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Synthesis of Indenoporphyrins, Highly Modified Porphyrins with Reduced Diatropic Characteristics†

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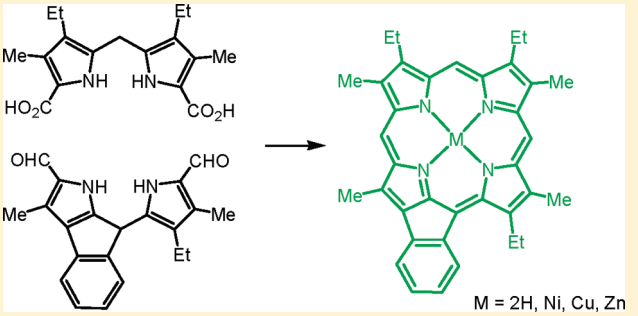
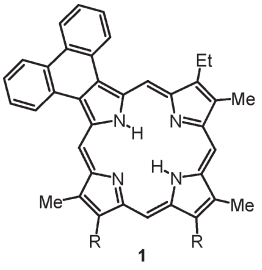
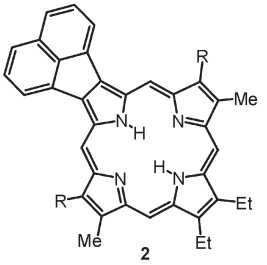
Supporting Information

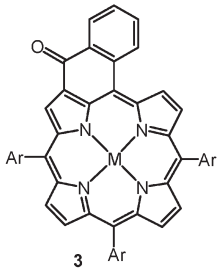
ABSTRACT: Indene-fused porphyrins have been synthesized starting from 2-indanone. Knorr-type reaction of oximes derived from benzyl or *tert*-butyl acetoacetate with 2-indanone and zinc dust in propionic acid gave good yields of indenopyrroles. Treatment with *N*-chlorosuccinimide then gave 8-chloro derivatives, and these reacted with 5-unsubstituted pyrroles to give dipyrroles incorporating the fused indene unit. Hydrogenolysis of the benzyl ester protective groups afforded the related dicarboxylic acids, but condensation with a dipyrrylmethane dialdehyde under MacDonald "2 + 2" reaction conditions gave poor yields of the targeted indenoporphyrins. However, when an indene-fused dipyrrole was converted into the corresponding dialdehyde with TFA−trimethyl orthoformate and then reacted with a dipyrrylmethane dicarboxylic acid, an indenoporphyrin was isolated in 26% yield. The porphyrin gave a highly modified UV−vis absorption spectrum with three strong bands showing up in the Soret region and a series of Q bands that extended beyond 700 nm. The proton NMR spectrum also showed a significantly reduced diamagnetic ring current where the *meso*-protons gave resonances near 9.3 ppm instead of typical porphyrin values of 10 ppm. Nickel(II), copper(II), and zinc complexes were also prepared, and these exhibited unusual UV−vis absorption spectra with bathochromically shifted Soret and Q absorptions. The diamagnetic nickel(II) and zinc complexes also showed reduced diatropic character compared to typical nickel(II) and zinc porphyrins.

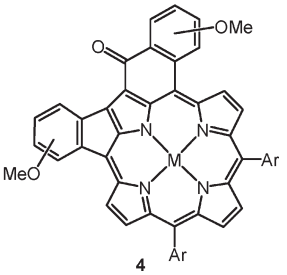


INTRODUCTION









Extended porphyrinoid chromophores have been widely investigated[1,2] because of their potential to produce long wavelength absorptions that could make them suitable for applications as photosensitizers in photodynamic therapy,[3] as biological sensors,[4] or in the development of novel optical materials.[5]

Fusion of aromatic units to the pyrrole rings in porphyrins can give rise to highly red-shifted chromophores,[1,2,6−13] but this is not always the case. For instance, phenanthroporphyrins (e.g., **1**) only show minor bathochromic shifts due to the presence of the fused tricyclic unit,[9] whereas structurally similar acenaphthylene-fused porphyrins **2** have considerably modified absorption bands.[11,14] Modification of the porphyrin system by cyclization onto the *meso*-positions can also produce unusual porphyrinoid chromophores.[15,16] Substantial efforts have been put into the synthesis of this type of system from tetraarylporphyrins, and these investigations commonly afford six-membered ring systems such as **3**.[15,16] The formation of fused five-membered ring structures such as **4** has also been noted, initially as minor byproducts.[15] These types of indene-fused systems are intriguing as they show highly modified UV−vis absorptions. Fox and Boyle reported a synthesis of metalated indenoporphyrins **5** by reacting nickel(II) or copper(II) 2-iodophenylporphyrins **6** with $Pd(PPh_3)_4$ and potassium phosphate (Scheme 1).[17] An alternative route was subsequently developed where nickel(II), copper(II), zinc, or free base 2-bromo tetraphenylporphyrins **8** were cyclized using $Pd_2(dba)_3$ and potassium carbonate (Scheme 1).[18] This ring closure can also be accomplished by the zinc-mediated cyclization of tetrarylporphyrin radicals.[19] The

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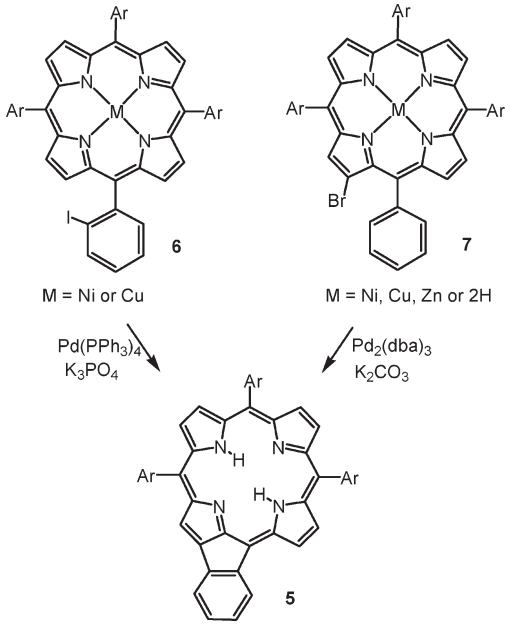
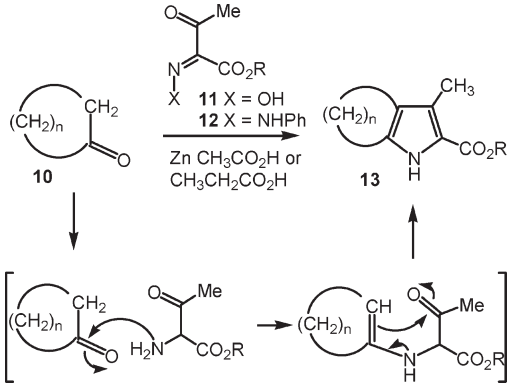
Scheme 1

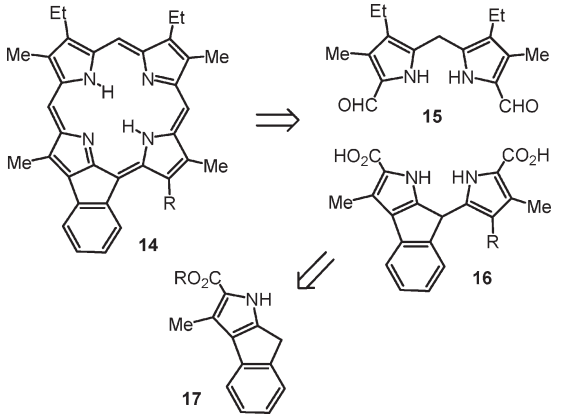


Scheme 2

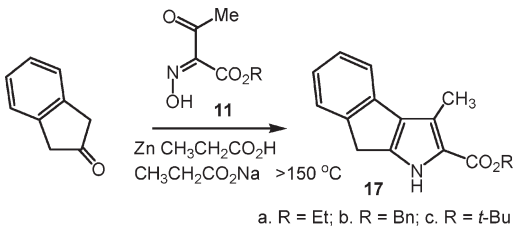


formation of **5** by the intramolecular Heck reaction of a tetraphenylporphyrin boronic ester has been noted,[20−22] and the preparation of more complex porphyrin systems that incorporate a fused indene unit have also been described.[23] We have developed versatile routes to cycloalkanoporphyrins (CAPs), including the porphyrin molecular fossils deoxophylloerythroetioporphyrin (DPEP, **8**) and butanoporphyrin **9**, starting from cyclic ketones.[24−26] CAPs are commonly found in petroleum and oil shales as their nickel(II) or vanadyl complexes,[27] and synthetic samples have been used to develop spectroscopic,[28] mass spectrometric,[29] and chromatographic methods[30] for the analysis of these materials. Cyclic ketones **10** were shown to react with oximes **11** or phenylhydrazones **12** in the presence of zinc dust and acetic or propionic acid to give the cycloalka[*b*]pyrroles **13** in good yields (Scheme 2).[24−26,31] In this variation on the Knorr pyrrole reaction,[32] an α-amino ketone is generated *in situ* and reacts with ketones **10** to afford pyrroles **13** (Scheme 2). Optimal yields are somewhat temperature-dependent, and syntheses using large ring ketones such as cyclododecanone or

