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Synthesis and Reactivity of Carbachlorins and Carbaporphyrins

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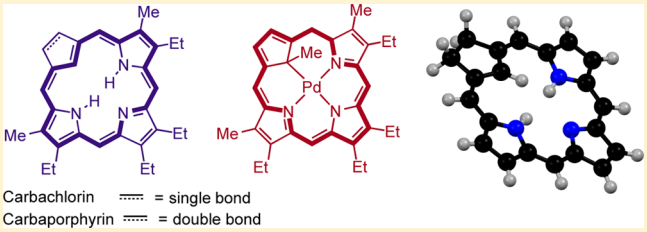
Supporting Information

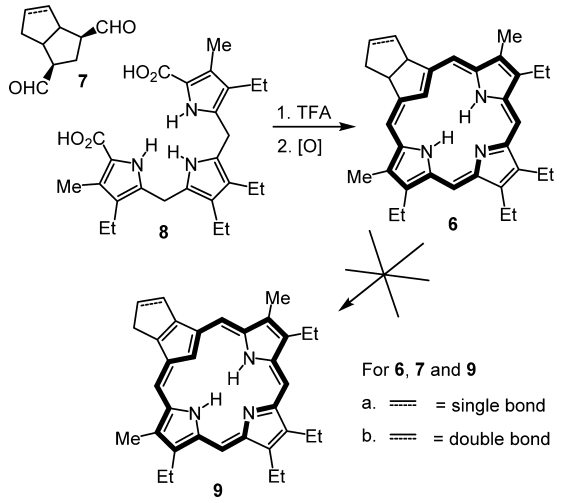
ABSTRACT: Acid-catalyzed condensation of 3-ethoxymethylenecyclopentene-1-carbaldehyde with a tripyrrane, followed by oxidation with aqueous ferric chloride solutions, afforded moderate yields of a carbachlorin. This porphyrinoid exhibited a porphyrin-like UV−vis spectrum with a slightly intensified peak at 650 nm. The proton NMR spectrum showed that the carbachlorin is highly diatropic, and this has been confirmed by nucleus independent chemical shift (NICS) calculations. Oxidation of the carbachlorin with DDQ gave the first example of a carbaporphyrin that is unsubstituted on the carbocyclic ring. Reaction of the carbachlorin with silver(I) acetate gave the corresponding silver(III) organometallic complex. When the carbachlorin was refluxed with methyl iodide and potassium carbonate in acetone, the 22-methyl derivative was formed. Treatment of the N-alkylation product with palladium(II) acetate afforded an unstable palladium(II) carbachlorin that was partially converted into a palladium(II) carbaporphyrin via an oxidation−methyl group migration process. Improved yields of the carbaporphyrin complex were obtained when the reaction mixture was stirred with aqueous ferric chloride solutions. These results open up the field of carbachlorin and carbaporphyrin chemistry for further study.



INTRODUCTION

Carbaporphyrinoids are porphyrin analogues with at least one carbon atom within the macrocyclic cavity[1] and include oxybenziporphyrins (**1**),[2] benzocarbaporphyrins (**2**),[3] azuliporphyrins (**3**),[4] and tropiporphyrins (**4**).[5] Oxybenziporphyrins and benzocarbaporphyrins retain porphyrin-like UV−vis spectra and are highly diatropic, as judged by proton NMR spectroscopy.[6] However, azuliporphyrins are cross-conjugated and have considerably reduced diatropic character, while tropiporphyrins have intermediary properties due to the nonplanar nature of the seven-membered ring. Chlorins (2,3-dihydroporphyrins **5**) are an important group of tetrapyrroles that provide the chromophore for many of the chlorophylls.[7] Chlorins have modified UV−vis spectra and show relatively strong absorptions near 650 nm that lead to their green coloration in solution. There is a great deal of interest in porphyrinoid chromophores with strong absorptions at 650 nm or higher wavelengths, due in part to their potential application as photosensitizers in photodynamic therapy,[8] and this has led to numerous investigations into the synthesis of chlorins.[9−13] However, there have been very few studies on the preparation of chlorin-like systems that may have equally useful properties.[14] Some time ago, we reported the synthesis of carbachlorins **6** using a "3 + 1" variant on the MacDonald condensation (Scheme 1).[15] Bicyclic dialdehydes **7** were found to condense with tripyrrane **8** in the presence of TFA to give, following oxidation with DDQ, propanocarbachlorin **6a** and propenocarbachlorin **6b** in moderate yields. These chlorin analogues retained aromatic properties, and the proton NMR spectra showed the inner CH protons upfield near −7 ppm.[15] The UV−vis spectra were also very porphyrin-like, showing a

Scheme 1



Soret band at 404 nm and a series of small absorptions that culminated in a medium-sized Q band at 650 nm.[15] However, although true chlorins are easily oxidized to give porphyrins, attempts to further oxidize **6a**,**b** to the corresponding carbaporphyrins **9** were unsuccessful.

In order to further explore the carbachlorin system, attempts were made to condense 1,3-cyclopentanedicarbaldehyde **10** with tripyrrane **8** to give porphyrinoid **11** (Scheme 2).[15]

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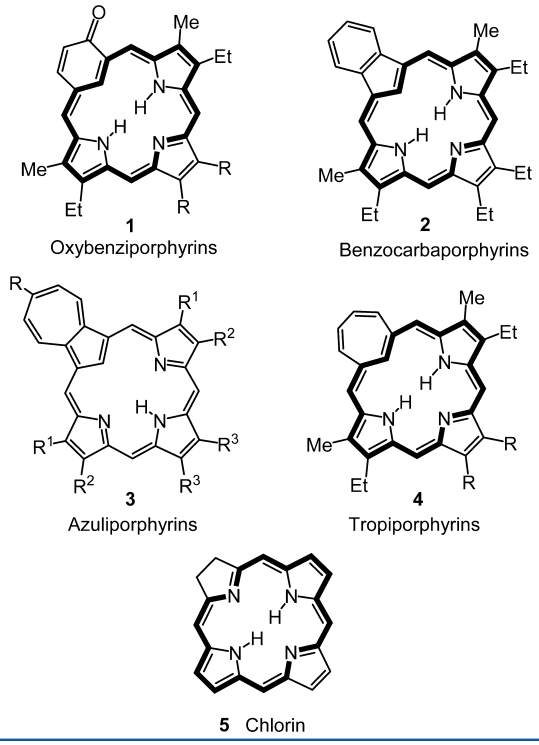
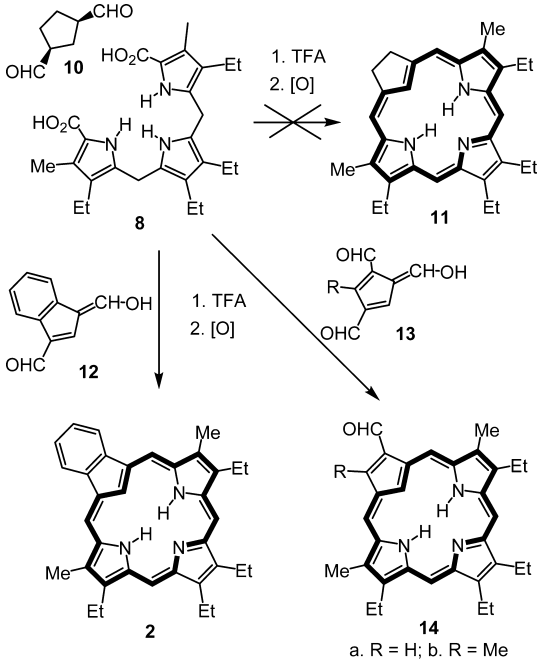


