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Porphyrins with exocyclic rings. Part 22: Synthesis of deoxophylloerythroetioporphyrin (DPEP), three ring homologues, and five related nonpolar bacteriopetroporphyrins using a western ring closure and an improved *b*-bilene methodology ☆

Timothy D. Lash,* Wei Li and Desiree M. Quizon-Colquitt

Department of Chemistry, Illinois State University, Normal, IL 61790-4160, United States

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Abstract—Dipyrrolic intermediates incorporating five-membered carbocyclic rings are easily prepared from cyclopenta[*b*]pyrroles, and this unit represents the southern half of the DPEP-type geoporphyrins found in organic-rich sediments such as oil shales and petroleum. Related dipyrroles with six-, seven- or eight-membered carbocyclic rings were shown to give *b*-bilenes when reacted with dipyrrylmethane carbaldehydes under mildly acidic conditions. Following deprotection of the terminal ester groups, cyclization with TFA–$CH(OMe)_3$ gave a series of ring homologues of deoxophylloerythroetioporphyrin (DPEP). The *b*-bilenes generated from the five-membered ring dipyrroles proved to be rather unstable and had to be used directly without purification. Cyclization gave DPEP contaminated with an etioporphyrin by-product, but these could be separated as the nickel(II) derivatives by flash chromatography. This approach gave superior yields of DPEP compared to previously reported methods. In addition, the methodology could be extended to the synthesis of related petroporphyrins, and a series of five molecular fossils derived from bacteriochlorophylls *d* were synthesized by this approach.

1. Introduction

The presence of metalloporphyrins in organic-rich sediments such as oil shales and petroleum was first recognized by Alfred Treibs in the 1930s.[1–3] Treibs tentatively identified metalated derivatives of etioporphyrin-III (**1a**) and deoxophylloerthroetioporphyrin (DPEP; **2a**) on the basis of degradative studies. These structures were appealing in that they contain the same carbon skeletons as heme and chlorophyll *a*, respectively, and the presence of metalloporphyrins provides supporting evidence for the biological origins of these sedimentary materials.[1–3] However, later analyses of 'petroporphyrin' extracts using mass spectrometry demonstrated that complex mixtures of metalloporphyrins were present, although pseudohomologous series related to etioporphyrin-III and DPEP could be identified.[2,4,5] It was not until the 1980s that individual porphyrin structures could be isolated in pure form and characterized by NMR spectroscopy. These investigations relied upon improvements in HPLC techniques,[6] as well as high field NOE difference proton NMR spectroscopy.[7] In addition to etioporphyrin-III[8] and the related chlorophyll degradation product **1b**,[8c,9] more than 50 examples of cycloalkanoporphyrins (CAPs) with five-, six- or seven-membered exocyclic rings (e.g., **2**–**4**, Chart 1) have been identified.[10–12] These structurally diverse CAPs are believed to be primarily derived from bacterial and algal chlorophylls,[13,21] and for that reason the most common structural motifs are DPEP-type porphyrins incorporating five-membered exocyclic rings.[3] In oil shales and petroleum, the petroporphyrins are primarily present as nickel(II) or vanadyl complexes,[14] although free base porphyrins and copper(II) derivatives are sometimes observed.[15] The presence of metalloporphyrins in petroleum allows them to be used as geochemical markers, as the distribution of structural types (e.g., etioporphyrins vs DPEPs) and molecular weights can be correlated to thermal maturity.[16] On the other hand, these metallo-derivatives can lead to difficulties in petrochemical processing by poisoning the catalysts.[17] Petroporphyrins are also being investigated for monitoring oil spills as the distribution of metalloporphyrins in the resulting tar balls can be used to identify the origin of the petroleum.[18] In a more academic sense, the porphyrins found in a deposit can give insights into the environment present when the sediment was laid down millions of years ago. For instance,

☆ For part 21 in the series, see Ref. 31e.
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* Corresponding author. Tel.: +1 309 438 8554; fax: +1 309 438 5538; e-mail: tdlash@ilstu.edu

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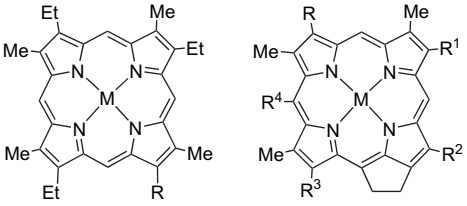
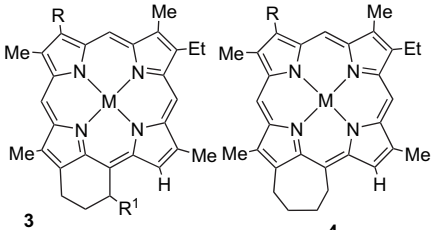


1 a. R = Et; b. R = H
M = Ni or VO

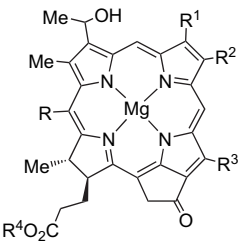
2 Deoxophylloerythroetioporphyrin and related cycloalkanoporphyrins

For structure **2**:
a. R = R^1 = R^3 = Et; R^2 = Me; R^4 = H; M = Ni or VO
b. R = R^1 = R^2 = Et; R^3 = P; R^4 = H; M = Ni
c. R = R^2 = Et; R^1 = Pr; R^3 = P; R^4 = H; M = Ni
d. R = R^2 = Et; R^1 = *i*-Bu; R^3 = P; R^4 = H; M = Ni
e. R = R^1 = R^3 = Et; R^2 = R^4 = Me; M = Ni or VO
f. R = R^2 = Me; R^1 = R^3 = Et; R^4 = H; M = Ni



3
a. R = Et or Me;
R^1 = Me; M = VO
b. R = H or Et;
R^1 = CH_2OH; M = Ni

4
M = Ni or VO
R = H, Me or Et



Bacteriochlorophylls c
R = R^1 = Me

Bacteriochlorophylls d
R = H; R^1 = Me

Bacteriochlorophylls e
R = Me; R^1 = CHO

Bacteriochlorophylls f
R = H; R^1 = CHO

R^2 = Et, Pr, *i*-Bu, neopentyl; R^3 = Me or Et
R^4 is usually farnesyl

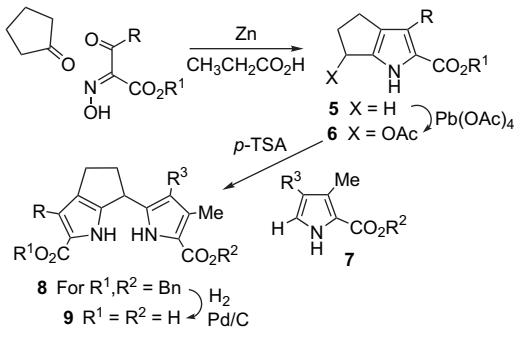
Chart 1.

a series of carboxylic acids **2b–d** were isolated[19] from the lacustrine Messel oil shale (Eocene) in Germany that showed the same substitution pattern that is found in the bacteriochlorophylls *d* (as well as bacteriochlorophylls *f*; see Chart 1) from the green sulfur bacteria (Chlorobiaceae).[20] As these photosynthetic bacteria are strictly anaerobic, this implies that an anoxic environment existed within the water column. The presence of a 20-methylDPEP **2e** in the Oulad Abdoun oil shale has also been noted,[21] and this species is presumably also derived from the *Chlorobium* chlorophylls (specifically from bacteriochlorophylls *c* or *e*).[20] It is worth noting that that the Chlorobiaceae can also generate bacteriochlorophylls (Chart 1) with neopentyl substituents at position 8,[20] although to date no examples of neopentylporphyrins have been identified in organic-rich sediments.