Scheme 3



Scheme 4



a. R = Et; b. R = Bn; c. R = *t*-Bu

cyclohexadecanone worked well only at temperatures >140 °C in propionic acid.[26i] Cyclopentanone gave good yields of cyclopenta[*b*]pyrroles only when the temperature was maintained at >150 °C in a mixture of sodium propionate and propionic acid.[25b] Multigram quantities of cycloalka[*b*]pyrroles are easily prepared by this approach, and these heterocycles are the key intermediates in the synthesis of cycloalkanoporphyrins like **8** and **9**.[24−26]

In principle, the synthesis of indenoporphyrins **14** could be approached in a similar fashion. A retrosynthetic analysis of **14** shows that this system could be obtained by using the MacDonald "2 + 2" methodology[33,34] from dipyrrylmethane dialdehyde **15** and the indene fused dipyrrole **16** (Scheme 3). Dipyrrole **16**, in turn, could be prepared from the indenopyrrole **17**. The successful application of this strategy and the spectroscopic properties of the resulting indenoporphyrins are presented below.[35]

RESULTS AND DISCUSSION

The synthesis of indenoporphyrins **14** required the availability of indenopyrroles **17**. In fact, an example of an indenopyrrole **17a** had been reported previously.[25b] Reaction of the oxime **11a** derived from ethyl acetoacetate with 2-indanone in propionic acid containing sodium propionate at 150 °C gave the indenopyrrole in 34% yield (Scheme 4).[25b] The corresponding benzyl ester **17b** was prepared similarly from oxime **11b** and 2-indanone in 47% yield. However, the related *tert*-butyl ester **17c** was obtained in very low yields under these conditions. Following a series of attempts, the yield was raised to 33% when the oxime and zinc dust were added to 2-indanone and sodium propionate in propionic acid at 140 °C and the reaction was stopped after 5 min once the addition had been completed. The same approach

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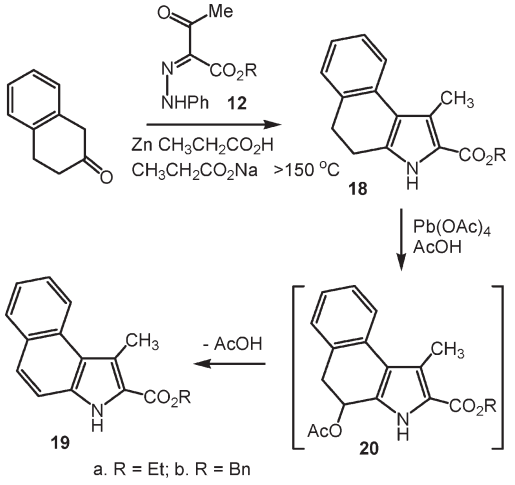
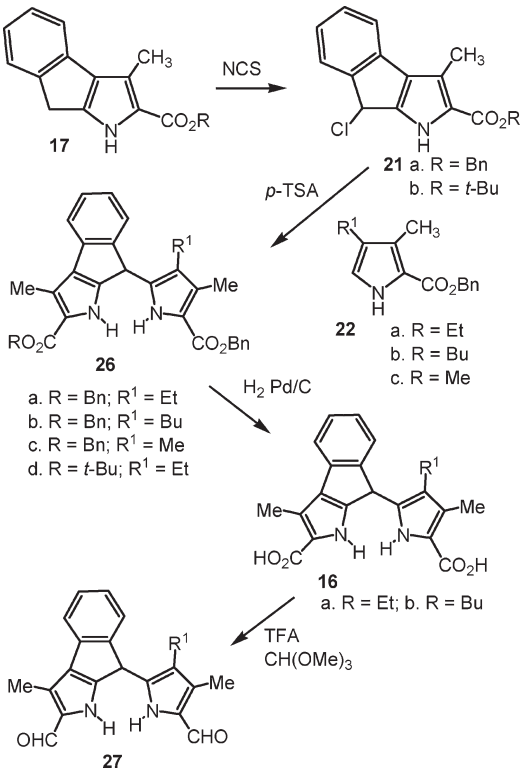
Scheme 5



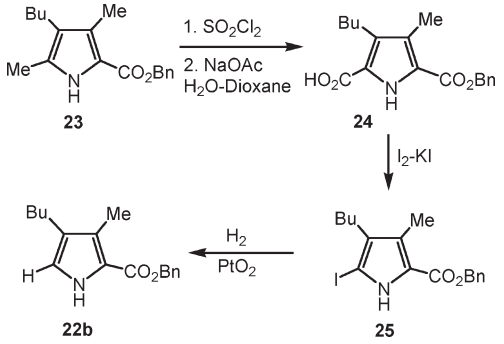
Scheme 6



was also used to prepare dihydrobenzo[*e*]indoles **18a** and **18b** from 2-tetralone, although in this case phenylhydrazones **12** gave better results than oximes **11** (Scheme 5). Again, high temperature conditions (>150 °C) were required to get the best results, and 8,9-dihydrobenzo[*e*]indoles **18** were formed in up to 65% yield.

In order to generate dipyrrolic intermediates from indenopyrroles **17**, it was necessary to introduce a suitable leaving group onto the five-membered carbocyclic ring. This had been accomplished for cycloalka[*b*]pyrroles **13** using lead tetraacetate,[24−26,31] but no stable product could be isolated from the reaction of pyrroles **17**

Scheme 7



with this reagent. Dihydrobenzoindoles **18** were also reacted with lead tetraacetate, but in this case the corresponding benzo[*e*]indoles **19** were formed (Scheme 5). Reaction of **18** with $Pb(OAc)_4$ would be expected to give the acetoxy-derivatives **20**, but these spontaneously eliminate acetic acid to give the fully conjugated tricycles **19**. This chemistry provides a useful route to benzo[*e*]indoles but cannot be applied to porphyrin synthesis. In an alternative strategy, **17b** was reacted with *N*-chlorosuccinimide (NCS) in carbon tetrachloride (Scheme 6). Under these conditions, benzyl ester **17b** underwent selective chlorination to give the 8-chloroindenopyrrole **21a**, and following recrystallization from toluene the derivative was isolated in 63% yield.

The formation of dipyrrolic products from **21a** required the availability of α-unsubstituted pyrroles **22a**−**c**. Pyrroles **22a** and **22c** are known compounds and may be prepared by modification of the related 5-methylpyrroles[36] or by using the Barton−-Zard reaction.[37,38] The necessary nitroalkane precursor to 4-butylpyrrole **22b** using the latter methodology is not readily available, and so this α-unsubstituted pyrrole was prepared from 5-methylpyrrole **23** (Scheme 7). Reaction with 3.3 equiv of sulfuryl chloride, followed by hydrolysis with sodium acetate in aqueous dioxane, gave carboxylic acid **24** in 40% yield. Iodinative decarboxylation with I_2/KI gave iodopyrrole **25** and subsequent hydrogenolysis over Adam's catalyst then gave the required α-free pyrrole **22b**. Chlorinated indenopyrrole **21a** was reacted with α-unsubstituted pyrroles **22a**−**c** in acetic acid at room temperature, using *p*-toluenesulfonic acid as a catalyst, to give dipyrroles **26a**−**c** in 40−66% yield (Scheme 6). A mixed ester dipyrrole **26d** was also prepared. Reaction of NCS with indenopyrrole *tert*-butyl ester **17c** gave poor results due to the instability of the chlorinated product **21b**. The crude product from this reaction was immediately reacted with **22a** in the presence of *p*-toluenesulfonic acid in acetic acid, but dipyrrole **26d** could only be isolated in 21% yield. Due to these low yields, the mixed ester dipyrrole **26d** was not further investigated.

The ^{1}H NMR spectra for indenodipyrrole **26a** in $CDCl_3$ and DMSO-d_6 indicate that solvent interactions can cause significant conformational changes. In $CDCl_3$, the ethyl substituent gives rise to a quartet and a triplet at 2.49 and 1.10 ppm, respectively, which fall into the expected range of a typical pyrrolic ethyl group. This coupling indicates that free rotation of the ethyl substituent occurs and that both protons for the potentially diastereotopic CH_2 unit have identical chemical shift values. However, in DMSO-d_6 the peaks associated with this CH_2 group give rise to two 1H multiplets centered on 1.47 and 1.56 ppm. Furthermore, the CH_3 group for the ethyl moiety is shifted upfield to 0.27 ppm (Figure 1). These signals suggest that a single

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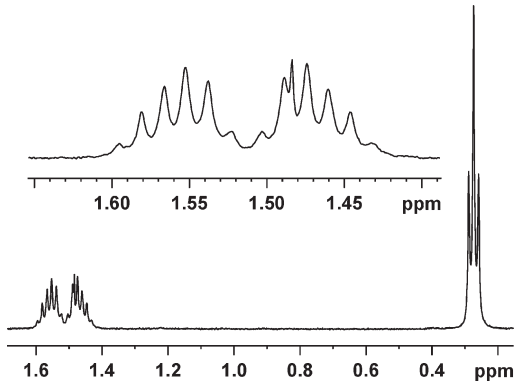


Figure 1. Partial 500 MHz proton NMR spectrum of dipyrrole **26a** in DMSO-d_6 showing the atypically upfield shifted resonances for the ethyl unit.