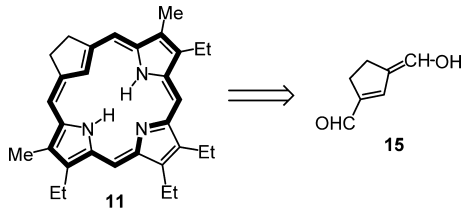
Scheme 2



However, no chlorinoid product could be isolated from these experiments. It was speculated that the presence of substituents, or the additional five-membered rings in structure 7, aids in the formation of porphyrinoid products by altering the conformation to the intermediates prior to cyclization. Indene dialdehyde **12** has been shown to be a particularly effective precursor to benzocarbaporphyrins **2**,[3] and cyclopentadiene trialdehyde **13** has also been reacted with **8** to give carbaporphyrin aldehyde **14**, albeit in low yields (Scheme 2).[3,16] The latter precursor is compromised by the presence of three aldehyde moieties, as only two of these are needed for macrocycle formation and the third unit may react to give unwanted byproducts.

In relation to these earlier studies, it is notable that conjugated dialdehydes such as **12** are more effective in the "3 + 1" condensation reactions than aliphatic dialdehydes such as **7** and **10**. Therefore, we speculated that the cyclopentene dialdehyde **15** might be a suitable precursor to chlorin **11** (Scheme 3). In this paper, the synthesis of carbachlorin **11** is

Scheme 3

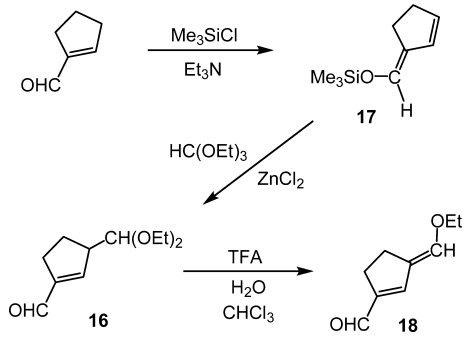


described together with its conversion to a carbaporphyrin.[17] In addition, preliminary investigations into the metalation of these porphyrinoids are described.

RESULTS AND DISCUSSION

Reports on the use of dialdehyde **15** in the synthesis of open-chain conjugated systems have appeared in the patent literature,[18] but we could find no published methods for the synthesis of this compound. However, a convenient synthesis of the related acetal derivative **16** has been reported.[19] Reaction of cyclopentene-1-carbaldehyde with trimethylsilyl chloride and triethylamine gives the silyl dienol ether **17**, and subsequent reaction with triethyl orthoformate and zinc chloride affords the related acetal **16** (Scheme 4).[19] Unfortunately, all attempts to

Scheme 4



carry out an acid-catalyzed hydrolysis of **16** to give dialdehyde **15** were unsuccessful, either giving starting material or leading to decomposition. However, treatment of a chloroform solution of **16** with aqueous trifluoroacetic acid gave the related enol ether **18** instead. We reasoned that the reactivity of **18** should be similar to that of **15** and that this aldehyde could be used in the preparation of **11**. As **18** proved to be rather unstable, a solution of the crude enol ether was generated and immediately used in reactions with tripyrrane **8** (Scheme 5). Tripyrrane **8** was treated with TFA and diluted with dichloromethane, and a freshly prepared solution of **18** in chloroform was added immediately. The mixture was allowed to react for 16 h and then oxidized by shaking the reaction mixture with 0.1% aqueous ferric chloride solution. Following purification by column chromatography and recrystallization, carbachlorin **11**

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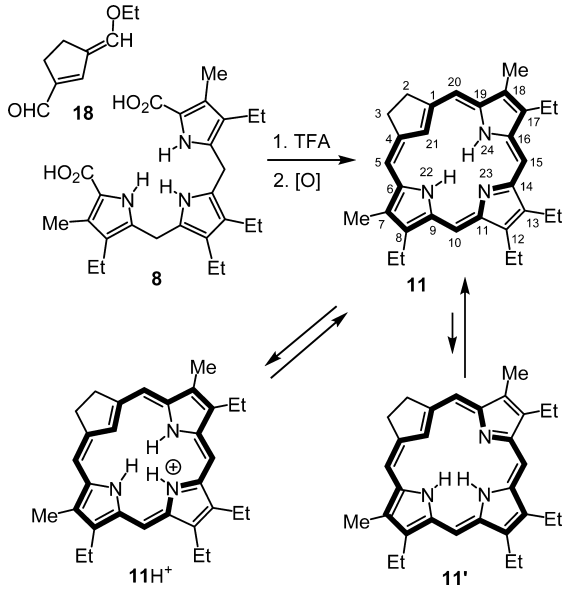
Scheme 5



was isolated in 11−16% yield. The proton and carbon-13 NMR spectra of **11** demonstrated that the porphyrinoid has a plane of symmetry and therefore must correspond to either tautomer **11** or a rapidly interconverting mixture of **11** and **11′** (Scheme 5). The proton NMR spectrum (Figure 1) also confirmed that this

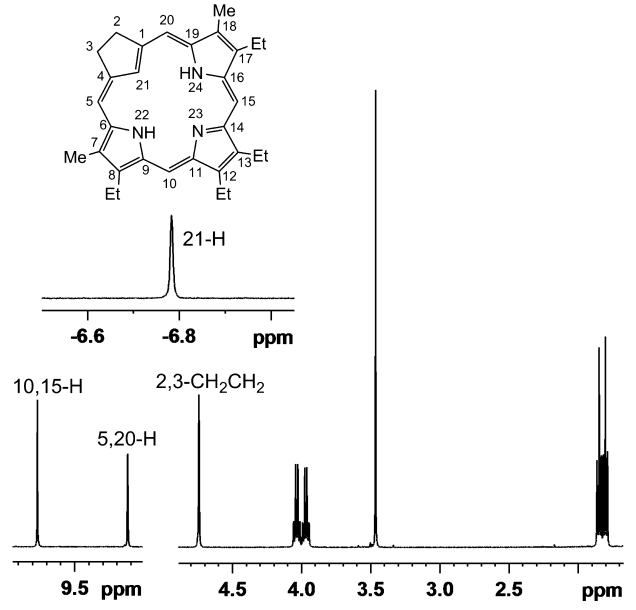


Figure 1. 500 MHz proton NMR spectrum of carbachlorin **11** in $CDCl_3$.

porphyrinoid is highly diatropic, as the internal CH was observed at −6.8 ppm, while the external *meso* protons were shifted downfield to give two 2H singlets at 9.14 and 9.77 ppm. The CH_2CH_2 unit of the carbachlorin ring gave a 4H singlet at 4.76 ppm due to its proximity to the macrocyclic ring current. The alkyl groups attached to the macrocycle are also strongly deshielded, and the methyl groups gave a 6H singlet at 3.47 ppm, while the CH_2 units of the four ethyl groups gave rise to two 4H quartets at 3.96 and 4.03 ppm. The carbon-13 NMR spectrum showed the internal CH at 122.1 ppm, while the *meso* carbons appeared at 96.2 (10,15-CH) and 97.4 ppm (5,20-CH). The UV−vis spectrum for **11** is very porphyrin-like, giving a Soret band at 401 nm and a series of Q bands at 495, 593, and 651 nm (Figure 2). As expected, the strongest of the

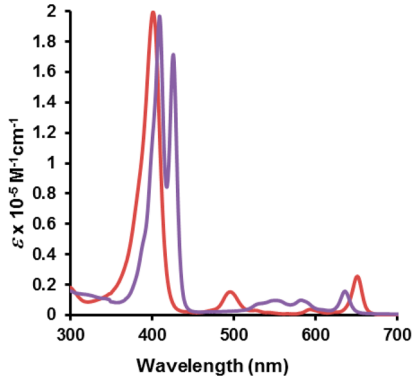


Figure 2. UV spectra of carbachlorin **11**: (red line) free base in 1% Et_3N−99% CH_2Cl_2; (blue line) cation **11**H$^+$ in 1% TFA−99% CH_2Cl_2.