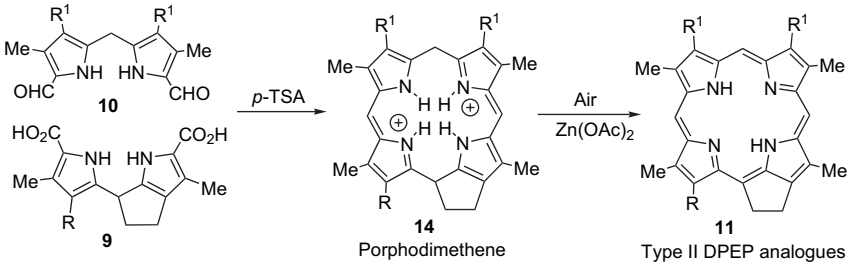
A synthesis of DPEP was first reported by Fischer in 1935 using pyrromethene intermediates, although the yield for the final step was very poor (<0.01%).[22] In 1966, Flaugh and Rapoport reported a *b*-bilene synthesis of DPEP where the cyclopentene unit had been incorporated prior to the cyclization step, but the final step afforded the porphyrin in only 6% yield.[23] Alternative routes have been reported where the five-membered exocyclic ring is introduced subsequent to porphyrin formation, but the additional steps required result in mediocre overall yields.[24] The limitations of these methods have allowed only a few of the known porphyrin molecular fossils to be synthesized.[25] Syntheses of DPEP from chlorophyll *a* have also been carried out,[26,27] and this provides an attractive route to **2a**, but this approach severely limits the substitution patterns that are accessible. Nevertheless, partial syntheses of bacteriopetroporphyrins **2b–d** from bacteriochlorophylls *d* have been accomplished.[28]

2. Results and discussion

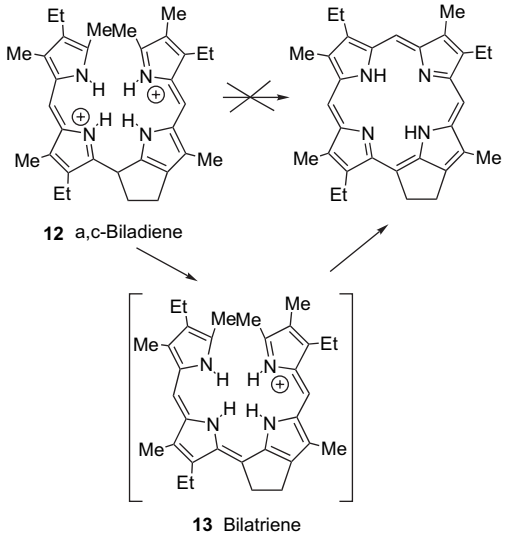
In our previous studies, we have developed synthetic routes to petroporphyrins starting from cyclic ketones.[29–33] Cyclopentanone reacts with oximes in the presence of zinc dust and sodium propionate in propionic acid at 150 °C to give cyclopenta[*b*]pyrroles **5**,[34] and these can be selectively oxidized with lead tetraacetate to afford the corresponding 6-acetoxy derivatives **6** (Scheme 1).[34] Further condensation with α-unsubstituted pyrroles **7** in the presence of *p*-toluenesulfonic acid afforded a series of dipyrroles **8** in good yields.[34] These dipyrroles correspond to the southern half of DPEP-type petroporphyrins. The corresponding dicarboxylic acids **9** were shown to condense with dipyrrylmethane dialdehydes **10** in the presence of *p*-toluenesulfonic acid to give, following air oxidation in the presence of zinc acetate, the type II CAPs **11** in up to 20% yield (Scheme 2).[33] This '2+2' methodology is a modification of the MacDonald condensation,[35] and the presence of the fused cyclopentene unit does not overtly disrupt the formation of the porphyrin macrocycle. However, in this method one of the condensing dipyrroles must be symmetrical to avoid the formation of two porphyrin isomers. Hence, this chemistry allowed a convenient synthesis of non-natural *meso*,β-ethanoporphyrins **11** but could not be used to prepare DPEP or other type III geoporphyrins.[33] Although a,c-biladiene intermediates are often used to prepare asymmetrical porphyrins,[36] this approach could not be used to prepare porphyrins with five-membered exocyclic rings.[33] Attempts to cyclize a,c-biladiene **12** failed to give more than trace amounts of porphyrin products under any of the conditions investigated (Scheme 3).[33] The failure of this study was attributed to two factors. Firstly, it is known that a,c-biladienes are initially oxidized to bilatrienes **13** prior to macrocyclization,[36,37] and this would introduce a deleterious steric interaction



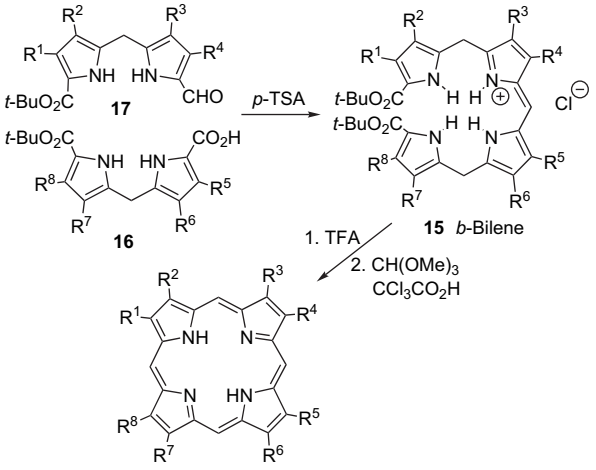
Scheme 1.



Scheme 2.



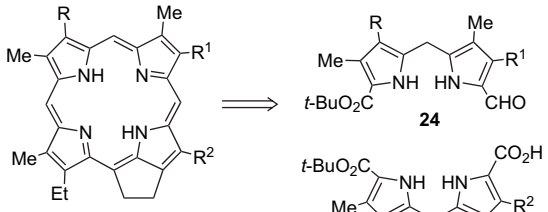
Scheme 3.



Scheme 4.

between the carbocyclic ring and the adjacent alkyl substituent. This is not a factor in the MacDonald synthesis (Scheme 2) as initial macrocycle formation occurs prior to oxidation, and the bridging carbon associated with the cyclopentene ring remains sp^3 hybridized so that the alkyl substituent and the carbocyclic ring are pivoted away from one another. The intermediary porphodimethene **14** can then slowly oxidize to porphyrin.[33] A second possibly more significant factor is that the five-membered ring introduces significant angle strain in the conjugated bilatriene **13** that appears to destabilize the tetrapyrrolic system leading to extensive decomposition.[33] Hence, a stepwise version of the MacDonald condensation that produces a single porphyrin isomer while retaining the beneficial oxidation state prior to cyclization is required to allow for the efficient synthesis of DPEP-type petroporphyrins.[38,39]

A *b*-bilene route that uses *tert*-butyl ester protective groups has been developed, which acts as a stepwise MacDonald route to porphyrins and overcomes any symmetry restrictions (Scheme 4).[40] In principle, this methodology fulfills the necessary requirements for synthesizing these geoporphyrins. The required tetrapyrrolic intermediates **15** can be obtained by reacting dipyrrylmethane aldehydes **16** with a second dipyrrylmethane **17** under mild acid catalyzed conditions.[40] Deprotection with TFA, followed by extraction, and cyclization with trimethyl orthoformate and trichloroacetic acid, afforded β-substituted porphyrins in 25–57% yields. In order to prepare DPEP or related petroporphyrins by this approach, the dipyrrolic intermediates shown in Scheme 5 were required. We were also interested in synthesizing petroporphyrins related to the bacteriochlorophyll derived sedimentary porphyrins **2b–d** that had been observed in the Messel oil shale.[19] In more mature sediments, these carboxylic acids would be expected to undergo decarboxylation to give the corresponding 17-ethylporphyrins **18a**, **18c**, and **18e**. As bacteriochlorophylls *d* commonly have an ethyl, *n*-propyl or isobutyl substituent at position 8, and a methyl or ethyl group at position 12, we targeted the five possible nonpolar petroporphyrin structures **18a–e** with this substitution pattern in addition to DPEP itself. Finally, a crystalline nickel(II) porphyrin mineral **18f** has been observed alongside oil shales that has a methyl substituent at the 3-position, but otherwise has the same arrangement of substituents as DPEP.[41] As this mineral, which is known as abelsonite, is