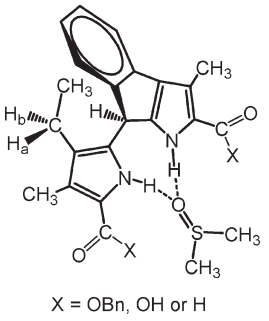


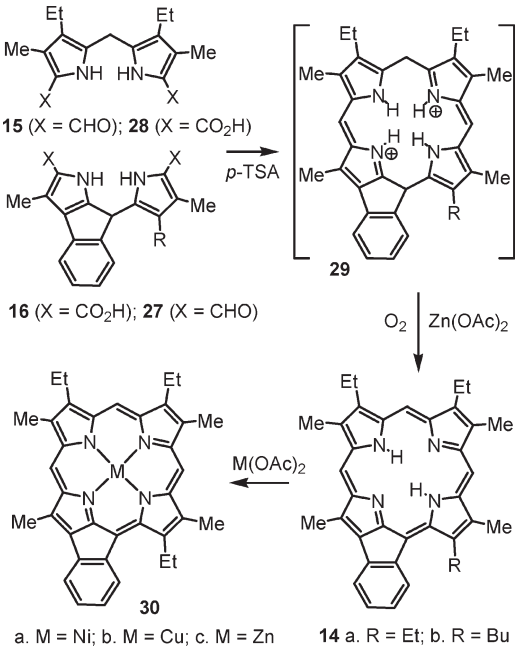
Figure 2. Proposed conformation for dipyrroles **16**, **26**, and **27** in DMSO-d_6.

conformation is favored in DMSO that results in restricted rotation of the ethyl substituent (Figure 2). It is postulated that DMSO is able to stabilize this conformation by hydrogen bonding to both pyrrolic NHs and that the pyrrole ring is oriented so that it causes the CH_3 of the ethyl group to be located over the benzene ring thereby leading to the observed shielding effect. This also causes an upfield shift to the CH_2 resonances and provides an environment that strongly differentiates between the diastereotopic protons. Conformational factors of this type can have a significant impact on macrocyclic ring formation.[26j,39]

Dipyrrole **26c** was poorly soluble in organic solvents and could not be deprotected. However, dipyrrole dibenzyl esters **26a** and **26b** were converted in quantitative yields into the related dicarboxylic acid **16** by hydrogenolysis over 10% palladium—charcoal. Dipyrroles **16a** and **16b** were reacted with dipyrrylmethane dialdehyde **15** in the presence of *p*-toluenesulfonic acid, followed by the addition of excess zinc acetate and air oxidation, but no more than trace amounts of porphyrins **14** were generated (Scheme 8). The reactions were repeated by adding a mixture of **15** and **16** to a solution of *p*-toluenesulfonic acid in methanol—dichloromethane over a period of 2 h. This method allows the concentration of reactants at any given moment to approximate to high dilution conditions that should aid in macrocycle formation,[40] but the targeted porphyrins could still only be isolated in 6—7% yield.

An alternative "2 + 2" condensation can be carried out with a dialdehyde **27** derived from the indene-fused dipyrrole and

Scheme 8



dipyrrylmethane **28**.[41] Dicarboxylic acid **16a** was decarboxylated with trifluoroacetic acid and then treated with trimethyl orthoformate to produce dialdehyde **27** (Scheme 6). Initially, trimethyl orthoformate was added at temperatures <0 °C and the reagents allowed to react at room temperature for 15 min, and this gave the dialdehyde in 33% yield. However, after a series of attempts the yield was raised to 81% when trimethyl orthoformate was introduced at temperatures between 20 and 25 °C, and the reaction was then allowed to proceed afterward for 10 min at 40 °C. The proton NMR spectra for **16** and **27** in DMSO-d_6 gave results similar to those with **26a**, showing that the ethyl group was held over the fused benzene ring, although the ethyl resonances for dialdehyde **27** were broadened. The carbon-13 NMR spectrum of **27** in DMSO-d_6 also showed broadened peaks, presumably due to hindered rotation for the alkyl substituent (see Supporting Information). Dialdehyde **27** was reacted with dipyrrole dicarboxylic acid **28** using the slow addition MacDonald "2 + 2" conditions described above (Scheme 8). The initial condensation gives rise to a porphodimethene intermediate **29**, but subsequent treatment with zinc acetate and air oxidation gave the indenoporphyrin. Following purification by column chromatography on neutral alumina and recrystallization from chloroform—methanol, indenoporphyrin **14a** was isolated as a dark green solid in 26% yield (Scheme 8).

As anticipated, the spectroscopic properties of this system are quite unusual and differ considerably from typical porphyrins. The UV—vis absorption spectra of **14** gave rise to a very distorted electronic absorption spectrum with no distinct Soret band, and instead three moderately intense absorption maxima are seen between 400 and 500 nm (Figure 3). Addition of TFA gives a diprotonated species $\mathbf{14}H_2^{2+}$ where the UV—vis spectrum is more porphyrin-like showing a Soret band at 434 nm with atypically broad peaks on either side (Figure 3). In addition, the modified chromophore gives rise to bathochromic shifts for both species pushing the absorbance wavelengths of the Q bands into the far red region. The chemical shifts in the proton NMR

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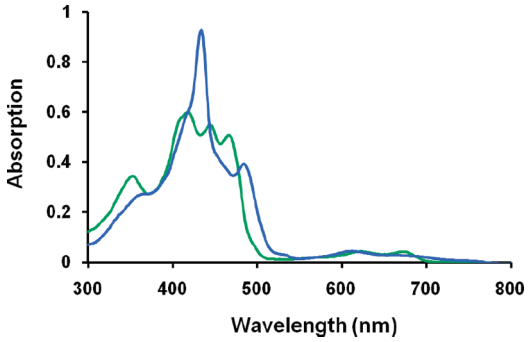

Figure 3. UV−vis spectra of indenoporphyrin **14a** in chloroform (green line) and 1% TFA−chloroform (dication **14a**H_2^{2+}, blue line).

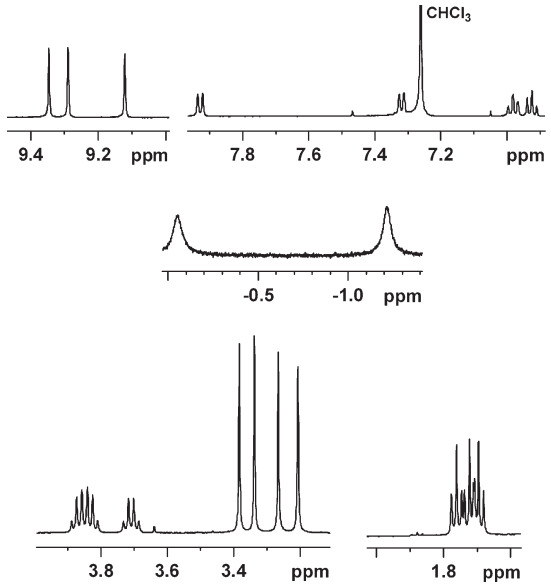

Figure 4. 500 MHz proton NMR spectrum of indenoporphyrin **14a** in $CDCl_3$.

spectra of **14** indicate that the system has somewhat compromised aromatic character. The *meso*-protons of the free base appear as three singlets between 9.12 and 9.35 ppm, while the internal NHs give rise to two broad singlets between −1.22 and 0 ppm (Figure 4). These NH resonances are downfield compared to a typical aromatic porphyrin in which the internal NH protons appear between −3 and −4 ppm, while the *meso*-protons have been shifted upfield from a typical value of +10 ppm.[42] The methyl substituents for porphyrins commonly show up near 3.6 ppm,[42] but for **14a** these substituents gave rise to four upfield singlets at 3.21, 3.27. 3.34 and 3.38 ppm. These shifts indicate that the indenoporphyrin has significantly reduced diatropic character. The corresponding porphyrin dication **14**H_2^{2+} can be generated in TFA−$CDCl_3$ and gives chemical shifts near 10 ppm for the external protons while the internal NHs show up at −1.74 and −0.97 ppm. These results suggest that protonation leads to a slight increase in the diamagnetic ring current, although these shifts are still not as large as those seen for typical porphyrin dications. The reduced aromaticity of this system is most likely due to unfavorable angle strain due to indene moiety, where all 5 carbons of the fused five-membered ring are sp^2 hybridized. However, a fused five-membered ring by itself (e.g., for

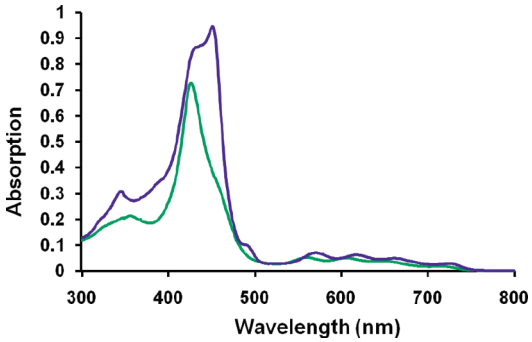

Figure 5. UV−vis spectra of nickel(II) indenoporphyrin **30a** (green line) and copper complex **30b** (purple line) in chloroform.

DPEP (**8**) and related porphyrins) does not significantly affect the diatropic character of the porphyrin macrocycle.[24,25]

Indenoporphyrin **14a** was reacted with metal acetates in refluxing chloroform−methanol to give the corresponding nickel(II), copper(II), or zinc porphyrins **30a**−**c** in excellent yields (Scheme 8). The proton NMR spectrum of nickel(II) complex **30a** shows that it has a slightly smaller diatropic ring current than the free base porphyrin **14a**, with the *meso*-protons appearing between 8.99 and 9.16 ppm. The methyl resonances were also shifted upfield to between 3.18 and 3.23 ppm. The decreased diatropicity of **30a** is attributed to the presence of a small nickel cation which causes the porphyrin macrocycle to distort or ruffle to allow optimal complexation.[43] The UV−vis spectrum for **30a** showed a Soret band at 427 nm and a series of Q bands that extended beyond 700 nm (Figure 5). Copper(II) porphyrins are paramagnetic and copper complex **30b** could not be characterized by NMR spectroscopy. The UV−vis spectrum for **30b** was similar to **30a** but showed two strong Soret bands near 450 nm (Figure 5). Porphyrins **14** and metallo-derivatives **30a**−**c** were all further characterized by mass spectrometry.

