s); $^{13}C$ NMR ($CDCl_3$): $\delta$ 13.2, 106.1, 108.7, 116.5, 127.8.

**5-Methylpyrrole-2,4-dicarboxaldehyde (13b).** A solution of oxalyl chloride in 1,2-dichloroethane (4 mL) was added dropwise over a period of 20 min to a mixture of DMF (2.00 g) and 1,2-dichloroethane (6 mL) while maintaining the temperature of the reaction mixture at 0 °C with the aid of an ice−salt bath. The resulting white precipitate was stirred at room temperature for 15 min. The mixture was then cooled with an ice bath and a solution of 2-methylpyrrole (**15**; 2.00 g) in 1,2-dichloroethane added dropwise over 20 min. The resulting solution was stirred at room temperature for a further 15 min, nitromethane (3.60 g) was added, and the mixture was cooled to 0 °C. Aluminum chloride (7.30 g) was cautiously added, followed by the rapid addition of dichloromethyl methyl ether (3.4 mL). After the highly exothermic reaction had subsided, the ice bath was removed and the mixture stirred at room temperature for 30 min. The mixture was poured into ice−water, further acidified with concentrated hydrochloric acid (5 mL), and exhaustively extracted with ether and ethyl acetate. The combined organic solutions were dried over sodium sulfate and evaporated, and the residue was recrystallized from ethanol to give the diformylpyrrole (1.59 g; 47%) as buff-colored crystals, mp 178−178.5 °C. Further recrystallization from ethanol gave an analytical sample as fluffy white microneedles: mp 178.5−179 °C; IR (Nujol mull): $\nu$ 3156 (NH str), 1661, 1639 (C=O str) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 2.66 (3H, s), 7.33 (1H, d, $J$ = 2.4 Hz), 9.51 (1H, s), 9.93 (1H, s), 10.10 (1H, br s); $^{13}C$ NMR ($CDCl_3$): $\delta$ 12.73, 122.70, 124.38, 132.04, 143.82, 179.82, 185.93; $^{13}C$ NMR (DMSO-$d_6$): $\delta$ 11.7, 121.3, 123.1, 131.9, 143.8, 179.7, 185.7. Anal. Calcd for $C_7H_7NO_2$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.17; H, 5.17; N, 10.15.

**5-Ethylpyrrole-2,4-dicarboxaldehyde (13c).** Prepared from 2-ethylpyrrole (1.00 g) by the foregoing procedure. Recrystallization from carbon tetrachloride gave the dialdehyde (0.95 g; 60%) as off-white crystals: mp 132 °C, with softening at 112 °C; IR (Nujol mull): $\nu$ 3242 (NH str), 1666, 1633 (C=O str) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): $\delta$ 1.36 (3H, t, $J$ = 7.6 Hz), 3.09 (2H, q, $J$ = 7.6 Hz), 7.37 (1H, d, $J$ = 2.3 Hz), 9.52 (1H, s), 9.95 (1H, s), 10.43 (1H, br s); $^{13}C$ NMR ($CDCl_3$): $\delta$ 13.8, 20.5, 123.3, 123.4, 131.8, 150.1, 179.8, 185.7. Anal. Calcd for $C_8H_9NO_2 \cdot {}^1/_{10}H_2O$: C, 62.82; H, 6.06; N, 9.15. Found: C, 62.86; H, 5.95; N, 9.11.