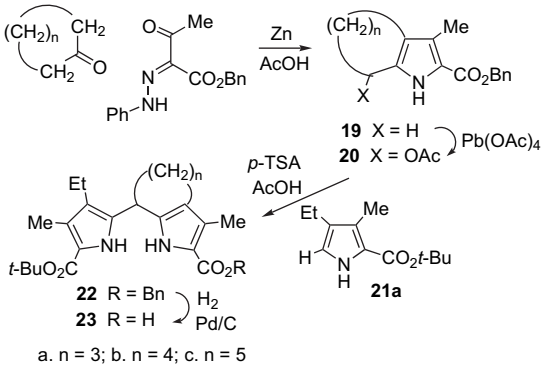


2a R = R¹ = Et; R² = Me
18a R = R¹ = R² = Et
18b R = Et; R¹ = Pr; R² = Me
18c R = R² = Et; R¹ = Pr
18d R = Et; R¹ = *i*-Bu; R² = Me
18e R = R² = Et; R¹ = *i*-Bu
18f R = R² = Me; R¹ = Et

Scheme 5.

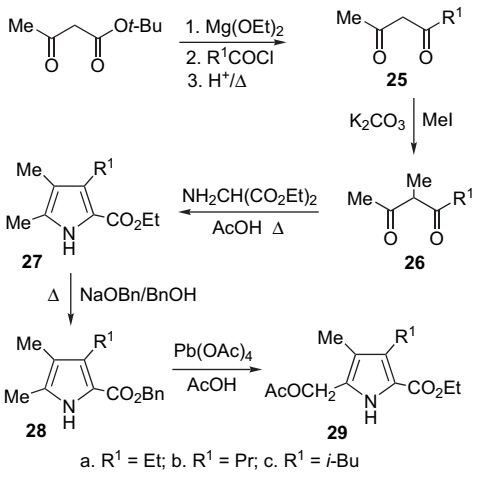
the only known example of this type it was somewhat surprising that it had not been synthesized previously. Therefore the synthesis of this system was also investigated. The planned syntheses would generate the eastern bridging connection first, and complete macrocycle formation with a western ring closure. Although these two steps could easily be reversed, this route was selected because it could in principle allow the introduction of an alkyl group at C20 at a late stage in the synthesis, thereby facilitating the production of petroporphyrin **2e** or related molecular fossils of bacteriochlorophyll *c* or *e*.[42]

As the five-membered ring in the DPEP-type systems has led to difficulties[33] that were not encountered in the synthesis of CAPs with six-, seven- or eight-membered rings,[31,32] ring expanded analogues of DPEP were prepared using the *b*-bilene route to see how well this methodology worked in the absence of ring strain factors. The cycloalka[*b*]pyrrole benzyl esters **19a–c** were easily prepared from the corresponding cyclic ketones using a variation on the Knorr pyrrole condensation (Scheme 6).[31,32,43] These were derivatized by reaction with lead tetraacetate to give the acetoxy compounds **20** in excellent yields as described previously.[31,32] The α-unsubstituted pyrrole *tert*-butyl ester **21a** is also easily prepared from *tert*-butyl isocyanoacetate[44] using the Barton–Zard pyrrole synthesis.[45] Acid catalyzed condensation of **20a–c** with **21a** gave the dipyrrolic intermediates **22a–c** with mixed ester protective groups in 61–88% yields. Subsequent hydrogenolysis of the benzyl esters over 10% Pd/C then gave the related carboxylic acids **23a–c**.

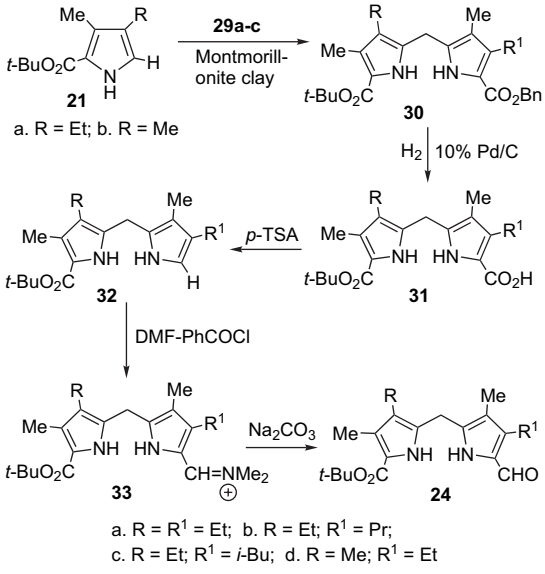


Scheme 6.

A series of dipyrrylmethane carbaldehydes **24** were also required in these syntheses. The magnesium enolate derivative of *tert*-butyl acetoacetate was reacted with propionyl chloride, butyryl chloride or isovaleryl chloride, and following cleavage of the *tert*-butyl ester and decarboxylation, a series of β-diketones **25a–c**, respectively, were generated (Scheme 7). Further alkylation with methyl iodide and potassium carbonate gave **26a–c**, and these condensed with diethyl aminomalonate[46] in refluxing acetic acid to give the pyrrole ethyl esters **27a–c**. Transesterification with benzyl alcohol and a catalytic amount of sodium benzyloxide afforded the related benzyl esters **28a–c** and these reacted with lead tetraacetate in acetic acid to give the acetoxymethylpyrroles **29a–c**. Pyrroles **29a–c** were reacted with **21a** in dichloromethane using K10 Montmorillonite clay as the catalyst[47] to give the dipyrrylmethanes **30a–c** in high yields (Scheme 8).



Scheme 7.



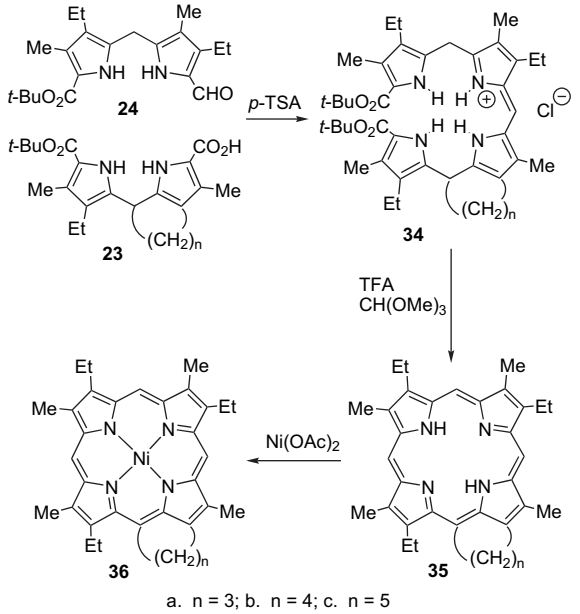
Scheme 8.