TLC on silica plates indicated that the zinc complex **30c** is more polar than the nickel or copper complexes **30a** and **30b**. Because of the poor solubility of the zinc complex in chloroform, difficulties were encountered in obtaining high quality proton NMR spectra. The zinc complex did dissolve to a limited extent and chemical shift values could be obtained. Addition of one drop of pyrrolidine greatly increased the solubility of the metalloporphyrin. Pyrrolidine forms an adduct with the zinc complex, disrupting porphyrin aggregation and thereby increasing solubility, making it easier to obtain NMR spectra. However, no significant changes in the chemical shifts were noted. The *meso*-protons of the zinc complex, with or without pyrrolidine, appear between 9.21 and 9.42 ppm, which is slightly downfield compared to the free base indenoporphyrin **14a** but upfield compared to typical zinc porphyrins. The UV−vis spectrum for zinc complex **30c** in chloroform gave a broad Soret band at 459 nm with a smaller broad absorption at 436 nm and Q-band absorptions extending into the far red region (Figure 6). All three metal complexes show two Soret absorptions, but in the nickel complex the lower wavelength absorption dominates, while both bands have comparable intensities for the copper complex and the longer wavelength band dominates for the zinc complex. In addition, the absorption bands shift to higher wavelengths going to higher atomic number (nickel to copper to zinc) as is observed for regular porphyrins.[2,44] Addition of pyrrolidine to solutions of **30c** in chloroform gives rise to further bathochromic shifts and an

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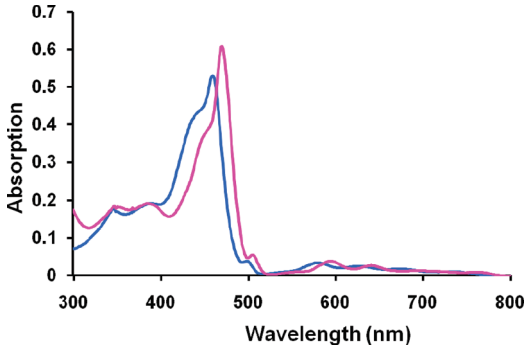

Figure 6. UV−vis spectra of zinc indenoporphyrin **30c** in chloroform (blue line) and 1% pyrrolidine−chloroform (pink line).

intensification of the Soret band (Figure 6). The Soret band is now observed at 470 nm and the Q bands extend to 768 nm.

CONCLUSIONS

A synthesis of *meso*-unsubstituted indenoporphyrins has been developed starting from 2-indanone. Following the formation of indenopyrroles, dipyrroles incorporating a fused indene unit can be generated in two steps and further transformed into a dialdehyde. MacDonald "2 + 2" condensation of the dialdehyde with a dipyrrylmethane dicarboxylic acid then gave an indenoporphyrin in 26% yield. The UV−vis spectra for indenoporphyrins are unusual, showing multiple bands in the Soret region and Q-band absorptions that extend into the far red. The proton NMR spectra for indenoporphyrins also show that the diamagnetic ring current for this porphyrin system is significantly reduced. Metalated derivatives show similarly modified characteristics. Hence, this system provides some insights into the aromatic characteristics of porphyrins and the novel optical properties of indenoporphyrins may lead to applications as photosensitizers or in the development of new optical materials.

EXPERIMENTAL SECTION

Benzyl 3-Methylindeno[2,1-*b*]pyrrole-2-carboxylate (17b). A stirred mixture of 2-indanone (6.60 g, 50.0 mmol), sodium propanoate (67.2 g) and propionic acid (224 mL) was heated to 150 °C. A solution of benzyl ester oxime **11b**[25b] (12.15 g, 55 mmol) in propionic acid (224 mL) was then added dropwise, simultaneously adding zinc dust (20 g) in small portions, while maintaining the reaction mixture at a temperature between 150 and 155 °C. Once the addition was complete, the resulting mixture was allowed to stir for 1 h while maintaining the temperature between 150 and 155 °C. The resulting mixture was cooled to 70 °C, poured into a beaker of ice water (1.5 L), and allowed to stand overnight. The precipitate was filtered, and the solid recrystallized from ethanol to give the indenopyrrole (7.155 g, 23.6 mmol, 47%) as a white solid, mp 166−167 °C; IR (nujol) ν 3309 (NH str.), 1669 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.63 (3H, s), 3.61 (2H, s), 5.35 (2H, s), 7.11 (1H, td, J = 1.1, 7.5 Hz), 7.29 (1H, t, J = 7.5 Hz), 7.33−7.42 (5H, m), 7.44−7.47 (1H, m), 7.52 (1H, d, J = 7.5 Hz), 9.07 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 11.9, 30.8, 65.9, 119.1, 122.1, 122.4, 123.9, 125.3, 127.2, 128.4, 128.8, 131.1, 136.6, 139.4, 142.6, 143.2, 161.8. Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.36; H, 5.50; N, 4.72.

***tert*-Butyl 3-Methylindeno[2,1-*b*]pyrrole-2-carboxylate (17c).** A mixture of 2-indanone (3.30 g, 25.0 mmol) and sodium propanoate (33.6 g) in propionic acid (112 mL) was prepared and heated while stirring to 140 °C. A solution of *tert*-butyl ester oxime **11c**[25b] (5.1 g, 27 mmol) in propionic acid (112 mL) was then added dropwise, simultaneously adding zinc dust (10 g) in small portions, while maintaining the reaction temperature at 140 °C. Once the addition was complete, the resulting mixture was allowed to stir for 5 min while maintaining the temperature at 140 °C and then poured into a beaker of ice water (750 mL) and allowed to stand for 2 h. The mixture was filtered, and the solid was dissolved in dichloromethane and washed with water. The residue was chromatographed on a silica column, eluting with a 50:50 mixture of chloroform and hexanes. The product fractions were identified by TLC and evaporated. Recrystallization from ethanol gave the indenopyrrole (2.23 g, 8.29 mmol, 33%) as off-white crystals, mp 201−202 °C. IR (nujol) ν 3302 (NH str.), 1663 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.65 (9H, s), 2.60 (3H, s), 3.61 (2H, s), 7.11 (1H, td, J = 1.1, 7.5 Hz), 7.29 (1H, t, J = 7.5 Hz), 7.39 (1H, d, J = 7.5 Hz), 7.53 (1H, d, J = 7.5 Hz), 9.63 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 11.9, 28.8, 30.7, 80.8, 118.9, 120.7, 123.6, 124.0, 125.2, 127.1, 130.7, 139.8, 141.9, 143.3, 162.2. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.57; H, 7.13; N, 5.25.

Ethyl 3-Methyl-7,8-dihydrobenzo[*f*]indole-2-carboxylate (18a). A stirred mixture of 2-tetralone (3.65 g, 25.0 mmol), sodium propanoate (33.6 g) and propionic acid (112 mL) was heated to 150 °C. A solution of phenylhydrazone **12a**[31] (5.85 g, 25 mmol) in propionic acid (112 mL) was then added dropwise, while simultaneously adding zinc dust (10 g) in small portions, maintaining the reaction mixture at a temperature between 150 and 155 °C. Once the addition was complete, the resulting mixture was allowed to stir for 1 h while maintaining the temperature between 120 and 130 °C. The resulting mixture was cooled to 70 °C, poured into a beaker of ice water (1.0 L), and allowed to stand overnight. The precipitate was filtered, and the solid recrystallized from ethanol to give the dihydrobenzoindole (4.14 g, 65%) as an off-white powder, mp 188−189 °C. IR (nujol) ν 3278 (NH str.), 1660 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (3H, t, J = 7.1 Hz), 2.68 (3H, s), 2.80 (2H, t, J = 7.5 Hz), 2.97 (2H, t, J = 7.5 Hz), 4.36 (2H, q, J = 7.1 Hz), 7.09 (1H, dt, J = 1.2, 7.4 Hz), 7.21−7.24 (1H, m), 7.25−7.27 (1H, m), 7.61 (1H, dd, J = 0.8, 7.7 Hz), 9.04 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.6, 14.8, 22.2, 30.1, 60.1, 118.5, 119.5, 123.0, 124.8, 125.1, 127.0, 128.4, 133.5, 134.3, 134.8, 162.2. Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.08; H, 6.68; N, 5.37.

Benzyl 3-Methyl-7,8-dihydrobenzo[*f*]indole-2-carboxylate (18b). Following the same procedure, tetralone (3.65 g, 25.0 mmol) was reacted with phenylhydrazone **12b**[26f] (7.40 g, 25.0 mmol). Recrystallization from ethanol gave the benzyl ester (4.90 g, 15.5 mmol, 62%) as an off-white solid, mp 134−135 °C. IR (nujol) ν 3289 (NH str.), 1655 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.73 (3H, s), 2.79 (2H, t, J = 7.5 Hz), 2.98 (2H, t, J = 7.5 Hz), 5.38 (2H, s), 7.13 (1H, dt, J = 1.2, 7.5 Hz), 7.23−7.30 (2H, m), 7.36−7.40 (1H, m), 7.41−7.45 (2H, m), 7.47−7.50 (2H, m), 7.64 (1H, d, J = 7.6 Hz), 9.03 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.7, 22.2, 30.0, 65.9, 118.1, 119.6, 123.1, 125.1, 125.4, 127.0, 128.4, 128.5, 128.8, 133.4, 134.3, 135.2, 136.7, 161.7. Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.37; H, 5.90; N, 4.20.