**8,12,13,17-Tetraethyl-3,7,18-trimethyl-2-aza-21-carbaporphyrin (14b).** Tripyrranedicarboxylic acid **12** (100 mg) was stirred with TFA (1 mL) under nitrogen at room temperature for 2 min. The mixture was diluted with dichloromethane (99 mL) and 5-methylpyrrole-2,4-dicarboxaldehyde (**13b**; 30 mg) 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 first on Grade II neutral alumina, eluting with chloroform, and then on silica gel eluting with 5% methanol−chloroform. Column fractions were assessed by TLC and UV−vis spectroscopy. The green product fractions were washed with 10% aqueous hydrochloric acid, evaporated, and recrystallized from chloroform−petroleum ether (60−90°) to give the hydrochloride salt (62−72 mg; 53−61%) as dark blue crystals, mp > 300 °C. Alternatively, the free base could be recrystallized from chloroform−methanol as a dull purple powder: mp > 300 °C; UV−vis (1% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\epsilon$) 353 (4.44), 422 (4.905), 516 (4.03), 554 (3.88), 614 (3.54), 678 (3.49); UV-vis (1 equiv of TFA−$CHCl_3$; monocation): $\lambda_{max}$ (log $\epsilon$) 338 (4.50), 421 (4.88), 442 (4.68), 529 (3.94), 571 (4.11), 637 (3.72), 697 (3.96); UV-vis (1% TFA−$CHCl_3$; dication): $\lambda_{max}$ (log $\epsilon$) 337 (4.48), 425 (4.88), 456 (3.94), 578 (3.87), 620 (3.87), 706 (3.97); $^1H$ NMR ($CDCl_3$; 20 °C): $\delta$ −6.30 (1H, s), −3.84 (1H, br s), −3.72 (1H, br s), 1.78−1.85 (12H, m), 3.51 (3H, s), 3.55 (3H, s), 3.60 (3H, s), 3.84−4.02 (8H, m), 9.54 (1H, s), 9.64 (1H, s), 9.70 (1H, s), 10.01 (1H, s); $^1H$ NMR (4 drops TFA−$CDCl_3$; dication): $\delta$ −4.04 (1H, s), −1.7 (1H, br s), −1.04 (1H, s), −0.94 (1H, s), 1.65 (3H, t), 1.68 (3H, t), 1.75 (6H, two overlapping triplets), 3.34 (3H, s), 3.42 (3H, s), 3.64 (3H, s), 3.8−3.91 (8H, m), 9.49 (1H, s), 9.54 (1H, s), 9.90 (1H, s), 10.00 (1H, s), 12.79 (1H, br s); $^1H$ NMR ($CDCl_3$ + 1 drop concentrated HCl): $\delta$ −4.43 (1H, s), 0.78 (1H, s), 0.86 (1H, s), 1.25 (1H, s), 1.67−1.79 (12H, m), 3.38 (3H, s), 3.40 (3H, s), 3.84 (3H, s), 3.81−3.87 (8H, m), 9.49 (1H, s), 9.57 (1H, s), 9.87 (1H, s), 10.47 (1H, s), 16.72 (1H, br s); $^1H$ NMR ($CDCl_3$ + 1 drop concentrated HBr): $\delta$ −4.39 (1H, s), 0.46 (1H, s), 0.53 (1H, s), 1.17 (1H, s), 1.63−1.78 (12H, m), 3.38 (6H, s), 3.84 (3H, s), 3.8−3.9 (8H, m), 9.49 (1H, s), 9.58 (1H, s), 9.88 (1H, s), 10.58 (1H, s), 16.55 (1H, br s); $^1H$ NMR ($CDCl_3$ + 1 drop concentrated HI): $\delta$ −3.93 (1H, s), 0.03 (1H, s), 0.10 (1H, s), 0.15 (1H, s), 1.65−1.80 (12H, m), 3.34 (3H, s), 3.37 (3H, s), 3.67 (3H, s), 3.77−3.86 (8H, m), 9.45 (1H, s), 9.52 (1H, s), 9.88 (1H, s), 10.37 (1H, s), 14.79 (1H, br s); $^{13}C$ NMR ($CDCl_3$): $\delta$ 11.4, 11.5, 17.4, 17.5, 17.6, 18.5, 18.6, 19.6, 19.7, 20.1, 94.3, 95.9, 101.6, 102.9, 106.6, 132.9, 134.1, 134.2, 134.9, 135.7, 136.8, 137.7, 137.9, 138.1, 144.7, 145.3, 154.0, 155.1, 165.9; $^{13}C$ NMR (TFA−$CDCl_3$): $\delta$ 11.2, 11.6, 14.7, 16.2, 16.3, 17.0, 17.1, 19.6 (2), 19.7, 19.8, 94.7, 96.3,

105.8, 110.2, 112.6, 124.7, 131.5, 140.3, 141.4, 142.2, 142.3, 142.4, 144.0, 144.9, 145.3, 145.5, 145.7, 147.5; FAB HR MS: Calcd for $C_{31}H_{36}N_4$ + H: 465.30182. Found: 465.30180. Anal. Calcd for $C_{31}H_{36}N_4 \cdot H_2O$: C, 77.14; H, 7.93; N, 11.61. Found: C, 77.67; H, 7.59; N, 11.25.