Similarly, **29a** condensed with *tert*-butyl 3,4-dimethylpyrrole-2-carboxylate (**21b**) to give the related dipyrrylmethane **30d**. All four dipyrrylmethanes were obtained as oils following chromatography and, as is often the case for dipyrrylmethane mixed diesters of this type,[47] could not be induced to crystallize. Cleavage of the benzyl esters with hydrogen over 10% Pd/C gave the corresponding carboxylic acids **31**. Conversion of these carboxylic acids to the related aldehydes could be carried out by reduction of the related acyl chlorides or some other derivatives,[48] but in practice the sacrifice of the carboxyl carbon and subsequent formylation is considerably more convenient. Decarboxylation of **31a–d** can be accomplished by stirring the dipyrrylmethanes with 2 equiv of *p*-toluenesulfonic acid at room temperature for 30 min while leaving the *tert*-butyl esters intact. In principle, the aldehyde groups may be introduced by using the Vilsmeier–Haack conditions, but we elected to use Clezy's milder conditions for this chemistry.[49] Benzoyl chloride and DMF were used to generate the required Vilsmeier intermediate and subsequent reaction with **32** gave the imine salts **33** in excellent yields. These were hydrolyzed with sodium

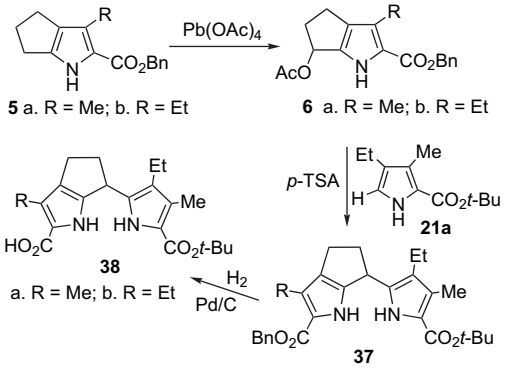
carbonate in ethanol–water to give the required dipyrrylmethane aldehydes **24**.

The condensation of the two dipyrrylmethane fragments must also be conducted under mildly acidic conditions in order to retain the *tert*-butyl ester protective groups. Reaction of **24a** with **23a** in the presence of 2 equiv of *p*-toluenesulfonic acid in methanol–dichloromethane, followed by extraction, washing with aqueous $NaHCO_3$ solution, and brief treatment with dry HCl gave the corresponding *b*-bilene hydrochloride salt **34a** (Scheme 9). Although these types of intermediates can be recrystallized from ether in many cases,[40] this proved to be impractical in our hands. The intermediate was also somewhat unstable and had to be used fairly quickly (<2 weeks). Initially, the crude *b*-bilene was taken on to porphyrin using literature conditions. This method called for deprotection of the *tert*-butyl esters by dissolving the *b*-bilene in TFA for 10 min, followed by extraction and cyclization with $CH(OMe)_3$ using trichloroacetic acid as a catalyst. However, this method gave poor results and only low yields of porphyrin **35a** were observed. In unrelated studies, we have used TFA to both deprotect *tert*-butyl esters and catalyze '3+1' MacDonald-type condensations of tripyrranes and dialdehydes.[50–52] The success of this approach suggested that a similar one pot procedure for *b*-bilene cyclizations should also be viable. Hence, *b*-bilene **34a** was dissolved in TFA and stirred for 10 min at room temperature under nitrogen. The mixture was diluted with dichloromethane, trimethyl orthoformate was added via a syringe, and the reaction stirred for 2 h. The solution was neutralized with triethylamine, 1 equiv of DDQ was added, and the mixture was stirred for an additional 1 h. Following extraction, chromatography, and recrystallization from chloroform–methanol, the six-membered ring homologue of DPEP **35a** was isolated in >30% yield. In some cases, the crude product in chloroform was heated with a saturated solution of nickel(II) acetate in methanol to give the corresponding nickel(II) complex **36a** in comparable overall yields. The seven-membered ring version **35b** was similarly obtained in 30–32% yield, while the *meso*,β-pentanoporphyrin **35c** was isolated in 50–51% yield. The nickel(II) complexes were also synthesized and characterized. In earlier studies, porphyrins with eight-membered exocyclic rings were obtained in relatively low yields using the MacDonald '2+2' condensation compared to the six- and seven-membered ring versions,[32] and this difference was attributed to conformational effects where the eight-membered ring favors a geometry that pulls the two ends of an open-chain tetrapyrrolic intermediate apart thereby inhibiting macrocyclization and favoring polymerization processes.[32] The relatively high yields obtained for the cyclization of the eight-membered ring *b*-bilene **34c** is therefore somewhat surprising, but the mild conditions presumably provide the molecule with more time to undergo a conformational change that facilitates cyclization.

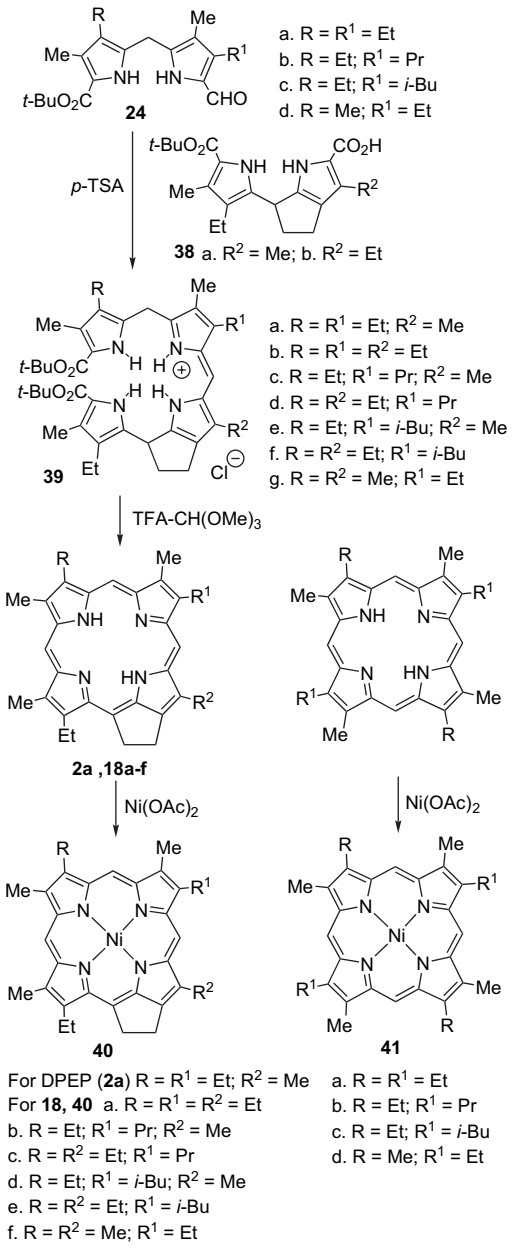
Porphyrins **35a–c** are structurally identical to DPEP apart from the expanded exocyclic rings, and can therefore be considered to be ring homologues of the natural system. Synthetic porphyrins from our studies have been used for extensive resonance Raman investigations that rely on the direct comparison of structural analogues as well as isomeric variations,[53–56] and these samples have therefore been of value in their own right.[57] However, in other respects these compounds are very similar to porphyrins previously synthesized using the MacDonald condensation.[31,32] The real challenge in these investigations was to extend the methodology to the preparation of DPEP and related geoporphyrins. The dipyrrolic intermediates bearing five-membered exocyclic rings were prepared from cyclopenta[*b*]pyrroles **5a**[34] and **5b** (Scheme 10). The 3-ethyl version **5b** was obtained by transesterification of the related ethyl ester.[34] Oxidation with lead tetraacetate gave the corresponding acetoxy derivatives **6** and these condensed with α-unsubstituted pyrrole **21a** to give the related dipyrroles **37** in 72–85% yields. Cleavage of the benzyl esters with hydrogen over 10% Pd/C gave the corresponding carboxylic acids **38** and these were used to prepare the *b*-bilene intermediates. The reaction of **38a** or **38b** with **24a** to generate *b*-bilenes **39** (Scheme 11) was initially conducted under the conditions used to prepare the 6–8 membered ring analogues **34a–c**, but these reactants gave products that underwent extensive decomposition during extraction. In the earliest of these studies, the crude *b*-bilenes were taken on using the original procedures where the protective groups were cleaved with TFA but cyclization was carried out using CCl_3CO_2H–$CH(OMe)_3$.[58]



Scheme 9.