Ethyl 3-Methylbenzo[*f*]indole-2-carboxylate (19a). Lead tetraacetate (95%, 0.93 g) was added to a stirred solution of **18a** (0.515 g, 2.02 mmol) in dichloromethane (10 mL). The resulting solution was stirred for 2 h at room temperature, then diluted with dichloromethane, washed with water, and dried over sodium sulfate. Recrystallization from ethanol gave the benzo[*f*]indole (0.26 g, 1.03 mmol, 51%) as a light yellow powder, mp 179−180 °C. IR (nujol) ν 3308 (NH str.), 1666 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (3H, t, J = 7.1 Hz), 3.06 (3H, s), 4.45 (2H, q, J = 7.1 Hz), 7.44−7.48 (2H, m), 7.59−7.63 (1H, m), 7.69 (1H, d, J = 8.9 Hz), 7.91 (1H, d, J = 8.0 Hz), 8.54 (1H, d, J = 8.3 Hz), 9.09 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 13.5, 14.7, 60.8, 113.1, 121.7, 122.0, 123.0, 123.4, 123.8, 126.8, 127.7, 129.4, 130.1, 130.5, 133.7, 162.7. Anal. Calcd for

$C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.83; H, 5.88; N, 5.56.

Benzyl 3-Methylbenzo[*f*]indole-2-carboxylate (19b). Benzyl ester **18b** (0.634 g, 2.00 mmol) was reacted with lead tetraacetate under the foregoing conditions. Recrystallization from ethanol gave the title compound (0.30 g, 0.95 mmol, 48%) as a yellow powder, mp 178−180 °C. IR (nujol) ν 3303 (NH str.), 1669 cm^{-1} (C═O str.); ^1H NMR (500 MHz, $CDCl_3$) δ 3.08 (3H, s), 5.43 (2H, s), 7.36−7.40 (1H, m), 7.41−7.51 (6H, m), 7.59−7.63 (1H, m), 7.69 (1H, d, J = 8.8 Hz), 7.91 (1H, d, J = 8.0 Hz), 8.53 (1H, d, J = 8.3 Hz), 9.10 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 13.6, 66.5, 113.1, 121.6, 121.7, 123.4, 123.6, 123.9, 126.9, 127.9, 128.6, 128.9, 129.4, 130.1, 130.4, 133.8, 136.2, 162.3. Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 79.61; H, 5.25; N, 4.35.

Benzyl 8-Chloro-3-methylindeno[2,1-*b*]pyrrole-2-carboxylate (21a). Indenopyrrole **17b** (3.60 g, 12 mmol) was dissolved in carbon tetrachloride (287 mL), *N*-chlorosuccinimide (1.60 g, 12 mmol) was added, and the solution was allowed to stir overnight under anhydrous conditions. The resulting mixture was diluted with dichloromethane, washed with water and 5% aqueous sodium bicarbonate solution, dried over sodium sulfate, and rotary evaporated. Recrystallization from toluene afforded the chlorinated indenopyrrole (2.51 g, 7.44 mmol, 63%) as a fluffy yellow-orange solid, mp 160−161 °C, darkens at 134 °C. IR (nujol) ν 3266 (NH str.), 1672 cm^{-1} (C═O str.); ^1H NMR (500 MHz, $CDCl_3$) δ 2.56 (3H, s), 5.33−5.40 (2H, AB quartet, J = 12.3 Hz), 5.50 (1H, s), 7.16 (1H, td, J = 0.9, 7.5 Hz), 7.28−7.49 (8H, m), 9.28 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 11.8, 50.6, 66.4, 119.6, 122.1, 124.4, 125.4, 125.9, 128.50, 128.54, 128.9, 129.6, 130.6, 136.3, 137.9, 140.9, 145.4, 161.5. Anal. Calcd for $C_{20}H_{16}NO_2Cl$: C, 71.11; H, 4.77; N, 4.15. Found: C, 70.67; H, 4.74; N, 4.20.

Benzyl 4-Butyl-3,5-dimethylpyrrole-2-carboxylate (23). A solution of sodium benzyloxide was prepared by reacting sodium metal (0.10 g) with benzyl alcohol (5 mL). Ethyl 4-butyl-3,5-dimethylpyrrole-2-carboxylate[45] (10.00 g; 44.8 mmol) in benzyl alcohol (10 mL) was heated on an oil bath raised from room temperature to 230 °C over a 90 min period. The sodium benzyloxide was added in small amounts periodically over the 90 min. When the vapor temperature above the solution reached 200 °C, an additional 0.5 mL of sodium benzyloxide solution was added, and the reaction continued for a further 5 min. The hot solution was poured into a chilled mixture consisting of methanol (32 mL), water (20 mL), and acetic acid (0.5 mL). The resulting precipitate was collected by suction filtration and recrystallized from 95% ethanol to yield the benzyl ester (10.54 g, 37.0 mmol, 82%) as white crystals, mp 73−75 °C (lit. mp[46] 75−76 °C); ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7.2 Hz), 1.28−1.43 (4H, m), 2.18 (3H, s), 2.28 (3H, s), 2.35 (2H, t, J = 7.5 Hz), 5.29 (2H, s), 7.30−7.34 (1H, m), 7.35−7.39 (2H, m), 7.41−7.43 (2H, m), 8.56 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 10.9, 11.8, 14.2, 22.7, 23.9, 33.3, 65.5, 116.5, 122.8, 128.2, 128.3, 128.7, 130.0, 136.9, 161.4. Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.75; H, 8.12; N, 4.91. Found: C, 75.75; H, 8.26; N, 5.01.

5-Benzyloxycarbonyl-3-butyl-4-methylpyrrole-2-carboxylic Acid (24). Freshly distilled sulfuryl chloride (9.3 mL, 15.4 g, 0.114 mol) was added dropwise to a stirred solution of benzyl 3,5-dimethyl-4-butylpyrrole-2-carboxylate (**23**) (10.00 g; 35.1 mmol) in ether (175 mL), maintaining the temperature at 20 °C throughout. The resulting solution was stirred for an additional 2 days at room temperature. The ether was removed under reduced pressure, and the resulting orange oil dissolved in dioxane (90 mL). A mixture of sodium acetate trihydrate (35.0 g) in water (50 mL) was added to the solution, and the stirred mixture heated at 70 °C for 1.5 h. The mixture was allowed to stand at room temperature overnight. The mixture was extracted with ether (3 × 80 mL), and the combined ether layers extracted with sodium bicarbonate solution (10%; 4 × 100 mL). The combined aqueous solution was acidified with conc hydrochloric acid, while maintaining the temperature below 10 °C. The resulting white precipitate was filtered, washed several times with hot water, and dried under vacuum. Recrystallization from ethanol−water gave the carboxylic acid (4.45 g, 14.1 mmol, 40%) as a white powder, mp 148 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 0.87 (3H, t, J = 7.3 Hz), 1.28 (2H, sextet, J = 7.5 Hz), 1.36−1.42 (2H, m), 2.19 (3H, s), 2.69 (2H, t, J = 7.6 Hz), 5.27 (2H, s), 7.31−7.35 (1H, m), 7.37−7.40 (2H, m), 7.37−7.40 (2H, m), 10.95 (1H, br s); ^{13}C NMR (DMSO-d_6) δ 10.0, 13.9, 21.1, 22.0, 23.5, 32.7, 65.0, 119.1, 125.8, 126.0, 127.88, 127.90, 128.4, 129.0, 136.5, 160.4, 162.9. Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.20; H, 6.80; N, 4.50.

Benzyl 4-Butyl-5-iodo-3-methylpyrrole-2-carboxylate (25). A solution of sodium bicarbonate (3.4 g) in water (35 mL) was added to a solution of 5-benzyloxycarbonyl-4-methyl-3-butylpyrrole-2-carboxylic acid (**24**) (4.00 g, 12.7 mmol) in methanol (35 mL), and the resulting mixture heated on a water bath to 60 °C. A solution of iodine (3.3 g) and potassium iodide (5.1 g) in water (135 mL) was added dropwise to the stirred mixture over a period of 1 h, while maintaining the reaction temperature at 60−65 °C, and stirring was continued for a further 1 h. The mixture was cooled, and the precipitate filtered, washed well with 1% aqueous sodium thiosulfate solution to remove traces of iodine and then with water. Recrystallization from ethanol−water gave the iodopyrrole (4.61 g, 91%) as a white powder, mp 107−108 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (3H, t, J = 7.2 Hz), 1.30−1.44 (4H, m), 2.32 (3H, s), 2.35 (2H, t, J = 7.5 Hz), 5.30 (2H, s), 7.32−7.43 (5H, m), 8.83 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 11.2, 14.2, 22.6, 26.5, 32.6, 66.1, 73.6, 123.6, 127.4, 128.5, 128.8, 131.3, 136.4, 160.5. Anal. Calcd for $C_{17}H_{20}INO_2$: C, 51.14; H, 5.07; N, 3.52. Found: C, 51.29; H, 4.93; N, 3.45.