**3,8,12,13,17-Pentaethyl-7,18-dimethyl-2-aza-21-carbaporphyrin (14c).** The hydrochloride salt was prepared by the procedure detailed above from tripyrrane **12** (100 mg) and diformylpyrrole **13c** (33 mg). The green product fractions were washed with 10% aqueous hydrochloric acid, evaporated, and recrystallized from chloroform-petroleum ether (60−90 °C) to give the desired N-confused porphyrin hydrochloride salt (30−50 mg; 28−47%) as purple crystals, mp > 300 °C. The corresponding free base was isolated as a purple powder by recrystallization from chloroform-methanol. UV−vis (1% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\epsilon$) 353 (4.44), 422 (4.96), 517 (4.00), 555 (3.87), 614 (3.43), 679 (3.27); UV−vis (1 equiv of TFA−$CHCl_3$; monocation): $\lambda_{max}$ (log $\epsilon$) 337 (4.51), 422 (4.92), 442 (4.69), 531 (3.88), 572 (4.11), 697 (3.99); UV-vis (2% TFA−$CHCl_3$; dication): $\lambda_{max}$ (log $\epsilon$) 337 (4.49), 426 (4.92), 456 (4.66), 549 (3.87), 594 (3.91), 706 (3.74); $^1$H NMR ($CDCl_3$; 25 °C): $\delta$ −6.26 (1H, s), −3.79 (1H, br s), −3.68 (1H, br s), 1.80−1.88 (12H, m), 1.96 (3H, t), 3.52 (3H, s), 3.54 (3H, s), 3.85−4.08 (10H, m), 9.57 (1H, s), 9.65 (1H, s), 9.73 (1H, s), 10.08 (1H, s); $^1$H NMR (TFA−$CDCl_3$): $\delta$ −4.11 (1H, s), −3.5 (1H, vb), −0.87 (1H, s), −0.76 (1H, s), 1.7−1.75 (12H, m), 1.84 (3H, t), 3.32 (3H, s), 3.39 (3H, s), 3.7−3.89 (8H, m), 4.07 (2H, q), 9.46 (1H, s), 9.52 (1H, s), 9.90 (1H, s), 9.96 (1H, s), 12.86 (1H, br s); $^{13}$C NMR ($CDCl_3$): $\delta$ 11.4, 11.5, 14.7, 17.4, 17.5, 18.6 (2), 19.6, 19.7, 20.1, 24.9, 94.2, 96.0, 101.3, 103.1, 106.8, 132.3, 134.1, 134.2, 134.9, 135.7, 136.8, 137.7, 137.9, 138.1, 144.7, 145.3, 148.2, 153.9, 155.1, 171.00; $^{13}$C NMR (TFA−$CDCl_3$): $\delta$ 11.2, 11.6, 13.3, 16.2, 17.0 (2), 19.6 (2), 19.8 (2), 22.7, 94.6, 96.2, 105.1, 109.9, 112.4, 123.8, 131.3, 140.2, 141.4, 142.4, 142.4, 142.6, 142.8, 144.3, 145.2, 145.6, 145.7, 145.9, 147.7, 164.6; EI MS: *m*/*z* (rel int) 478 (100), 463 (6.8), 449 (26), 239 (12); HR MS: Calcd for $C_{32}H_{38}N_4$: 478.30965. Found: 478.30896. Anal. Calcd for $C_{32}H_{38}N_4 \cdot H_2O$: C, 77.38; H, 8.11; N, 11.28. Found: C, 77.28; H, 7.77; N, 11.03.

**8,12,13,17-Tetraethyl-7,18-dimethyl-2-aza-21-carbaporphyrin (14a).** The hydrochloride salt was prepared by the procedure detailed above for **14b** from tripyrrane **12** (100 mg) and diformylpyrrole **13a** (27 mg). Recrystallization from chloroform−petroleum ether (60−90 °C) gave the porphyrin analogue (16 mg; 16%) as dark blue crystals, mp > 300 °C. The corresponding free base was isolated as a purple powder: UV−vis (1% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\epsilon$) 352 (4.53), 420 (5.12), 515 (4.11), 552 (3.87), 618 (3.38), 681 (3.56); UV-vis (1 equiv of TFA−$CHCl_3$; monocation): $\lambda_{max}$ (log $\epsilon$) 336 (4.88), 418 (5.05), 437 (4.76), 527 (3.94), 569 (4.22), 647 (3.74), 707 (4.17); UV-vis (5% TFA−$CHCl_3$; dication): $\lambda_{max}$ (log $\epsilon$) 341 (4.63), 423 (4.99), 451 (4.64), 507 (3.42), 545 (3.78), 590 (3.81), 669 (3.67), 714 (3.86); $^1$H NMR ($CDCl_3$): $\delta$ −6.30 (1H, s), −3.87 (2H, br s), 1.75−1.83 (12H, m), 3.45 (3H, s), 3.55 (3H, s), 3.80−3.99 (8H, m), 9.44 (1H, s), 9.54 (1H, s), 9.56 (1H, s), 9.70 (1H, s), 10.12 (1H, s); $^1$H NMR (TFA−$CDCl_3$): $\delta$ -3.30 (1H, s), 0.37 (1H, br s), 0.48 (1H, s), 0.87 (1H, s), 1.6−1.74 (12H, m), 3.30 (3H, s), 3.34 (3H, s), 3.74−3.82 (8H, m), 9.26 (1H, s), 9.30 (1H, s), 9.44 (1H, s), 9.97 (1H, s), 10.01 (1H, s), 13.59 (1H, br s); $^{13}$C NMR ($CDCl_3$): $\delta$ 11.4, 11.5, 17.4, 17.5, 18.5, 18.6, 19.6 (2), 20.0, 94.2, 95.5, 101.3, 104.1, 108.0, 132.6, 134.8, 134.8, 135.8, 137.7, 137.8, 138.1, 138.4, 145.0, 145.4, 149.1, 154.7, 155.5, 156.4; FAB HR MS: Calcd for $C_{30}H_{34}N_4$ + H: 451.28617. Found: 451.28630.