Scheme 10.



Scheme 11.

Further decomposition was evident by the color changes that were observed during the extraction processes, but DPEP and its 13-ethyl analogue **18a** could be isolated in 2% yield.[58] The one pot procedure also gave poor results, primarily because the *b*-bilene underwent decomposition during workup. In order to avoid this problem, reaction mixture obtained by reacting **38a** and **24a** was evaporated to dryness, treated with TFA, diluted with dichloromethane, and cyclized with trimethyl orthoformate. This method avoided any manipulation of the *b*-bilene intermediate **39**, but even then poor results were obtained using DDQ as an oxidant. In the MacDonald synthesis of *meso*,β-ethanoporphyrins **11**, the intermediates were air oxidized in the presence of zinc acetate.[33,59] Using these mild conditions, substantial amounts of porphyrin products were generated. Unfortunately, the desired DPEP product was contaminated with an etioporphyrin by-product in a ratio of approximately 2:1. These porphyrins could not be separated on alumina, but chromatography on silica gel was not feasible as this leads to oxidation of the cyclopentene ring.[60] However, the latter problem can be avoided by converting the porphyrin mixtures into the corresponding nickel(II) complexes **40** (Scheme 11). The nickel(II) porphyrins are reasonably stable to silica, and this allowed separation of the two porphyrins by flash chromatography. Due to the low solubility of the nickel(II) porphyrins, chromatography had to be performed two or more times to separate the two porphyrin components. Nevertheless, nickel(II) DPEP was isolated in 28% yield, and this represents a significant improvement in the overall yield compared to any other previously published methodology. Demetalation can be carried out with 5% sulfuric acid in TFA, although it should be noted that the natural porphyrins occur in metalated form. The method was used to prepare the series of five nonpolar bacteriopetroporphyrins, and the nickel complexes **40** were isolated in 12–23% yield. Demetalation could also be carried out using 5% H_2SO_4–TFA to give the free base porphyrins **18a–e**. However, reaction of dimethyl dipyrrylmethane aldehyde **24d** with **38a** gave mixtures of products that could not be separated due to the very poor solubility of the resulting nickel(II) porphyrins **40f** and **41d**. This prevented us from completing the synthesis of abelsonite by this method, although an alternative approach was later developed that allowed this synthesis to be accomplished.[61] Nevertheless, the present route allowed DPEP to be prepared in superior yield, and also allowed a series of nonpolar bacteriopetroporphyrins to be synthesized for the first time.

The preparation of **2a** and **18a** gave etioporphyrin **41a** as a by-product, and this presumably arises by a head-to-tail self-condensation of the unreacted dipyrrylmethane aldehyde **24a**. Although one might expect the product to be nickel(II) etioporphyrin-I (**41a**), the proton and carbon-13 NMR spectra for the nickel complex showed additional peaks which suggest that some scrambling has occurred to give other types of isomers. The related dipropyl etio-type porphyrin **41b** obtained as a by-product from the synthesis of **18b** and **18c** gave NMR data that indicated only a trace amount of isomer contamination, while the diisobutylporphyrin **41c** that was isolated in preparations of **18d** and **18e** appeared to be only the type I isomer.

The proton NMR spectra for the nickel(II) DPEP-type derivatives were often broad and poorly resolved at room temperature, although the spectra were much improved at 40–50 °C. This phenomenon was attributed to aggregation of the metalloporphyrins in solution. Nevertheless, the nickel(II) complexes gave good spectroscopic results and demonstrated isomeric purity by proton and carbon-13 NMR spectroscopy. For instance, nickel(II) complex **40b** of the 8-propyl analogue of DPEP showed a well resolved 400 MHz proton NMR spectrum at 40 °C (Fig. 1), although significant broadening is noted at 20 °C (Fig. 1, inset C). Three separate *meso*-protons resolve at 9.75 ppm, while the *meso*-linked CH_2 of the ethano unit gives a multiplet at 5.1 ppm and the three methyl groups give singlets near 3.5 ppm. Carbon-13 NMR spectroscopy has been shown to be a sensitive technique for characterizing porphyrin isomers, particularly in the *meso*-carbon region.[62] Three of the *meso*-carbon resonances for the 100 MHz carbon-13 NMR spectrum of **40b** show up between 96 and 98 ppm,

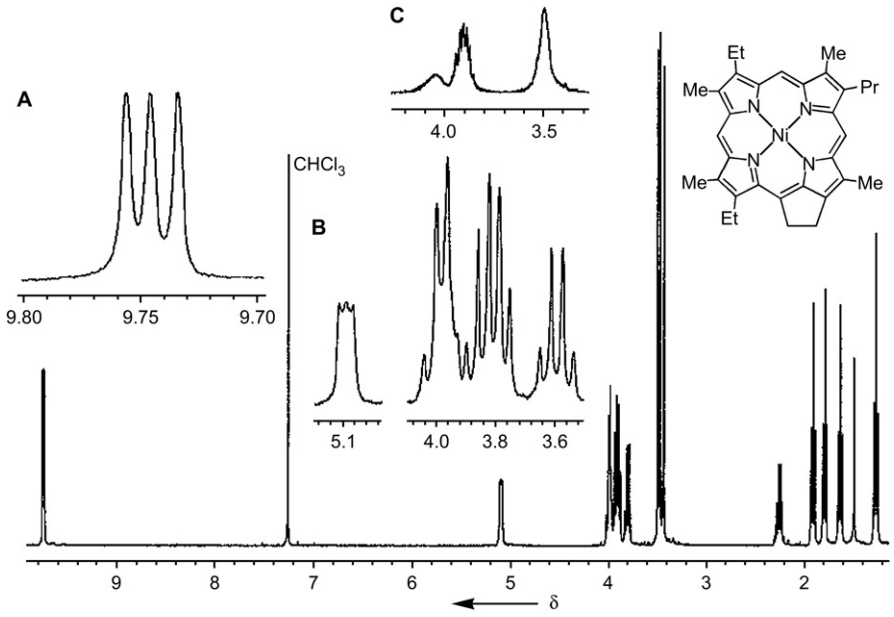


Figure 1. Proton NMR spectrum (400 MHz) of nickel porphyrin **40b** in $CDCl_3$ at 40 °C. Inset A shows the three singlets for the *meso*-protons at 9.7–9.8 ppm. Inset B shows an expansion of the methylene units directly connected to the porphyrin macrocycle. Inset C shows part of the same region for this sample at 20 °C illustrating poorer resolution due to aggregation.

while the fourth *meso*-carbon associated with the exocyclic ring is shifted downfield to 118 ppm (Fig. 2). The proton NMR data for the free base porphyrins are well resolved at room temperature and also confirm the identities of these structures. For example, the 8-isobutyl-12-ethylDPEP **18e** shows the expected *meso*-resonances at 9.98, 10.01, and 10.05 ppm, and the *meso*-CH_2 unit gives a multiplet at 5.45 ppm (Fig. 3). The internal NH resonances are strongly deshielded, and give two well separated resonances at −3.7 and −2.9 ppm. The well resolved NH resonances for DPEP-type porphyrins are typical for this system, but it is worth noting that this implies that NH exchange is slow at room temperature and that a single tautomer is favored for the free base system.