Benzyl 4-Butyl-3-methylpyrrole-2-carboxylate (22b). Benzyl 4-butyl-5-iodo-3-methylpyrrole-2-carboxylate (**25**) (4.00 g, 10.1 mmol), anhydrous sodium acetate (1.6 g), platinum oxide (24 mg), and ethanol (160 mL) were placed in a hydrogenation vessel, and the mixture was shaken under a hydrogen atmosphere at room temperature and 30 psi for 24 h. The mixture was filtered to remove the catalyst, and the solvent evaporated on a rotary evaporator. The residue was taken up in chloroform, washed with water, dried over sodium sulfate, and evaporated under reduced pressure to give the α-unsubstituted pyrrole (2.70 g, 10.0 mmol, 99%) as a pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7.3 Hz), 1.35−1.42 (2H, m), 1.50−1.56 (2H, m), 2.32 (3H, s), 2.42 (2H, t, J = 7.7 Hz), 5.33 (2H, s), 6.68 (1H, d, J = 2.9 Hz), 7.33−7.45 (5H, m), 8.75 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 10.6, 14.2, 22.7, 24.9, 32.7, 65.8, 119.1, 120.1, 126.3, 126.8, 128.30, 128.33, 128.8, 136.7, 161.6; HR MS (EI) calcd for $C_{17}H_{21}NO_2$: 271.1572, found 271.1581.

Benzyl 8(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylindeno[2,1-*b*]pyrrole-2-carboxylate (26a). A solution of chlorinated indenopyrrole **21a** (400 mg, 1.185 mmol), α-free pyrrole **22a**[38c] (300 mg, 1.23 mmol), and *p*-toluenesulfonic acid (20 mg) in glacial acetic acid (13 mL) was stirred for 2 h at room temperature. The solution was diluted with dichloromethane, washed with water and 5% aqueous sodium bicarbonate solution, dried over sodium sulfate, and rotary evaporated to give a brown oil. The crude residue was purified by column chromatography on silica, eluting with dichloromethane, and the product fractions were identified by TLC, combined, and evaporated. Recrystallization from toluene gave the indenodipyrrole (425 mg, 0.781 mmol, 66%) as a white solid, mp 200 °C, dec. IR (nujol) ν 3297, 3255 (NH str.), 1658 cm^{-1} (C═O str.); ^1H NMR (500 MHz, $CDCl_3$) δ 1.10 (3H, t, J = 7.5 Hz), 2.30 (3H, s), 2.46−2.52 (2H, q, J = 7.5 Hz), 2.63 (3H, s), 4.95 (1H, s), 5.21 (2H, s), 5.25−5.35 (2H, AB quartet, J = 12.4 Hz), 7.07 (1H, td, J = 0.9, 7.5 Hz), 7.15 (1H, d, J = 7.5 Hz), 7.27−7.44 (11H, m), 7.52 (1H, d, J = 7.6 Hz), 8.14 (1H, br s), 8.88 (1H, br s); ^1H NMR (500 MHz, DMSO-d_6) δ 0.27 (3H, t, J = 7.4 Hz), 1.41−1.51 (1H, m), 1.51−1.61 (1H, m), 2.09 (3H, s), 2.54 (3H, s), 5.15 (1H, s),

5.23−5.33 (4H, m), 7.01 (1H, td, J = 0.9, 7.4 Hz), 7.06 (1H, d, J = 7.4 Hz), 7.23 (1H, d, J = 7.4 Hz), 7.29−7.50 (11H, m), 11.60 (1H, br s), 11.95 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 10.9, 12.0, 16.4, 17.5, 40.0, 65.8, 66.1, 118.3, 119.5, 122.1, 123.0, 124.6, 125.1, 125.6, 127.1, 128.0, 128.13, 128.15, 128.31, 128.33, 128.6, 128.7, 129.5, 130.4, 136.3, 136.5, 138.6, 143.9, 146.5, 161.7, 161.9; HR MS (EI) calcd for $C_{35}H_{32}N_2O_4$: 544.2362, found 544.2366. Anal. Calcd for $C_{35}H_{32}N_2O_4$: C, 77.18; H, 5.92; N, 5.14. Found: C, 77.20; H, 5.82; N, 4.97.

Benzyl 8(5-Benzyloxycarbonyl-3,4-dimethyl-2-pyrrolyl)-3-methylindeno[2,1-*b*]pyrrole-2-carboxylate (26c). Chlorinated indenopyrrole **21a** (805 mg, 2.52 mmol), α-free pyrrole **22c**[38c] (600 mg, 2.62 mmol), and *p*-toluenesulfonic acid (20 mg) were reacted under the foregoing conditions. Recrystallization from toluene gave the indenodipyrrole (852 mg, 1.61 mmol, 64%) as a white solid, mp 217−218 °C, dec; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.04 (3H, s), 2.26 (3H, s), 2.62 (3H, s), 4.97 (1H, s), 5.09−5.32 (4H, m), 7.06 (1H, dt, J = 1.1, 7.5 Hz), 7.15 (1H, d, J = 7.7 Hz), 7.27−7.41 (11H, m), 7.51 (1H, d, J = 7.5 Hz), 8.38 (1H, br s), 9.31 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 9.2, 11.0, 12.0, 40.1, 65.8, 66.1, 118.1, 118.7, 119.5, 122.2, 123.2, 124.7, 125.1, 127.9, 128.1, 128.2, 128.4, 128.7, 128.8, 129.8, 130.6, 136.4, 136.6, 138.5, 143.4, 146.3, 161.6, 161.8; HR MS (EI) calcd for $C_{34}H_{30}N_2O_4$: 530.2205, found 530.2200. Anal. Calcd for $C_{34}H_{30}N_2O_4 \cdot {}^1/_5H_2O$: C, 76.44; H, 5.74; N, 5.24. Found: C, 76.27; H, 5.48; N, 5.00.

Benzyl 8(5-Benzyloxycarbonyl-3-butyl-4-methyl-2-pyrrolyl)-3-methylindeno[2,1-*b*]pyrrole-2-carboxylate (26b). Chloroindenopyrrole **21a** (1.24 g, 3.67 mmol) was reacted with pyrrole **22b** (1.00 g, 3.69 mmol) under the foregoing conditions. Recrystallization from acetone−hexanes gave the dipyrrole (840 mg, 1.47 mmol, 40%) as an off-white powder, mp 143.5−145 oC; 1H NMR (500 MHz, CDCl3) δ0.89 (3H, t, J = 7.1 Hz), 1.29−1.42 (4H, m), 2.27 (3H, s), 2.37−2.44 (2H, m), 2.63 (3H, s), 4.94 (1H, s), 5.12−5.18 (2H, AB quartet, J = 12.6 Hz), 5.21 (1H, br d, J = 12.3 Hz), 5.28 (1H, br d, J = 12.3 Hz), 7.07 (1H, dt, J = 1.0, 7.5 Hz), 7.15 (1H, d, J = 7.5 Hz), 7.27−7.41 (11H, m), 7.52 (1H, d, J = 7.5 Hz), 8.41 (1H, s, br), 9.20 (1H, br s); 13C NMR (CDCl3) δ11.0, 11.9, 14.1, 23.0, 24.0, 34.0, 40.2, 65.8, 66.1, 118.3, 119.5, 123.0, 124.3, 124.6, 125.1, 127.5, 128.1, 128.20, 128.23, 128.37, 128.40, 128.7, 128.8, 129.6, 130.4, 136.4, 138.6, 146.4, 161.6. Anal. Calcd for $C_{37}H_{36}N_2O_4$: C, 77.60; H, 6.33; N, 4.89. Found: C, 77.41; H, 6.18; N, 5.03.

***tert*-Butyl 8(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylindeno[2,1-*b*]pyrrole-2-carboxylate (26d).** Indenopyrrole *tert*-butylester **17c** (200 mg, 0.74 mmol) was dissolved in carbon tetrachloride (18 mL), *N*-chlorosuccinimide (100 mg, 0.75 mmol) was added, and the solution was allowed to stir for 3 h. The reaction mixture was then washed with water and 5% aqueous sodium bicarbonate solution, dried over sodium sulfate, and rotary evaporated to give the crude chloro-derivative **21b** as a brown oil. The crude residue was dissolved in glacial acetic acid (7 mL) along with α-free pyrrole **22a**[38c] (160 mg, 0.666 mmol) and *p*-toluenesulfonic acid (10 mg) and allowed to stir at room temperature for 2 h. The solution was diluted with dichloromethane, washed with water and 5% aqueous sodium bicarbonate solution, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified on a silica column, eluting with dichloromethane, and the product fractions were identified by TLC, combined, and evaporated. The resulting brown oil crystallized from ethanol to yield the indenodipyrrole **26d** (81 mg, 0.159 mmol, 21%) as a pale green solid, mp 219−220 °C. IR (nujol) ν 3287 (NH str.), 1665 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (3H, t, J = 7.5 Hz), 1.58 (9H, s), 2.31 (3H, s), 2.51 (2H, q, J = 7.5 Hz), 2.59 (3H, s), 4.95 (1H, s), 5.21 (2H, s), 7.06 (1H, td, J = 0.8, 7.5 Hz), 7.15 (1H, d, J = 7.5 Hz), 7.27−7.38 (6H, m), 7.51 (1H, d, J = 7.5 Hz), 8.17 (1H, br s), 8.79 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 10.9, 11.8, 16.3, 17.5, 28.7, 40.1, 65.8, 81.1, 118.3, 119.4, 120.9, 124.4, 124.8, 125.1, 125.6, 127.3, 128.1, 128.19, 128.24, 128.7, 129.5, 130.3, 136.6, 138.8, 142.3, 146.3, 161.56, 161.60; HR MS (EI) calcd for $C_{32}H_{34}N_2O_4$: 510.2519, found 510.2517. Anal. Calcd for $C_{32}H_{34}N_2O_4 \cdot 1/4H_2O$: C, 74.61; H, 6.75; N, 5.44. Found: C, 74.38; H, 6.87; N, 5.48.