Q bands was the longest wavelength absorption. Addition of TFA afforded the cationic species **11**H$^+$ (Scheme 5), and this gave a split Soret band at 409 and 426 nm (Figure 2). The UV−vis data closely resemble those previously reported for carbachlorins **6**.[15] The proton NMR spectrum for cation **11**H$^+$ in TFA−$CDCl_3$ demonstrated the presence of a slightly enhanced diatropic ring current. The inner CH gave a resonance at −6.95 ppm, while the NH protons afforded peaks at −5.52 (1H) and −4.19 ppm (2H). The external *meso* protons gave two 2H singlets at 9.53 and 10.02 ppm, while the carbachlorin methylene groups gave rise to a 4H singlet at 4.80 ppm. The proton and carbon-13 NMR spectra both confirmed that the cation retains a plane of symmetry.

In order to gain further insights into the carbachlorin system, the parent structure **19** was assessed using density functional theory calculations.[20] Chlorin tautomers **19** and **19′** and the related cation **19**H$^+$ were minimized using B3LYP/6-311++G(d,p). Although the B3LYP functional has been shown to be reliable for calculating porphyrinoid geometries and frequencies,[21,22] the sensitivity of the relative energies to the choice of functionals needed to be assessed.[23,24] Single-point energy calculations were performed on the minimized structures using M06-2X/6-311++C(d,p) and B3LYP-D/6-311++G(d,p) (Table 1).[25,26] By these measures tautomer **19′** is calculated to be between 4.79 and 5.00 kcal/mol less stable than tautomer **19**. In **19**, the NH units flank the imine nitrogen and are in a better position for hydrogen-bonding interactions. The carbachlorin structures are not completely planar, due to steric crowding within the macrocycle (Table 2). For **19**, ring *a* is pivoted by nearly 10° relative to the mean macrocyclic plane, although the remaining rings are only slightly tilted (Table 2). Tautomer **19′** is slightly more distorted, but this is magnified in cation **19**H$^+$, where four internal hydrogens have to be accommodated. The bond lengths in **19** are consistent with the presence of an 18-π-electron delocalization pathway (Figure 3). The C6−C7, C8−C9, C16−C17, and C18−C19 bonds are relatively short in comparison to the C11−C12 and C13−C14 bonds, while the C7−C8 and C17−C18 bonds are longer than the C1−-C13 bond, as would be predicted by the [18]annulene model for porphyrinoid aromaticity.[27] Nucleus independent

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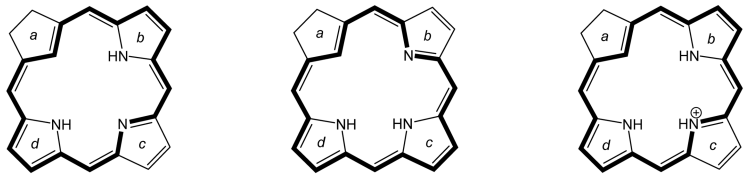
Table 1. Calculated Energies (hartrees), Relative Energies (kcal/mol), and NICS Values (ppm) for Tautomers of Carbachlorin 19 and the Related Cation 19H$^+$.



	19	**19'**	**19H$^+$**
B3LYP Minimum	-974.9472257	-974.9395878	-975.3458152
ΔG (298 K)	0.00	4.59	***
*B3LYP/**B3LYP-D**/M06-2X*	0.00/**0.00**/0.00	4.79/**4.84**/5.00	***
NICS(0)	-14.03	-13.97	-13.95
NICS(*a*)	+5.81	+6.14	+6.07
NICS(*b*)	-14.02	-3.83	-14.61
NICS(*c*)	-5.11	-14.25	-15.84
NICS(*d*)	-14.02	-15.60	-14.61

Table 2. Angles (deg) between the Plane of Each of the Five-Membered Rings and the Overall Plane of the Macrocycle

molecule	ring *a*	ring *b*	ring *c*	ring *d*
19	11.10	1.97	1.26	1.99
19′	6.93	0.65	3.04	8.23
19H$^+$	13.69	11.74	12.47	11.74

chemical shifts (NICS)[28] were also performed on **19**, **19′**, and **19H$^+$**. The NICS(0) values for all three structures were close to −14 ppm, which is in accord with expectations for a highly diatropic porphyrinoid. The NICS values for the center of the individual subunits were also calculated. The pyrrole rings in **19** gave values of −14.02 ppm. The observed ring current is due to a combination of all of the possible delocalization pathways, but the 18-π-electron pathway is likely to be dominant. As rings *b* and *d* lie within the aza[18]annulene pathway, large negative values would be expected. Nevertheless, the ring current due to the pyrrole ring itself may also be a significant factor. The pyrrolenine ring (*c*) gives a much smaller value of −5.11 because the center of this ring lies outside of the 18-π-electron delocalization pathway and this leads to deshielding. Ring *a* gives a value of +5.81, which is to be expected, as this ring also lies outside of the aza[18]annulene core and does not contribute a ring current of its own. Similar trends can be discerned for tautomer **19′**. In cation **19H$^+$**, all three pyrrole rings give similar strongly negative values. This is due to resonance contributors such as **19′H$^+$** and **19″H$^+$**, which facilitate three different versions of the aza[18]annulene pathway (Figure 4). However, ring *a* remains outside of these pathways, and this results in a deshielded NICS(a) value of +6.07 ppm.

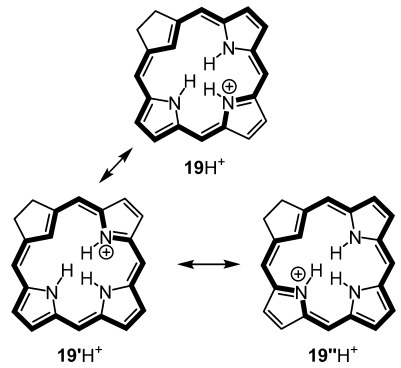


Figure 4. Alternative 18-π-electron delocalization pathways in cation **19H$^+$**.