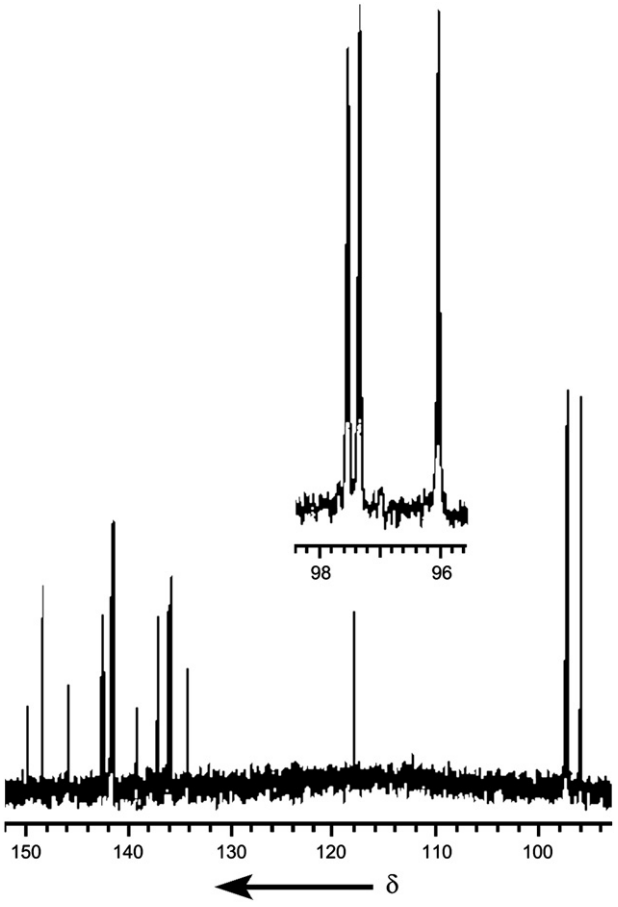


Figure 2. Downfield region of the 100 MHz carbon-13 NMR spectrum for nickel(II) porphyrin **40b** in $CDCl_3$ showing the aromatic region. Three unsubstituted *meso*-carbons are evident between 96 and 98 ppm.

When our initial low yielding synthesis of **18a** was completed,[58,63] the only known molecular fossils of the bacteriochlorophylls *d* were the carboxylic acids **1b–d**.[19] However, nickel(II) isobutylDPEP **35d** was subsequently identified in a marl from the evaporitic Mulhouse Basin (Oligocene) in Alsace, France.[64] Again this provided evidence for the existence of an anoxic photic zone that could allow the growth of obligate anaerobes. In another study, the iron porphyrin fraction of Kupferschiefer, an organic-rich sedimentary rock deposited in the Zechstein Sea (Permian, ca. 235 million years before present) was shown to contain three nonpolar bacteriopetroporphyrins **18a**, **18c**, and **18e**.[63,65] The NMR data for these molecular fossils of the *Chlorobium* chlorophylls were in good agreement with our synthetic samples. Again, these studies confirm that a photic anoxic zone existed in this ancient environment that allowed the growth of the Chlorobiaceae.[65,66]

3. Conclusions

By using a *b*-bilene route that mimics the beneficial results observed for the MacDonald condensation, a superior route to the major sedimentary porphyrin deoxophylloerythoetioporphyrin (DPEP) has been developed. This methodology works particularly well in the synthesis of DPEP ring

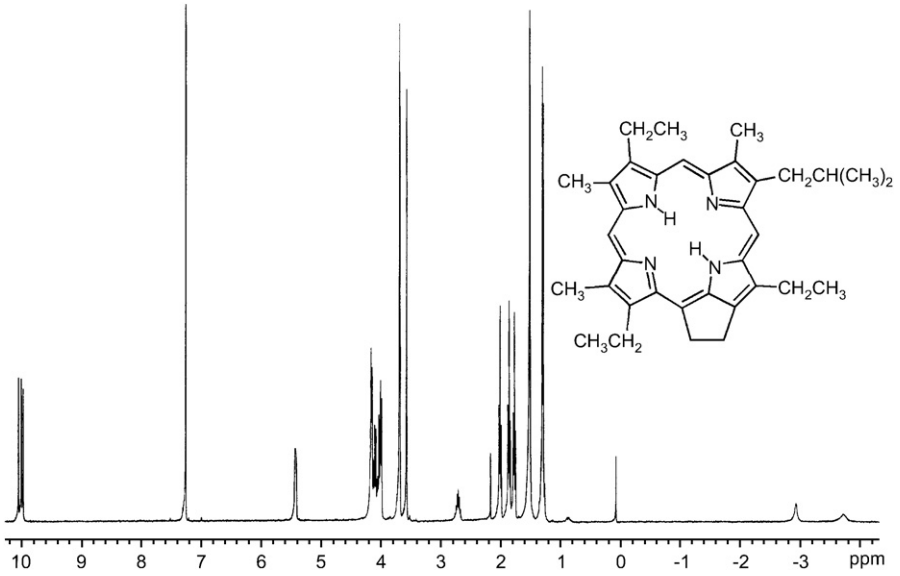


Figure 3. Proton NMR spectrum (400 MHz) of DPEP-type porphyrin **18e** in $CDCl_3$.

homologues with six-, seven- or eight-membered exocyclic rings, but tolerates the presence of the more demanding cyclopentene moiety. This approach has also been extended to the synthesis of five related nonpolar bacteriopetroporphyrins that derive from the photosynthetic pigments of the strictly anaerobic Chlorobiaceae. As etioporphyrins are formed as by-products in these procedures, the methodology only works when the nickel(II) porphyrins are sufficiently soluble to allow separation by flash chromatography. For this reason, the synthesis of the porphyric mineral abelsonite could not be accomplished by this approach. Nevertheless, the chemistry described in this paper can be applied to the synthesis of a wide range of porphyrin molecular fossils.

4. Experimental

4.1. General

Ethyl acetoacetate, *tert*-butyl acetoacetate, diethyl malonate, propanoyl chloride, butyryl chloride, isovaleryl chloride, benzyl alcohol, cyclopentanone, cyclohexanone, cycloheptanone, cyclooctanone, 3-nitro-2-pentanol, trimethyl orthoformate (SureSeal bottle), acetic anhydride, DMAP, *p*-toluenesulfonic acid, DDQ, lead tetraacetate, triethylamine, and K10 Montmorillonite clay were purchased from Aldrich or Acros, and were used without further purification. Chromatography was performed using grade III neutral alumina or 70–230 mesh silica gel. Melting points were determined in open capillary tubes on an Mel-Temp apparatus and are uncorrected. UV–vis absorption spectra were run on a Beckmann DU-40 spectrophotometer or a Varian Cary Spectrophotometer. Proton and carbon-13 NMR data were obtained on a Varian Gemini 300 or 400 MHz FT-NMR spectrometer. Mass spectral determinations were conducted at the Mass Spectral Laboratory, School of Chemical Sciences, University of Illinois at Urbana-Champaign, and elemental analyses were obtained from Micro-Analysis, Inc., Wilmington, DE, or the School of Chemical Sciences Microanalysis Laboratory at the University of Illinois.

4.2. Synthetic procedures

4.2.1. 2,4-Heptanedione (25b). Magnesium turnings (26.7 g), absolute ethanol (135 mL), and carbon tetrachloride (5 mL) were placed in a 2 L round-bottomed flask and gently heated until the evolution of hydrogen gas subsided. Dry benzene (200 mL) was added to the stirred mixture and heating was resumed until the gas evolution ceased completely (approx. 4 h). Dry ether (500 mL) was added to the cooled mixture, followed by the addition of *tert*-butyl acetoacetate (161 g), at such a rate as to maintain a gentle reflux. The reaction mixture was heated under reflux for an additional 30 min. The mixture was cooled to room temperature and treated with butyryl chloride (106.5 g) by slow addition. Once the reaction subsided, the mixture was refluxed for 1 h and allowed to stand overnight. The solution was cooled in an ice bath and treated with 5 M sulfuric acid (200 mL) and sufficient water to dissolve the precipitate. The organic layer was separated and the aqueous phase was further extracted with ether (3×50 mL). The combined organic extracts were washed with a saturated sodium chloride solution (3×200 mL) and dried over sodium sulfate. The solvents were removed under reduced pressure and the residual oil treated with *p*-toluenesulfonic acid (1.2 g) and heated at 150 °C until carbon dioxide evolution ceased (approx. 2 h). The product was distilled and collected as pale yellow oil (92.91 g; 73%), bp 158–171 °C; IR (neat): ν 1617 cm^{-1} (s, sh, C═O).