8(5-Carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methylindeno-[2,1-*b*]pyrrole-2-carboxylic Acid (16a). Dibenzyl ester **26a** (507.5 mg, 0.933 mmol), acetone (150 mL), methanol (20 mL), and triethylamine (20 drops) was placed into a hydrogenation vessel. The air was displaced with nitrogen, 10% palladium on activated carbon (150 mg) was added, and the mixture was shaken at room temperature with hydrogen at 30 psi for 16 h. The catalyst was removed by suction filtration and evaporation of the solvent gave an oil. The residue was dissolved in 5% aqueous ammonia and diluted with enough water was added to give a total volume of 40 mL. The solution was cooled to less than 5 °C, and acidified to litmus with glacial acetic acid while maintaining the temperature below 5 °C, and then allowed to stand at <5 °C for several hours. Suction filtration of the precipitate, followed by vacuum desiccation, gave the dipyrrole dicarboxylic acid (338 mg, 0.929 mmol, 99%) as a light purple solid, mp 133 °C, dec; ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.30 (3H, t, J = 7.5 Hz), 1.43−1.52 (1H, m), 1.53−1.62 (1H, m), 2.07 (3H, s), 2.52 (3H, s), 5.08 (1H, s), 6.99 (1H, td, J = 0.8, 7.5 Hz), 7.06 (1H, d, J = 7.5 Hz), 7.21 (1H, t, J = 7.5 Hz), 7.45 (1H, d, J = 7.5 Hz), 11.34 (1H, s), 11.72 (1H, s), 11.91 (2H, br s); ^{13}C NMR (d_6-DMSO) δ 10.1, 11.7, 14.6, 16.3, 40.5, 117.4, 118.4, 119.6, 122.2, 123.1, 123.7, 124.9, 125.9, 127.3, 128.5, 130.1, 138.3, 144.3, 147.5, 162.6, 162.9. Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.22; H, 5.33; N, 7.69. Found: C, 69.31; H, 5.65; N, 7.63.

8(3-Ethyl-5-formyl-4-methyl-2-pyrrolyl)-3-methylindeno-[2,1-*b*]pyrrole-2-carbaldehyde (27). Dipyrrole dicarboxylic acid **26a** (1.00 g, 2.75 mmol) was dissolved in trifluoroacetic acid (15.5 mL) and stirred for 2 min at room temperature. Trimethyl orthoformate (3.1 mL) was added while maintaining the temperature at <25 °C, and the resulting solution was heated to 40 °C and allowed to stir for an additional 10 min. The mixture was then poured into ice−water (600 mL). Concentrated aqueous ammonia (15.5 mL) was added to neutralize the acid, and the solution was allowed to stand overnight and then suction filtered. Recrystallization from ethanol−water gave the dialdehyde (742 mg, 2.24 mmol, 81%) as a dark powder, mp 230 °C, dec A small amount of product was chromatographed on a silica column eluting with 30% ethyl acetate in toluene followed by recrystallization from ethanol to give an analytical sample as brown crystals. IR (nujol) ν 3256, 3195 (NH str.), 1638, 1621 cm^{-1} (C═O str.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7.5 Hz), 2.28 (3H, s), 2.37−2.43 (2H, q, J = 7.5 Hz), 2.60 (3H, s), 5.05 (1H, s), 7.11 (1H, td, J = 0.9, 7.5 Hz), 7.18 (1H, d, J = 7.5 Hz), 7.33 (1H, t, J = 7.5 Hz), 7.51 (1H, d, J = 7.5 Hz), 8.93 (1H, br s), 9.39 (1H, s), 9.53 (1H, s), 9.87 (1H, br s); ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.39 (3H, br s), 1.62 (1H, br s), 1.68 (1H, br s), 2.13 (3H, s), 2.57 (3H, s), 5.16 (1H, s), 7.04−7.11 (2H, m), 7.28 (1H, td, J = 1.2, 7.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 9.51 (1H, s), 9.58 (1H, s), 11.84 (1H, br s), 12.25 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 8.9, 10.2, 15.8, 17.1, 40.2, 120.0, 125.3, 125.4, 126.2, 128.5, 129.1, 130.9, 131.7, 133.7, 134.2, 137.9, 145.7, 147.9, 176.8, 177.4; ^{13}C NMR (DMSO-d_6) δ 8.6 (br), 10.2 (br), 14.5, 16.1, 40.4, 119.3, 123.7 (br), 124.6, 125.0, 127.8, 128.3, 129.5 (br), 133.8, 134.4 (br), 137.5, 146.7, 148.1 (br), 177.0 (br), 177.9 (br); HR MS (EI) calcd for $C_{21}H_{20}N_2O_2$: 332.1525, found 332.1524. Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.83; H, 5.76; N, 8.39.

Indenoporphyrin 14a. A solution of *p*-toluenesulfonic acid (190 mg) in dichloromethane (70 mL) and methanol (14 mL) was prepared in a 500 mL round-bottom flask. A solution of dialdehyde **27** (100 mg, 0.301 mmol) and dipyrrole dicarboxylic acid **28**[41] (101 mg, 0.316 mmol) in dichloromethane (56 mL) and methanol (3.5 mL) was added dropwise to the reaction flask over 2 h. The solution was allowed to stir overnight in the dark, a saturated solution of zinc acetate in methanol (4.5 mL) was added, and the reaction mixture was allowed to stir for

5 days open to the air for oxidation. The resulting solution was washed with water and carefully back extracted with chloroform. The organic solvent was then evaporated, and the residue was dissolved in trifluoroacetic acid (12 mL), diluted with chloroform, and washed with water and 5% aqueous sodium bicarbonate solution. The solvent was removed via rotary evaporation, and the residue was purified on a short grade 3 neutral alumina column, eluting with dichloromethane. The first 600 mL of colored eluant was evaporated and rechromatographed on grade 2 neutral alumina, eluting with toluene. The product fractions were combined and rotary evaporated, and subsequent recrystallization from chloroform and methanol gave the indenoporphyrin (40.6 mg, 0.077 mmol, 26%) as a dark green solid, mp >300 °C, dec; UV−vis (1% Et_3N−$CHCl_3$) λ_{max} (log ε) 352 (4.62), 418 (4.86), 445 (4.82), 467 (4.79), 622 (3.71), 672 nm (3.68); UV−vis (1% TFA−$CHCl_3$) λ_{max} (log ε) 434 (5.05), 485 (4.67), 613 nm (3.73); ^{1}H NMR (500 MHz, $CDCl_3$) δ −1.22 (1H, br s), −0.05 (1H, br s), 1.70 (3H, t, J = 7.6 Hz), 1.72 (3H, t, J = 7.6 Hz), 1.76 (3H, t, J = 7.6 Hz), 3.21 (3H, s), 3.27 (3H, s), 3.34 (3H, s), 3.38 (3H, s), 3.71 (2H, q, J = 7.6 Hz), 3.80−3.90 (4H, m), 6.92 (1H, t, J = 7.1 Hz), 6.98 (1H, dt, J = 0.9, 7.4 Hz), 7.32 (1H, d, J = 7.1 Hz), 7.93 (1H, d, J = 7.4 Hz), 9.12 (1H, s), 9.29 (1H, s), 9.35 (1H, s); ^{1}H NMR (500 MHz, TFA−$CDCl_3$) δ −1.74 (1H, br s), −0.97 (1H, br s), 1.61 (3H, t, J = 7.7 Hz), 1.66 (3H, t, J = 7.7 Hz), 1.76 (3H, t, J = 7.6 Hz), 3.36 (3H, s), 3.41 (3H, s), 3.42 (3H, s), 3.44 (3H, s), 3.87−3.98 (6H, m), 7.12 (1H, t, J = 7.3 Hz), 7.22 (1H, td, J = 0.8, 7.6 Hz), 7.57 (1H, d, J = 7.2 Hz), 8.04 (1H, d, J = 7.6 Hz), 9.84 (1H, s), 10.01 (1H, s), 10.04 (1H, s); ^{13}C NMR (TFA−$CDCl_3$) δ 11.60, 11.66, 12.3, 12.7, 15.6, 16.3, 16.4, 20.06, 20.07, 21.4, 100.81, 100.84, 101.4, 112.5, 125.5, 128.9, 130.2, 131.1, 133.5, 137.0, 137.3, 138.1, 139.8, 140.2, 140.6, 141.3, 141.9, 142.1, 143.7, 143.8, 144.9, 145.1, 147.6, 150.2, 152.3; HR MS (EI) calcd for $C_{36}H_{36}N_4$: 524.2940, found 524.2940. Anal. Calcd for $C_{32}H_{36}N_4$: C, 81.99; H, 7.08; N, 10.93. Found: C, 82.35; H, 6.92; N, 10.57.