Attempts to oxidize carbachlorins **6** to the corresponding carbaporphyrins had been unsuccessful, but this may be due in part to the presence of a fused five-membered ring which would not favor the presence of sp^2-hybridized carbons due to the associated angle strain.[15] When **11** was heated with DDQ in

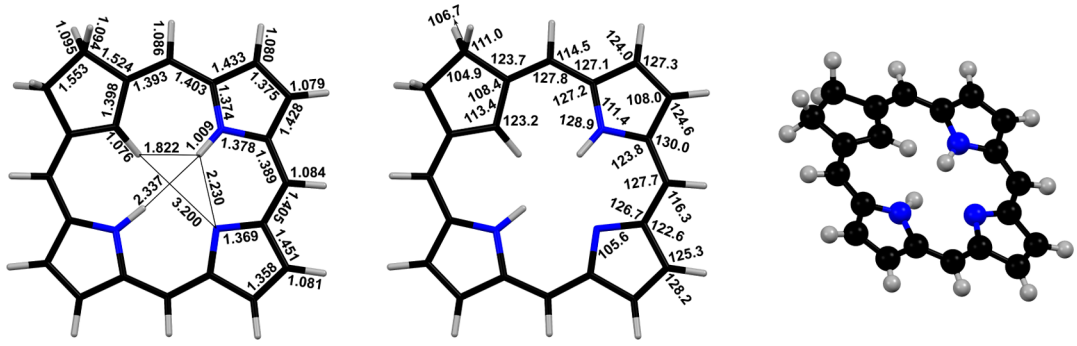


Figure 3. Bond lengths (Å) and angles (deg) and the 3D geometry for the minimized conformation of carbachlorin **19**.

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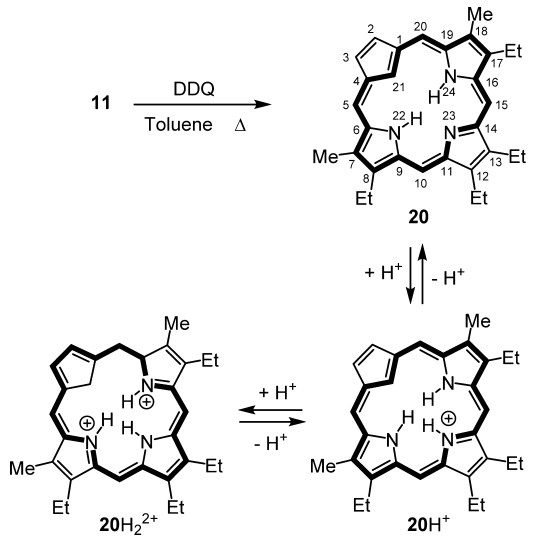
toluene, dehydrogenation readily occurred to give the corresponding carbaporphyrin **20** (Scheme 6). Most of the

Scheme 6



research on carbaporphyrins has made use of the readily available benzo-fused structures **2**;[3] therefore, access to **20** is an important advance in this area.[29−31] Carbaporphyrin **11** is also highly diatropic and shows the internal CH as a singlet at −6.91 ppm, while the NHs produce a broad resonance at −3.92 ppm. The *meso* protons appear downfield as two 2H singlets at 9.77 and 9.83 ppm, and the external cyclopentadiene protons appear as a 2H doublet (J = 1.6 Hz) at 8.15 ppm (Figure 5). The

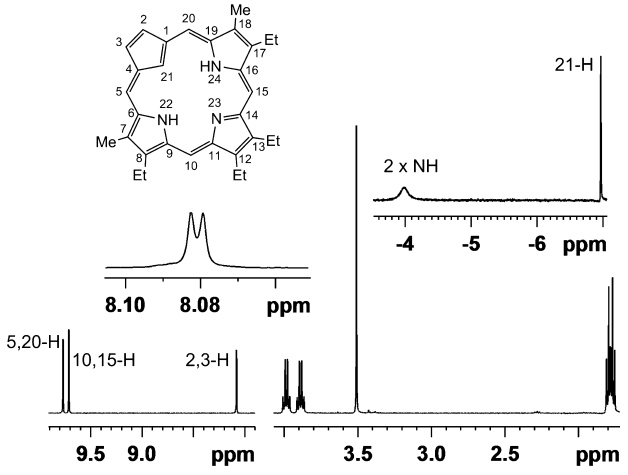


Figure 5. 500 MHz proton NMR spectrum of carbaporphyrin **20** in $CDCl_3$.

doublet results from coupling to the inner CH (confirmed by $^1H-^1H$ COSY), but this coupling is not resolved for the 21-H resonance. The proton and carbon-13 NMR spectra for **20** show that the macrocycle has a plane of symmetry, and this result is consistent with the depicted tautomer (the favorability of this tautomer is also supported by DFT calculations[30] and is due in part to favorable hydrogen-bonding interactions within the macrocyclic cavity). The carbon-13 NMR spectrum in $CDCl_3$ showed the inner CH at 100.8 ppm, the *meso* carbons at 94.8 and 105.9 ppm, and the external cyclopentadiene carbons at 128.7 ppm. The UV−vis spectrum of **20** was less porphyrin-like, showing two broad absorptions in the Soret region at 377 and 421 nm and broad Q bands at higher wavelengths (Figure 6). This is in contrast with the case for benzocarbaporphyrins **2**

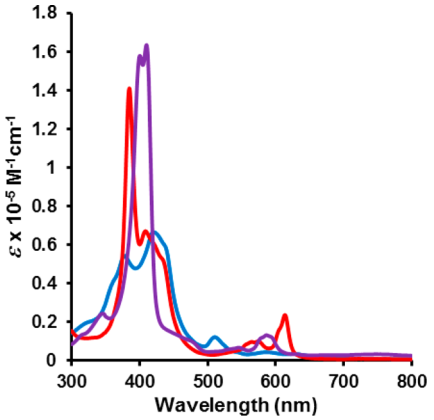


Figure 6. UV−vis spectra of carbaporphyrin **20**: (blue line) free base in 1% triethylamine−99% dichloromethane; (red line) monocation **20**H^+ with 10 equiv of TFA in CH_2Cl_2; (purple line) dication **20**H_2^{2+} in 10% TFA−90% CH_2Cl_2.

and formylcarbaporphyrins **14**, which show strong Soret bands and better defined Q bands in their UV−vis spectra. Addition of trace amounts of TFA produced a new species attributed to the monocation **20**H^+, which showed a strong Soret band at 385 nm, together with a broad absorption at 409 nm and Q bands at 563, 574, and 614 nm (Figure 6). Further addition of TFA gave rise to a third species corresponding to the C-protonated dication **20**H_2^{2+}. In 10% TFA−90% CH_2Cl_2, a strong split Soret band appeared at 400 and 410 nm, together with weaker absorptions at higher wavelengths (Figure 6). Benzocarbaporphyrins **2** are also reported to form C-protonated dications,[3] but diprotonation is only complete in approximately 50% TFA solutions, whereas diprotonation of **20** is essentially complete in 5% TFA solutions. The proton NMR spectrum of **20**H_2^{2+} shows the presence of a very strong diamagnetic ring current, and the internal CH_2 gives a resonance at −8.27 ppm while the external cyclopentadiene protons appear at 11.11 ppm and the *meso* protons give rise to two 2H singlets at 11.00 and 11.45 ppm. These data show that the dication has enhanced diatropicity in comparison to the free base form. However, the downfield shift of the outer cyclopentadiene protons is due in part to the 18-π-electron delocalization pathway being relocated through the five-membered carbon ring (see bold pathway for **20**H_2^{2+} in Scheme 6).