**Nickel(II) Complex 25.** Trimethyl N-confused porphyrin **14b** (35 mg) and nickel(II) acetate (30 mg) were dissolved in DMF (35 mL) and heated at 145 °C under nitrogen for 30 min. The mixture was cooled, diluted with chloroform, and washed with water, and the solvents were removed under reduced pressure. The purple residue was chromatographed on Grade II alumina, eluting with 0.5% methanol−chloroform, and the organometallic product was collected as a dark red band. Trituration with methanol, followed by recrystallization of the filtrate from chloroform−hexanes, gave the nickel complex (18 mg; 46%) as purple crystals: mp > 300 °C; UV-vis (1% $Et_3N$−$CHCl_3$): $\lambda_{max}$ (log $\epsilon$) 337 (4.57), 405 (4.645), 453 (4.31), 557 (4.15), 682 (3.53), 750 (3.46); UV-vis (DMSO): $\lambda_{max}$ (log $\epsilon$) 336 (4.55), 405 (4.70), 420 (4.67), 456 (4.34), 557 (4.16), 674 (3.49), 740 (3.43); UV-vis (1% TFA−$CHCl_3$): $\lambda_{max}$ (log $\epsilon$) 326 (4.48), 409 (4.73), 550 (4.06); $^1$H NMR ($CDCl_3$): $\delta$ 1.55−1.68 (12H, m), 2.75 (3H, s), 2.86 (3H, s), 2.97 (3H, s), 3.39−3.53 (8H, m), 7.83 (1H, br s), 8.53 (1H, br s), 8.65 (1H, br s), 8.68 (1H, br s), 9.09 (1H, br s, exchanges with $D_2O$); $^1$H NMR (DMSO-$d_6$): $\delta$ 1.55 (6H, t), 1.62 (6H, two overlapping triplets), 3.02 (3H, s), 3.07 (3H, s), 3.44 (3H, s), 3.48−3.55 (8H, m), 8.70 (1H, s), 8.77 (2H, s), 9.15 (1H, s), 13.78 (1H, s); $^1$H NMR (TFA−$CDCl_3$): $\delta$ −4.93 (1H, br d), 1.63−1.77 (12H, m), 3.16 (3H, s), 3.22 (3H, s), 3.77 (3H, s), 3.61−3.8 (8H, m), 9.37 (1H, s), 9.43 (1H, s), 9.75 (1H, s), 10.01 (1H, s), 14.77 (1H, br s); $^{13}$C NMR (DMSO-$d_6$): $\delta$ 10.6 (2), 12.9, 16.6, 17.0, 17.5, 17.6, 18.4, 18.6, 94.2, 95.6, 103.7, 109.8, 114.8, 124.2, 131.7, 135.4, 136.9, 138.7, 139.6, 141.3, 141.5, 142.8, 142.9, 144.8, 146.5, 146.7, 149.1, 157.7; EI MS: *m*/*z* (rel int) 524 (9), 523 (16), 522 (45), 521 (37), 520 (100), 519 (10), 509 (2.6), 508 (4.7), 507 (8.5), 506 (9.9), 505 (16), 504 (3.0), 260 (13); HR MS: Calcd for $C_{31}H_{36}N_4Ni$: 520.21369. Found: 520.21342.

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**Supporting Information Available:** Copies of proton and carbon-13 NMR spectra for **13**−**15** and **25**, and UV-vis spectra for porphyrinoids **14a**−**c** and nickel chelate **25**. This material is available free of charge via the Internet at http://pubs.acs.org.

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