4.2.2. 6-Methyl-2,4-heptanedione (25c). The title diketone was prepared from *tert*-butyl acetoacetate (161 g) and isovaleryl chloride (120.5 g) by the procedure detailed above. The product was purified by distillation and collected as a pale yellow oil (78.9 g; 56%), bp 178–188 °C; IR (neat): ν 1615 cm^{-1} (s, sh, C═O).

4.2.3. 3-Methyl-2,4-heptanedione (26b). Anhydrous potassium carbonate (95 g) was added to a stirred mixture of 2,4-heptanedione (92.9 g) and iodomethane (127.0 g) in reagent grade acetone (140 mL). The mixture was stirred vigorously

under reflux at 80 °C overnight. The cooled mixture was filtered and the solid potassium carbonate was washed liberally with acetone. The solvent was removed under reduced pressure, and the residual oil purified by distillation to give the desired diketone as a pale yellow oil (75.9 g; 74%), bp 165–170 °C.

4.2.4. 3,6-Dimethyl-2,4-heptanedione (26c). The title diketone was prepared from 6-methyl-2,4-heptanedione **25c** (30.83 g) and iodomethane (47.44 g) by the procedure described above. The product was purified by distillation and collected as a yellow oil (25.59 g; 76%), bp 150–152 °C.

4.2.5. Ethyl 4,5-dimethyl-3-propylpyrrole-2-carboxylate (27b). A mixture of diethyl aminomalonate (89.34 g) and 3-methyl-2,4-heptanedione (72.34 g) was added in a steady stream to gently boiling glacial acetic acid (106 mL). After the evolution of carbon dioxide and ethanol had subsided, the reaction mixture was gently boiled for a further 3 h. The solution was diluted with ice water to fill the flask and the resulting precipitate filtered off and washed with a small amount of cold 60% ethanol–water. The product was recrystallized from 95% ethanol to give the title pyrrole (50.66 g; 47%) as a yellow powder, mp 101–102 °C (lit. mp[67] 100–102 °C); IR (Nujol mull): ν 3306 (s, sh, NH), 1656 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 0.94 (3H, t, J=7.3 Hz), 1.34 (3H, t, J=7.2 Hz), 1.46–1.56 (2H, m), 1.92 (3H, s), 2.18 (3H, s), 2.67 (2H, t, J=7.6 Hz), 4.29 (2H, q, J=7.6 Hz), 8.79 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.9, 11.6, 14.3, 14.7, 24.2, 27.5, 59.7, 116.6, 116.9, 129.7, 132.6, 161.9.

4.2.6. Ethyl 3-isobutyl-4,5-dimethylpyrrole-2-carboxylate (27c). The title pyrrole was prepared from 3,6-dimethyl-2,4-heptanedione (10.0 g) and diethyl aminomalonate (11.24 g) by the procedure described above. Recrystallization from 95% ethanol gave the pyrrole (4.76 g; 33%) as off-white crystals, mp 112.5–113.5 °C; IR (Nujol mull): ν 3297 (s, sh, NH), 1657 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 0.90 (6H, d, J=6.6 Hz), 1.34 (3H, t, J=7.1 Hz), 1.78–1.88 (1H, m), 1.90 (3H, s), 2.18 (3H, s), 2.56 (2H, d, J=7.2 Hz), 4.28 (2H, q, J=7.1 Hz), 8.96 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.3, 11.6, 14.7, 22.7, 30.3, 34.5, 59.7, 116.9, 117.3, 129.8, 131.8, 162.0. Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.91; H, 9.74; N, 6.41.

4.2.7. Benzyl 4,5-dimethyl-3-propylpyrrole-2-carboxylate (28b). In a 50 mL Erlenmeyer flask, a mixture of ethyl 4,5-dimethyl-3-propylpyrrole-2-carboxylate (**27b**; 4.50 g) and benzyl alcohol (13 mL) (freshly distilled from potassium carbonate) was stirred and heated on an oil bath. A thermometer was placed near the neck of the flask to measure the vapor temperature. A fresh solution of sodium benzyloxide was prepared by dissolving two pellets of sodium metal in benzyl alcohol (20 mL). The catalyst was added in small portions to the heated mixture, while the temperature of the oil bath was allowed to gradually rise. The catalyst was added periodically until the vapor temperature reached 200 °C (at this point, the temperature of the oil bath was approx. 240 °C). The reaction was immediately quenched by the cautious addition of the hot mixture to a stirred solution of ice cold methanol (34 mL) in water (24 mL) and acetic acid (0.4 mL). The mixture was cooled in an ice bath and the resulting precipitate filtered. The solids were washed with 50% aqueous methanol and then water. Recrystallization from ethanol afforded the transesterified pyrrole (4.93 g; 85%) as fluffy white crystals, mp 84–85 °C; IR (Nujol mull): ν 3300 (s, sh, NH), 1666 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 0.88 (3H, t, J=7.3 Hz), 1.46–1.54 (2H, m), 1.91 (3H, s), 2.15 (3H, s), 2.67 (2H, t), 5.28 (2H, s), 7.30–7.41 (5H, m), 9.05 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.9, 11.6, 14.3, 24.3, 27.5, 65.7, 116.1, 117.0, 128.1, 128.2, 128.6, 130.4, 133.1, 136.8, 161.6. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16. Found: C, 75.05; H, 7.64; N, 5.06.

4.2.8. Benzyl 3-isobutyl-4,5-dimethylpyrrole-2-carboxylate (28c). The title pyrrole was prepared from ethyl 3-isobutyl-4,5-dimethylpyrrole-2-carboxylate (**27c**; 21.42 g) and benzyl alcohol (57.7 mL) by the previously described method. Recrystallization from absolute ethanol gave the desired pyrrole (17.96 g; 66%) as fluffy off-white crystals, mp 103–103.5 °C; IR (Nujol mull): ν 3309 (s, sh, NH), 1673 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 0.82 (6H, d, J=6.8 Hz), 1.75–1.82 (1H, m), 1.89 (3H, s), 2.15 (3H, s), 2.55 (2H, d, J=7.8 Hz), 5.26 (2H, s), 7.29–7.41 (5H, m), 9.13 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.3, 11.6, 22.6, 30.3, 34.4, 65.7, 116.5, 117.4, 128.2, 128.5, 128.6, 130.4, 132.3, 136.7, 161.7. Anal. Calcd for $C_{18}H_{23}NO_2 \cdot 1/5H_2O$: C, 74.81; H, 8.16; N, 4.85. Found: C, 75.09; H, 7.88; N, 4.75.

4.2.9. Benzyl 3-ethyl-4,5-dimethylpyrrole-2-carboxylate (28a). The benzyl ester was prepared from ethyl 3-ethyl-4,5-dimethylpyrrole-2-carboxylate[46a] (**27a**; 5.00 g) and benzyl alcohol (15 mL) by the previously described method. Recrystallization from ethanol gave the title compound (5.40 g; 82%) as fluffy white crystals, mp 87.5–89 °C (lit. mp[68] 88–90 °C); IR (Nujol mull): ν 3308 (s, sh, NH), 1657 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 1.10 (3H, t, J=7 Hz), 1.93 (3H, s), 2.17 (3H, s), 2.74 (2H, q, J=7 Hz), 5.29 (2H, s), 7.32–7.43 (5H, m), 8.66 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.7, 11.6, 15.3, 18.7, 65.6, 115.8, 116.7, 128.3, 128.5, 128.7, 130.2, 134.8, 136.9, 161.3.