Carbaporphyrinoids such as **1**, **2**, and **4** react with silver(I) acetate to give silver(III) organometallic derivatives.[32,33] For instance, benzocarbaporphyrin **2** afforded good yields of the nonpolar silver(III) complexes **21** (Scheme 7).[33] This chemistry occurs rapidly in mixtures of dichloromethane and methanol at room temperature in the presence of 3 equiv of silver(I) acetate. However, carbachlorin **11** reacted rather slowly under these conditions. After 16 h, the silver(III) derivative **22** was isolated in 11% yield (Scheme 8). When the reaction was continued for several days, the yield was raised to 31%. However, when 7 equiv of silver(I) acetate was used, only low yields (6%) of impure silver(III) carbaporphyrin **23** could be isolated. Attempts to react carbaporphyrin **20** with silver(I)

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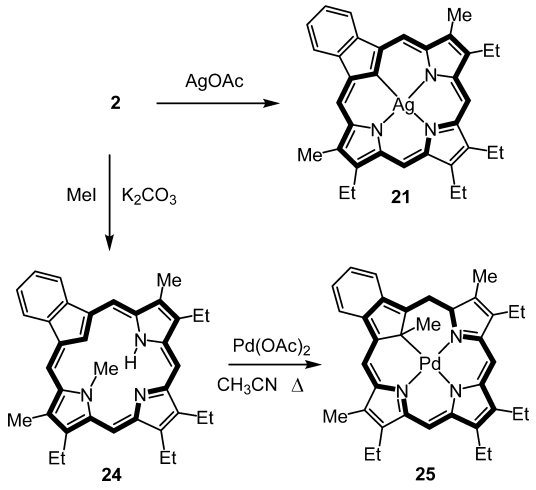
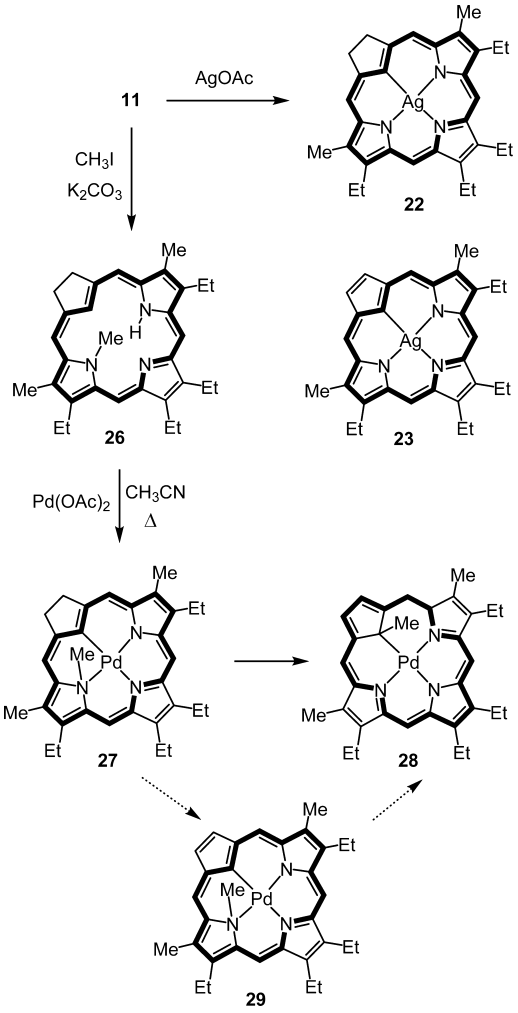
Scheme 7



Scheme 8



acetate led to decomposition. These results indicate that the exposed carbocyclic ring is prone to oxidative degradation, and the presence of a fused benzene ring in **2** is clearly beneficial in stabilizing these structures. The UV−vis spectrum for **22** is porphyrin-like, showing a strong Soret band at 411 nm and a relatively strong Q band at 599 nm (Figure 7). The proton NMR spectrum for **22** indicates that the complex retains

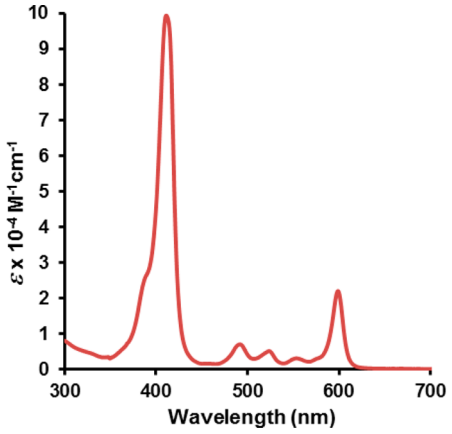


Figure 7. UV−vis spectrum of silver(III) carbachlorin **22** in dichloromethane.

strongly aromatic properties, as the *meso* protons show up downfield at 9.23 and 9.90 ppm and the carbachlorin CH_2CH_2 unit gives a 4H singlet at 5.02 ppm. The presence of a plane of symmetry was evident in the proton and carbon-13 NMR spectra, and the molecular formula was confirmed by high-resolution electron impact mass spectrometry.

Benzocarbaporphyrin does not give any isolatable products in reactions with palladium(II) salts. However, the *N*-alkyl derivatives **24** reacted with palladium(II) acetate in refluxing acetonitrile to give palladium(II) complexes **25** (Scheme 7).[34] This chemistry is intriguing, because metalation is associated with an alkyl group migration from the nitrogen to the internal carbon atom.[34] A similar alkylation−metalation sequence was conducted on carbachlorin **11**. Reaction of **11** with methyl iodide and potassium carbonate in refluxing acetone for 16 h gave the *N*-methyl derivative **26** in 34% yield. Prolonged reaction times did not improve the yield, as unidentified side products were formed. The site of alkylation can be deduced from the proton and carbon-13 NMR spectra, as the product shows a complete loss of symmetry (Figure 8). For instance, the *meso* protons now show up as four 1H singlets at 8.89, 9.04, 9.37, and 9.58 ppm. The alkylation introduces steric crowding within the macrocyclic cavity, but the NMR data show that the chlorin retains most of its diatropic character. The internal methyl group gave a 3H singlet at −4.27 ppm, while the inner CH gave a resonance at −6.31 ppm (Figure 8). As the methyl group is too large to pass through the cavity, carbachlorin **26** is chiral, and this leads to some complexity in the proton NMR spectrum. The 6 methylene units are all nonequivalent, and the individual protons are diastereotopic; thus, in principle this can lead to 12 different resonances. In reality there is a significant amount of overlap, but the carbachlorin CH_2CH_2 unit gives rise to three multiplets at 4.40 (1H), 4.54 (1H), and 4.79 ppm (2H). The UV−vis spectrum for **26** in CH_2Cl_2 is somewhat broadened in comparison to the spectrum for **11**. The resulting weakened Soret band appeared at 407 nm, and less well-defined Q bands appeared between 500 and 664 nm (Figure 9). These differences presumably result from distortion of the carbachlorin chromophore due to the presence of the internal methyl group. Addition of TFA resulted in the formation of the cation **26**H^+ with a split Soret band at 415 and 428 nm (Figure 9), and again the spectrum was somewhat broadened in comparison to **11**H^+. Methylated chlorin **26** was refluxed with palladium(II) acetate in acetonitrile for 30 min. Column chromatography on silica gel gave two fractions with similar

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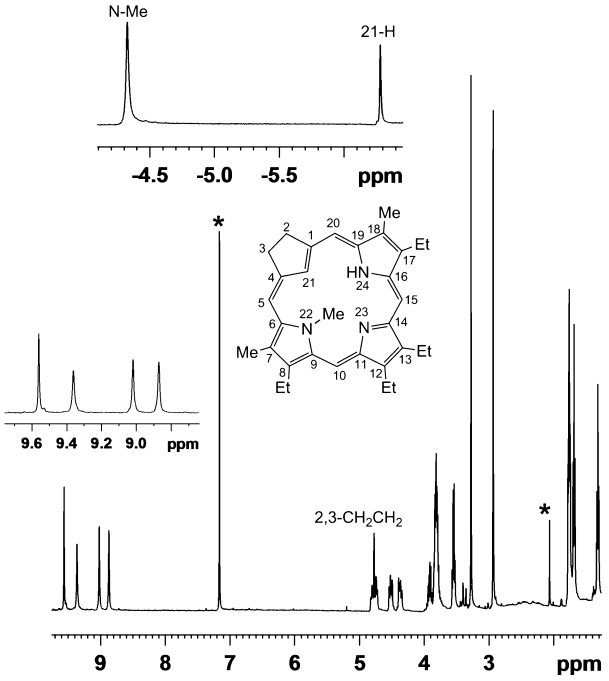

Figure 8. 500 MHz proton NMR spectrum of *N*-methylchlorin **26** in $CDCl_3$. Asterisks denote solvent impurities.