Indenoporphyrin 14b. A solution of *p*-toluenesulfonic acid (160 mg) in dichloromethane (60 mL) and methanol (12 mL) was prepared in a foil wrapped 500 mL round-bottom flask. A solution of indenodipyrrole dicarboxylic acid **16b** (100 mg, 0.255 mmol) and dipyrrole dialdehyde **15**[26f] (69 mg, 0.254 mmol) in dichloromethane (50 mL) and methanol (5 mL) was added slowly to the reaction flask over a period of 2 h. The solution was allowed to stir overnight in the dark, then a saturated solution of zinc acetate in methanol (4 mL) was added, and the reaction mixture was allowed to stir for 3 days open to the air for oxidation. The resulting solution was washed with water and carefully back extracted with chloroform. The organic solvent was then evaporated, and the residue was dissolved in trifluoroacetic acid (10 mL), diluted with chloroform, and washed with water and 5% aqueous sodium bicarbonate solution. The solvent was removed under reduced pressure, and the residue was purified on a short grade 3 neutral alumina column, eluting with dichloromethane. The colored eluants were combined, evaporated, and rechromatographed on grade 3 neutral alumina, eluting with toluene. The product fractions were combined and evaporated under reduced pressure. Recrystallization from chloroform−methanol gave the indenoporphyrin (8.1 mg, 0.015 mmol, 6%) as a dark green solid, mp >260 °C, dec; UV−vis (1% Et_3N−$CHCl_3$) λ_{max} (log ε) 352 (4.61), 418 (4.85), 445 (4.81), 467 (4.77), 622 (3.78), 672 nm (3.78); ^{1}H NMR (500 MHz, TFA−$CDCl_3$) δ −2.37 (1H, s), 2.27 (1H, br s), −1.52 (1H, s), −1.40 (1H, v br), 0.99 (3H, t, J = 7.9 Hz), 1.49 (2H, sextet, J = 7.4 Hz), 1.62 (3H, t, J = 7.7 Hz), 1.67 (3H, t, J = 7.7 Hz), 2.05−2.11 (2H, m), 3.37 (3H, s), 3.44 (3H, s), 3.45 (3H, s), 3.46 (3H, s), 3.90−3.95 (6H, m), 7.15 (1H, t, J = 7.4 Hz), 7.24 (1H, t, J = 7.8 Hz), 7.59 (1H, d, J = 7.1 Hz), 8.04 (1H, d, J = 7.5 Hz), 9.92 (1H, s), 10.08 (1H, s), 10.11 (1H, s); ^{13}C NMR (TFA−$CDCl_3$) δ 11.5, 11.6, 12.4, 12.6, 13.7, 16.2, 16.3, 20.1, 23.1, 28.1, 29.9, 33.2, 100.9, 101.0, 101.6, 113.1, 125.8, 129.2, 130.7, 131.3, 134.2, 137.1, 137.8, 138.8, 139.6, 140.6, 140.7, 141,2, 141.9, 142.1, 143.7, 145.7, 145.8, 147.2, 150.1, 152.2; HR MS (EI) calcd for $C_{38}H_{40}N_4$: 552.3253, found 552.3252.

Nickel(II) Complex 30a. A solution of saturated nickel(II) acetate in methanol (5 mL) was added to a solution of indenoporphyrin **14a** (10.5 mg, 0.020 mmol) in chloroform (10 mL), and the resulting mixture was stirred under reflux overnight. The reaction mixture was then diluted with chloroform (30 mL) and washed with water, and the chloroform layer evaporated under reduced pressure. The residue was chromatographed on grade 3 neutral alumina, eluting with dichloromethane. The product fractions were combined and recrystallized from chloroform−methanol to give the nickel complex in quantitative yield as a dark green solid, mp 276−278 °C; UV−vis ($CHCl_3$) λ_{max} (log ε) 358 (4.18), 427 (4.72), 561 (3.58), 605 (3.56), 651 (3.45), 716 nm (3.16); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.63−1.67 (6H, 2 overlapping triplets, J = 7.7 Hz), 1.68 (3H, t, J = 7.6 Hz), 3.18 (3H, s), 3.21 (6H, s), 3.23 (3H, s), 3.63−3.69 (4H, 2 overlapping quartets, J = 7.7 Hz), 3.79 (2H, q, J = 7.6 Hz), 6.97−7.05 (2H, m), 7.41 (1H, dd, J = 1.4, 6.6 Hz), 7.82 (1H, d, J = 7.2 Hz), 8.99 (1H, s), 9.11 (1H, s), 9.16 (1H, s); ^{13}C NMR ($CDCl_3$) δ 11.2, 11.3, 11.8, 12.3, 16.9, 17.46, 17.51, 19.63, 19.67, 21.3, 97.3, 99.4, 101.6, 111.9, 122.9, 127.3, 127.7, 127.9, 132.1, 135.6, 139.7, 140.6, 140.8, 141.1, 141.6, 141.7, 141.8, 142.1, 144.1, 144.2, 144.4, 144.5, 145.2, 149.4, 152.4; HR MS (EI) calcd for $C_{36}H_{34}N_4Ni$: 580.2137, found 580.2144.

Copper(II) Complex 30b. A solution of saturated copper(II) acetate in methanol (5 mL) was added to a solution of indenoporphyrin **14a** (11 mg, 0.021 mmol) in chloroform (10 mL), and the resulting mixture was allowed to reflux for 2 h. The reaction mixture was then diluted with chloroform (30 mL) and washed with water, and the chloroform layer evaporated under reduced pressure. The residue was purified on a grade 3 neutral alumina column, eluting with dichloromethane. The product fractions were combined and recrystallized from chloroform−methanol to give the copper complex (12.3 mg, 0.021 mmol, 100%) as a dark green solid, mp >300 °C; UV−vis ($CHCl_3$) λ_{max} (log ε) 346 (4.34), 430 (4.78), 451 (4.83), 492 (3.85), 571 (3.70), 618 (3.65), 662 (3.55), 725 nm (3.33); HR MS (EI) calcd for $C_{36}H_{34}N_4Cu$: 585.2079, found 585.2072.

Zinc Complex 30c. A solution of saturated zinc acetate in methanol (5 mL) was added to a solution of indenoporphyrin **14a** (10 mg, 0.019 mmol) in chloroform (10 mL), and the resulting mixture was allowed to reflux for 1 h. The reaction mixture was then diluted with chloroform (30 mL) and washed with water, and the chloroform layer evaporated under reduced pressure. The residue was purified on a grade 3 neutral alumina column, eluting with dichloromethane. However, due to low solubility, the crude product had to be loaded on to the column with a few drops of pyrrolidine in dichloromethane due to its ability to increase the solubility of zinc porphyrins in chlorinated solvents. The product fractions were combined and recrystallized from chloroform−hexanes to give the zinc complex (8.2 mg, 0.014 mmol, 73%) as a very dark blue solid, mp >300 °C; UV−vis ($CHCl_3$) λ_{max} (log ε) 347 (4.53), 389 (4.56), 436 (4.89), 459 (5.00), 498 (3.86), 580 (3.79), 624 (2.67), 674 (3.51), 737 nm (3.27); UV−vis (1% Pyrrolidine-$CHCl_3$) λ_{max} (log ε) 348 (4.54), 385 (4.56), 446 (4.83), 470 (5.06), 505 (4.01), 594 (3.85), 641 (3.71), 768 nm (3.18); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70−1.80 (9H, m), 3.31 (3H, s), 3.35 (3H, s), 3.37 (3H, s), 3.39 (3H, s), 3.79 (2H, q, J = 7.7 Hz), 3.82−3.89 (4H, m), 7.00 (1H, t, J = 7.2 Hz), 7.06 (1H, t, J = 7.5 Hz), 7.47 (1H, d, J = 7.2 Hz), 8.08 (1H, d, J = 7.5 Hz), 9.24 (1H, s), 9.36 (1H, s), 9.42 (1H, s); ^{1}H NMR (500 MHz, pyrrolidine-$CDCl_3$) δ 1.68−1.74 (6H, m), 1.76 (3H, t, J = 7.6 Hz), 3.30 (3H, s), 3.34 (3H, s), 3.35 (3H, s), 3.36 (3H, s), 3.77 (2H, q, J = 7.7 Hz), 3.81 (2H, q, J = 7.6 Hz), 3.84 (2H, q, J = 7.5 Hz), 6.89 (1H, t, J = 7.3 Hz), 6.97 (1H, td, J = 1.0, 7.5 Hz), 7.39 (1H, dd, J = 0.8, 7.0 Hz), 8.03 (1H, d, J = 7.5 Hz), 9.21 (1H, s), 9.31 (1H, s), 9.34 (1H, s); ^{13}C NMR (pyrrolidine-$CDCl_3$) δ 11.3, 11.4, 11.9, 12.4, 16.9, 17.77, 17.78, 19.7, 19.8, 21.8, 97.3, 99.6, 101.6, 112.8, 122.8, 126.5, 127.0, 128.0, 131.7, 134.8, 135.0, 139.7, 140.1, 140.8, 141.9, 142.9, 143.5, 147.7, 148.7, 149.2, 150.2, 150.3, 152.0, 153.2, 160.4, 167.1; HR MS (EI) calcd for $C_{36}H_{34}N_4Zn$: 586.2075, found 586.2073.

■ ASSOCIATED CONTENT

Supporting Information. Selected ^{1}H NMR, ^{1}H−^{1}H COSY, HMQC, ^{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

†Porphyrins with Exocyclic Rings. Part 27. For Part 26 of this series, see ref 13e.

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