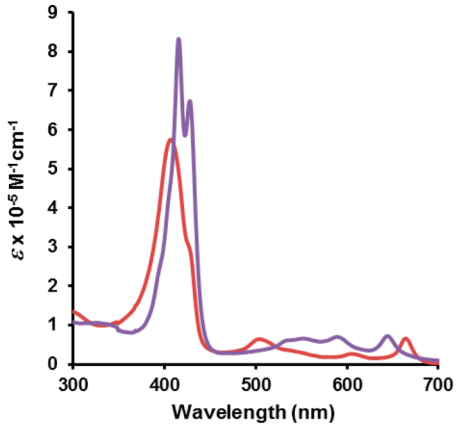

Figure 9. UV−vis spectra of *N*-methylchlorin **26**: (red line) free base in 1% triethylamine−99% dichloromethane; (blue line) cation **26**H^+ in 1% TFA−99% CH_2Cl_2.

polarities corresponding to metalated products. It had been anticipated that the product of this chemistry would be the *N*-methyl palladium(II) complex **27**. Methyl group migration would not be expected in this case, as this would interrupt the macrocyclic conjugation pathway. Unexpectedly, the main product was identified as palladium(II) carbaporphyrin **28**, where an oxidation had occurred in addition to the methyl group migration. Palladium complex **28** was isolated in 17% yield. The remaining fraction appeared to consist primarily of the expected palladium(II) chlorin **27**, but this could not be isolated in pure form. The samples were always contaminated with **28**, and it soon became apparent that **27** was slowly converting into **28**. In order to speed up the oxidation, the crude reaction solution was diluted with dichloromethane and stirred vigorously with an aqueous ferric chloride solution for 24 h. Following workup, the yield of palladium(II) complex **28** was raised to 34%. It is likely that initial oxidation affords the *N*-methyl palladium(II) carbaporphyrin **29** and this subsequently undergoes a rearrangement to give **28**. The mechanism of the rearrangement is not known but could be a stepwise process involving the transient formation of a Pd−methyl bond. Alternatively, the conversion could be considered to be a [3,3]-sigmatropic shift.[34] Palladium complex **28** has regained a plane of symmetry and retains strongly diatropic characteristics. The proton NMR spectrum showed the internal methyl group at −4.46 ppm, while the *meso* protons appeared downfield as two 2H singlets at 10.00 and 10.42 ppm. The cyclopentadiene protons are directly connected to the 18-π-electron delocalization pathway and as a result are deshelded to give a 2H singlet at 9.60 ppm. The UV−vis spectrum is less distinctive, giving broad bands in the Soret region at 394 and 440 nm. The molecular formula for **28** was confirmed by high-resolution electron impact mass spectrometry.

CONCLUSION

The synthesis of a carbachlorin using a "3 + 1" methodology has been accomplished, and this system retains highly aromatic characteristics. Oxidation with DDQ affords a related carbaporphyrin, and this also shows highly diatropic properties. The carbachlorin was metalated with silver(I) acetate to give a stable silver(III) organometallic derivative. In addition, the chlorin was reacted with methyl iodide to give a chiral *N*-methyl derivative. Reaction of the alkylated product with palladium(II) acetate afforded a palladium(II) complex via a metalation−oxidation−methyl group migration sequence. These results open this area up for the study of carbachlorins and carbaporphyrins without fused benzene units.

EXPERIMENTAL SECTION

General Considerations. Melting points are uncorrected. NMR spectra were recorded using 400 and 500 MHz NMR spectrometers. ^{1}H NMR values are reported as chemical shift δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak), and coupling constant (J). Chemical shifts are reported in parts per million (ppm) relative to $CDCl_3$ (^{1}H residual $CHCl_3$ δ 7.26, ^{13}C $CDCl_3$ triplet δ 77.23 ppm), and coupling constants are taken directly from the spectra. NMR assignments were made with the aid of ^{1}H−^{1}H COSY, HSQC, DEPT-135, and NOE difference proton NMR spectroscopy. 2D NMR experiments were performed using standard software. High-resolution mass spectra (HRMS) were carried out by using a double-focusing magnetic sector instrument. ^{1}H and ^{13}C NMR spectra for all new compounds are reported in the Supporting Information.

8,12,13,17-Tetraethyl-7,18-dimethylcarbachlorin (11). Chloroform (20 mL) and a 50% aqueous trifluoroacetic acid solution (10 mL) were mixed, cooled to 0 °C, and then added to monoacetal **16** (200 mg, 1.31 mmol). The mixture was stirred at 0 °C for 3 h and then transferred to a separatory funnel. The organic layer was separated and the aqueous layer extracted with 30 mL of chloroform. The combined organic layers were washed with water, saturated sodium bicarbonate solution, and water. The organic layer was dried over sodium sulfate and filtered, and the resulting enol ether **18** solution was immediately used in the next step.

Tripyrranedicarboxylic acid **8**[35] (200 mg, 0.47 mmol) was stirred with trifluoroacetic acid (4 mL) under nitrogen for several minutes. The solution was diluted with dichloromethane (200 mL), the aforementioned enol ether solution (approximately 100 mL) was added, and the resulting mixture was stirred under nitrogen at room temperature overnight. The solution was transferred to a separatory funnel and shaken with an aqueous ferric chloride solution (0.1%, 200 mL) for 5 min. The organic phase was separated and washed with water, saturated sodium bicarbonate solution, and water. The organic layer was dried over sodium sulfate and filtered, and the solvent was

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removed under reduced pressure. The residue was chromatographed on a neutral grade 3 alumina column, with dichloromethane as eluent. The first fraction eluted as a purple solution which was evaporated under reduced pressure. The residue was further purified on a silica gel flash column, initially with dichloromethane and then with chloroform and 0.5% methanol−99.5% chloroform as eluents. A purple fraction was collected and recrystallized from chloroform−hexanes or chloroform−methanol to give the carbachlorin (21.2−31.9 mg, 0.047−0.070 mmol, 11−16%) as dark purple crystals: mp 246−247 °C; UV−vis (1% Et_3N−99% CH_2Cl_2) λ_{max} (log ε) 401 (5.30), 495 (4.18), 526 (sh, 3.51), 593 (3.57), 651 nm (4.41); UV−vis (1% TFA−99% CH_2Cl_2) λ_{max} (log ε) 409 (5.29), 426 (5.23), 530 (sh, 3.87), 552 (3.99), 582 (3.99), 636 nm (4.19); ^{1}H NMR (500 MHz, $CDCl_3$) δ −6.77 (1H, s, 21-H), 1.80 (6H, t, J = 7.7 Hz, 12,13-CH_2CH_3), 1.84 (6H, t, J = 7.7 Hz, 8,17-CH_2CH_3), 3.47 (6H, s, 7,18-CH_3), 3.96 (4H, q, J = 7.7 Hz, 12,13-CH_2), 4.03 (4H, q, J = 7.7 Hz, 12,13-CH_2), 4.76 (4H, CH_2CH_2), 9.14 (2H, s, 5,20-H), 9.77 (2H, s, 10,15-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.4 (7,18-CH_3), 17.6 (8,17-CH_2CH_3), 18.9 (12,13-CH_2CH_3), 19.8 (8,17-CH_2), 20.2 (12,13-CH_2), 35.8 (2,3-CH_2), 96.2 (10,15-CH), 97.4 (5,20-CH), 122.1 (21-CH), 128.7, 132.4, 136.1, 137.8, 142.7, 148.1, 149.5; ^{1}H NMR (500 MHz, TFA-$CDCl_3$) δ −6.95 (1H, s, 21-H), −5.52 (1H, s, 24-NH), −4.19 2H, br s, 23,25-NH), 1.63 (6H, t, J = 7.7 Hz, 8,17-CH_2CH_3), 1.81 (6H, t, J = 7.7 Hz, 12,13-CH_2CH_3), 3.41 (6H, s, 7,18-CH_3), 4.01 (4H, q, J = 7.7 Hz, 8,17-CH_2), 4.08 (4H, q, J = 7.7 Hz, 12,13-CH_2), 4.80 (4H, s, CH_2CH_2), 9.53 (2H, s, 5,20-H), 10.02 (2H, s, 10,15-H); ^{13}C NMR (125 MHz, TFA−$CDCl_3$) δ 11.6 (7,18-CH_3), 16.8 (8,17-CH_2CH_3), 17.8 (12,13-CH_2CH_3), 19.9 (12,13-CH_2), 20.1 (8,17-CH_2), 36.3 (2,3-CH_2), 93.6 (10,15-CH), 103.3 (5,20-CH), 131.0 (21-CH), 132.1, 133.6, 134.2, 139.5, 141.5, 142.6, 153.5; HR MS (EI) calcd for $C_{31}H_{37}N_3$ 451.2987, found 451.2992.

8,12,13,17-Tetraethyl-7,18-dimethylcarbaporphyrin (20). DDQ (10.0 mg, 0.044 mmol) was added to a solution of carbachlorin **11** (20.0 mg, 0.044 mmol) in toluene (10 mL). The mixture was stirred under reflux for 30 min and then cooled to room temperature. The solution was transferred to a separatory funnel, diluted with chloroform (50 mL), and washed with water. The aqueous layer was discarded, the organic layer was dried over sodium sulfate and filtered, and the solvent was removed under reduced pressure. The residue was chromatographed on grade 3 alumina, with 50% dichloromethane−50% hexanes as eluent. The first fraction (yellow) corresponded to carbaporphyrin **20**. Recrystallization from chloroform−methanol gave **20** (14.2 mg, 0.0316 mmol, 71%) as dark green crystals: mp >300 °C; UV−vis (1% Et_3N−99% CH_2Cl_2) λ_{max} (log ε) 377 (4.73), 421 (4.82), 510 (4.08), 585 nm (3.63); UV−vis (10 equiv TFA−CH_2Cl_2) λ_{max} (log ε) 385 (5.15), 409 (4.83), 433 (sh, 4.72), 555 (sh, 3.91), 563 (3.98), 574 (4.00), 614 nm (4.37); UV−vis (10% TFA−90% CH_2Cl_2) λ_{max} (log ε) 345 (4.39), 400 (5.20), 410 (5.21), 474 (sh, 4.01), 546 (3.83), 578 (sh, 4.07), 586 (4.12), 749 nm (3.51); ^{1}H NMR (500 MHz, $CDCl_3$) δ −6.91 (1H, s, 21-H), −3.92 (2H, br s, 2 × NH), 1.84 (6H, t, J = 7.7 Hz, 8,17-CH_2CH_3), 1.87 (6H, t, J = 7.7 Hz, 12,13-CH_2CH_3), 3.58 (6H, s), 3.96, (4H, q, J = 7.7 Hz, 12,13-CH_2), 4.05 (4H, q, J = 7.7 Hz, 8,17-CH_2), 8.15 (2H, d, J = 1.6 Hz), 9.77 (2H, s, 10,15-H), 9.83 (2H, s, 5,20-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.5 (7,18-CH_3), 17.6 (8,17-CH_2CH_3), 18.7 (12,13-CH_2CH_3), 19.7 (8,17-CH_2), 20.1 (12,13-CH_2), 94.8 (10,15-CH), 100.8 (21-CH), 105.9 (5,20-CH), 128.7 (2,3-CH), 133.4, 135.2, 136.6, 137.5, 138.2, 144.8, 153.8; ^{1}H NMR (500 MHz, TFA-$CDCl_3$) δ −8.27 (2H, s, 21-CH_2), −4.42 (2H, br, 2 × NH), 1.78 (6H, t, J = 7.7 Hz, 12,13-CH_2CH_3), 1.82 (6H, t, J = 7.7 Hz, 8,17-CH_2CH_3), 3.76 (6H, s, 7,18-CH_3), 4.21 (4H, q, J = 7.7 Hz, 8,17-CH_2), 4.26 (4H, q, J = 7.7 Hz, 12,13-CH_2), 11.00 (2H, s, 10,15-H), 11.11 (2H, s, 2,3-H), 11.45 (2H, s, 5,20-H); ^{13}C NMR (125 MHz, TFA-$CDCl_3$) δ 11.9 (7,18-CH_3), 16.6 (8,17-CH_2CH_3), 17.6 (12,13-CH_2CH_3), 20.36, 20.39 (8,12,13,17-CH_2), 103.3 (10,15-CH), 113.6 (5,20-CH), 140.1, 141.4, 142.5, 146.3, 146.7, 147.6, 150.3 (2,3-CH), 151.9; HR MS (EI) calcd for $C_{31}H_{35}N_3$ 449.2831, found 449.2836.

[8,12,13,17-Tetraethyl-7,18-dimethylcarbachlorinato]silver(III) (22). A solution of carbachlorin **11** (20.0 mg, 0.044 mmol) in dichloromethane (20 mL) was added to an suspension of 3.5 equiv of silver(I) acetate (25.9 mg, 0.154 mol) in methanol (20 mL), and the mixture was stirred at room temperature for 4 days. The mixture was washed with water, and the solvent was removed under reduced pressure. The residue was purified by silica gel flash column, with dichloromethane as eluent. A green-pink fraction was collected and further recrystallized from chloroform−methanol to give the silver(III) carbachlorin (7.6 mg, 0.014 mmol, 31%) as a dark purple solid: mp >300 °C; UV−vis (CH_2Cl_2) λ_{max} (log ε) 387 (sh, 4.40), 411 (5.00), 492 (3.85), 524 (3.71), 553 (3.49), 599 nm (4.34); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (6H, t, J = 7.7 Hz, 8,17-CH_2CH_3), 1.88 (6H, t, J = 7.7 Hz, 12,13-CH_2CH_3), 3.46 (6H, s, 7,18-CH_3), 4.00−4.05 (8H, m, 8,12,13,17-CH_2), 5.02 (4H, s, CH_2CH_2), 9.23 (2H, s, 5,20-H), 9.90 (2H, s, 10,15-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7 (7,18-CH_3), 17.7 (8,17-CH_2CH_3), 18.5 (12,13-CH_2CH_3), 19.9, 20.5 (8,12,13,17-CH_2), 36.3 (CH_2CH_2), 98.3 (10,15-CH), 100.5 (5,20-CH), 129.6, 133.7, 134.2, 135.5, 136.5, 138.1, 140.4; HR MS (EI) calcd for $C_{31}H_{34}N_3Ag$ 555.1804, found 555.1799.

8,12,13,17-Tetraethyl-7,18,22-trimethylcarbachlorin (26). Carbachlorin **11** (30.0 mg, 0.0665 mmol) was stirred with potassium carbonate (360 mg), 54 drops of iodomethane, and acetone (36 mL) under reflux for 16 h. The mixture was then cooled, diluted with dichloromethane (50 mL), and washed with water, and the solvent was removed under reduced pressure. The residue was run through a silica gel flash column with chloroform as eluent, and the starting material was initially collected as a dark green fraction. The major product fraction subsequently eluted, the solvent was removed under reduced pressure, and the residue was recrystallized from chloroform−methanol to yield the *N*-methylcarbachlorin (10.4 mg, 0.0224 mmol, 34%) as dark purple crystals: mp 173−174 °C; UV−vis (1% Et_3N−99% CH_2Cl_2) λ_{max} (log ε) 407 (4.76), 504 (3.81), 605 (3.42), 664 nm (3.82); UV−vis (1% TFA−99% CH_2Cl_2) λ_{max} (log ε) 415 (4.92), 428 (4.83), 534 (sh, 3.79), 552 (3.82), 589 (3.85), 644 nm (3.86); ^{1}H NMR (500 MHz, $CDCl_3$) δ −6.31 (1H, s, 21-H), −4.27 (3H, s, N-CH_3), −1.56 (1H, br s, NH), 1.38 (3H, t, J = 7.7 Hz), 1.77 (3H, t, J = 7.7 Hz), 1.83−1.87 (6H, two overlapping triplets) (4 × CH_2CH_3), 2.94 (3H, s), 3.29 (3H, s) (7,18-CH_3), 3.52−3.60 (2H, m), 3.78−3.86 (5H, m, 3.89−3.97 (1H, m) (4 × CH_2CH_3), 4.36−4.43 (1H, m), 4.51−4.56 (1H, m), 4.74−4.84 (2H, m) (CH_2CH_2), 8.89 (1H, s), 9.04 (1H, s), 9.37 (1H, s), 9.58 (1H, s) (4 × *meso*-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.55, 11.57, 16.3, 17.7, 18.55, 18.57, 19.82, 19.85, 20.0, 20.1, 30.9 (N-Me), 34.8, 36.4, 94.4, 98.2, 100.8, 101.7, 123.0, 128.3, 132.5, 132.7, 139.3, 140.1, 140.6, 141.2, 141.9, 143.5, 144.0, 145.7, 148.2, 148.5, 151.1; ^{1}H NMR (500 MHz, TFA-$CDCl_3$) δ −7.09 (s, 1H), −6.18 (1H, s), −6.15 (1H, s) (2 × NH), −4.53 (3H, s, N-CH_3), 1.37 (3H, t, J = 7.7 Hz), 1.70 (3H, t, J = 7.7 Hz), 1.84−1.89 (6H, two overlapping triplets) (4 × CH_2CH_3), 3.13 (3H, s), 3.48 (3H, s) (7,18-CH_3), 3.70−3.79 (2H, m), 4.00−4.09 (2H, m), 4.11−4.19 (4H, m) (4 × CH_2CH_3), 4.59−4.65 (1H, m), 4.67−4.72 (1H, m), 5.08−5.19 (2H, m) (CH_2CH_2), 9.50 (1H, s), 9.63 (1H, s), 10.05 (1H, s), 10.07 (1H, s) (4 × *meso*-H); HR MS (EI) calcd for $C_{32}H_{39}N_3$ 465.3144, found 465.3136.

[8,12,13,17-Tetraethyl-7,18,21-trimethylcarbaporphyrinato]palladium(II) (28). Palladium(II) acetate (20 mg, 0.089 mmol) was added to a solution of *N*-methylcarbachlorin **26** (20.0 mg, 0.0430 mmol) in acetonitrile (20 mL), and the solution was stirred under reflux for 30 min. The mixture was cooled and diluted with chloroform (50 mL), and an aqueous solution of ferric chloride (0.1%, 60 mL) was added. The biphasic mixture was vigorously stirred at room temperature for 24 h. The two layers were separated, and the organic phase was washed with water and then evaporated to dryness. The residue was chromatographed with silica, with 30% dichloromethane−70% hexanes as eluent, and the product was collected as an emerald green fraction. Recrystallization from chloroform−methanol gave the palladium(II) complex (8.4 mg, 0.0148 mmol, 34%) as dark purple crystals: mp 229−230 °C; UV−vis (CH_2Cl_2) λ_{max} (log ε) 394 (4.48), 440 (4.33), 524 (3.74), 578 (sh, 3.76), 612 nm (3.86); ^{1}H NMR (500 MHz, $CDCl_3$) δ −4.46 (3H, s, 21-CH_3), 1.83−1.88 (12H, two overlapping triplets, 4 × CH_2CH_3), 3.49 (6H, s, 7,18-CH_3), 3.93−3.99 (8H, m, 4 × CH_2CH_3), 9.60 (2H, s, 2,3-H), 10.00 (2H, s, 10,15-H), 10.42 (2H, s, 5,20-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.8 (7,18-

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CH_3), 17.8 (8,17-CH_2CH_3), 18.7 (12,13-CH_2CH_3), 19.8, 20.2 (4 × CH_2CH_3), 22.2 (21-CH_3), 36.1, 102.3 (10,15-CH), 111.2 (5,20-CH), 133.9 (2,3-CH), 135.0, 141.6, 142.2, 142.9, 145.3, 148.0, 165.5; HR MS (EI) calcd for $C_{32}H_{35}N_3Pd$ 567.1866, found 567.1859.

Computational Studies. All calculations were performed using Gaussian 09[36] Rev D.01 running on a Linux-based PC. Energy minimization and frequency calculations of the porphyrinoid systems were performed at the density functional theory (DFT) level of theory with the B3LYP functional and a 6-311++G(d,p) basis set. Single-point energy calculations were performed on the minimized structures using both the B3LYP-D and M06-2X functionals with a 6-311++G(d,p) basis set. Mercury 3.1 running on an OS X platform, as provided by the CCDC (www.ccdc.cam.ac.uk/mercury/), was used to visualize the optimized structures. The resulting Cartesian coordinates of the molecules can be found in the Supporting Information.

NICS values were computed using the GIAO method,[37] at the DFT level of theory with the B3LYP functional and a 6-31+G(d,p) basis set, at several positions in each molecule. NICS(0) was calculated at the mean position of all the non-hydrogen atoms. NICS(*a*), NICS(*b*), NICS(*c*), and NICS(*d*) values were obtained by applying the same method to the mean positions of the non-hydrogen atoms that comprise the individual rings of each macrocycle.

■ ASSOCIATED CONTENT

Supporting Information

Tables and figures giving Cartesian coordinates, HOMO and LUMO surfaces, and selected ^{1}H NMR, ^{1}H−^{1}H COSY, HSQC, ^{13}C NMR, MS, and UV−vis spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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