4.2.10. Benzyl 3-ethylcyclopenta[*b*]pyrrole-2-carboxylate (5b). The title pyrrole was synthesized from ethyl 3-ethylcyclopenta[*b*]pyrrole-2-carboxylate[34] (4.20 g) and benzyl alcohol (12 mL) by the procedure described above. The product was recrystallized from ethanol to afford the benzyl ester (4.30 g; 79%) as off-white crystals, mp 91.5–92.5 °C; IR (Nujol mull): ν 3316 (s, sh, NH), 1668 cm^{-1} (s, sh, C═O); ^1H NMR ($CDCl_3$): δ 1.14 (3H, t, J=7.5 Hz), 2.33–2.43 (2H, m), 2.56–2.67 (4H, m), 2.77 (2H, q, J=7.5 Hz), 5.26 (2H, s), 7.29–7.39 (5H, m), 8.59 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 14.7, 19.9, 24.7, 25.3, 29.1, 65.5, 120.6, 128.2, 128.7, 129.5, 130.8, 136.9, 142.1, 161.5. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.85; H, 7.23; N, 5.30.

4.2.11. Benzyl 5-acetoxymethyl-3-ethyl-4-methylpyrrole-2-carboxylate (29a). Lead tetraacetate (9.03 g) was added in several portions to a stirred solution of benzyl 3-ethyl-4,5-dimethylpyrrole-2-carboxylate (**28a**; 5.00 g) in glacial acetic acid (80 mL) and acetic anhydride (4 mL). The mixture was stirred for 3 h and poured into ice water

(250 mL). After 3 h, the resulting precipitate was filtered off and washed well with water. The vacuum dried product was recrystallized from chloroform–hexane to give the acetoxymethylpyrrole (5.15 g; 84%) as fluffy white crystals, mp 113–114 °C (lit. mp[68] 111–112 °C); IR (Nujol mull): ν 3328 (s, sh, NH), 1736 (s, sh, acetoxy C=O), 1662 cm^{-1} (pyrrole ester C=O); ^1H NMR ($CDCl_3$): δ 1.09 (3H, t, J=7.5 Hz), 2.03 (3H, s), 2.07 (3H, s), 2.74 (2H, q, J=7.5 Hz), 5.01 (2H, s), 5.31 (2H, s), 7.32–7.43 (5H, m), 8.98 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.6, 15.2, 18.5, 21.1, 57.2, 66.0, 118.4, 119.7, 127.5, 128.3, 128.7, 128.9, 133.9, 136.6, 161.2, 171.7.

4.2.12. Benzyl 5-acetoxymethyl-4-methyl-3-propylpyrrole-2-carboxylate (29b). Lead tetraacetate (17.18 g) was added in several portions to a stirred solution of benzyl 4,5-dimethyl-3-propylpyrrole-2-carboxylate (**28b**; 10.00 g) in glacial acetic acid (82 mL) and acetic anhydride (4 mL). The mixture was stirred for 3 h and poured into ice water (250 mL). After 3 h, the resulting precipitate was filtered off, washed well with water, and dried in vacuo overnight. Recrystallization from chloroform–hexane gave the desired pyrrole (10.29 g; 85%) as fluffy white crystals, mp 97–98 °C; IR (Nujol mull): ν 3299 (s, sh, NH), 1731 (s, sh, acetoxy C=O), 1668 cm^{-1} (s, sh, pyrrole C=O); ^1H NMR ($CDCl_3$): δ 1.00 (3H, t, J=7.4 Hz), 1.61 (2H, sextet), 2.14 (3H, s), 2.18 (3H, s), 2.79 (2H, t, J=7.5 Hz), 5.13 (2H, s), 5.41 (2H, s), 7.44–7.54 (5H, m), 9.22 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.8, 14.3, 21.1, 24.2, 27.3, 57.2, 66.0, 118.7, 120.1, 127.5, 128.3, 128.7, 132.3, 136.4, 161.3, 171.7. Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 68.96; H, 6.90; N, 4.13.

4.2.13. Benzyl 5-acetoxymethyl-3-isobutyl-4-methylpyrrole-2-carboxylate (29c). The title pyrrole was prepared from **28c** (10.00 g) and lead tetraacetate (16.35 g) by the procedure previously described for **29a**. Recrystallization from chloroform–hexanes afforded the acetoxymethylpyrrole (9.57 g; 80%) as fluffy white crystals, mp 129–130 °C; IR (Nujol mull): ν 3304 (s, sh, NH), 1732 (s, sh, acetoxy C=O), 1668 cm^{-1} (s, sh, pyrrole C=O); ^1H NMR ($CDCl_3$): δ 0.84 (6H, d, J=6.7 Hz), 1.74–1.88 (1H, m), 2.01 (3H, s), 2.07 (3H, s), 2.57 (2H, d, J=7.4 Hz), 5.02 (2H, s), 5.29 (2H, s), 7.31–7.44 (5H, m), 9.09 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.2, 21.1, 22.6, 30.2, 34.1, 57.3, 66.1, 119.1, 120.5, 127.4, 128.4, 128.6, 128.7, 131.5, 136.4, 161.2, 171.7. Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.74; H, 7.50; N, 4.24.

4.2.14. Benzyl 6-acetoxy-3-ethylcyclopenta[*b*]pyrrole-2-carboxylate (6b). Lead tetraacetate (0.865 g) was added in several portions to a stirred solution of benzyl 3-ethylcyclopenta[*b*]pyrrole-2-carboxylate (**5b**; 0.50 g) in acetic acid (10 mL) and acetic anhydride (0.5 mL) and the resulting mixture was stirred for an additional 2 h. The mixture was diluted with dichloromethane and washed with water, 5% aqueous sodium bicarbonate solution, and water. The solution was dried over sodium sulfate and evaporated under reduced pressure to give the crude acetoxy derivative as a yellow oil that solidified on standing. The solid was recrystallized from hexanes to give **6b** (0.38 g; 63%) as a yellow powder, mp 103–105 °C; IR (Nujol mull): ν 3296 (NH str), 1725, 1667 cm^{-1} (s, sh, C=O); ^1H NMR ($CDCl_3$): δ 1.15 (3H, t, J=7.5 Hz), 2.03 (3H, s), 2.44–2.61 (2H, m), 2.72–2.83 (4H, m), 5.23–5.34 (2H, AB quartet), 5.68 (1H, d, J=6.5 Hz), 7.28–7.42 (5H, m), 8.91 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 14.6, 19.7, 21.3, 22.9, 35.6, 65.9, 72.4, 122.9, 128.3, 128.4, 128.5, 128.7, 129.6, 131.8, 136.6, 138.3, 161.3, 172.4. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.99; H, 6.25; N, 4.37.

4.2.15. *tert*-Butyl 4-ethyl-3-methylpyrrole-2-carboxylate (21a). A solution of 3-nitro-2-pentanol (5.00 g), acetic anhydride (8.0 g), and DMAP (200 mg) in methylene chloride (25 mL) was stirred at room temperature overnight. Methanol (25 mL) was then added to destroy the excess acetic anhydride. After stirring for an additional 1 h, the solution was carefully poured into a dilute aqueous sodium bicarbonate solution (11 g in 60 mL of water) and extracted with methylene chloride. The combined organic extracts were dried over sodium sulfate and filtered through a short silica column. The solvent was evaporated to afford the corresponding acetoxynitroalkane as a clear yellow liquid. A solution of *tert*-butyl isocyanoacetate (2.00 g) and DBU (4.51 g) in a 50:50 v/v mixture of THF–2-propanol (38 mL) was added in portions to a stirred solution of the acetoxynitroalkane (2.53 g) in the same THF–2-propanol solvent mixture (13 mL), keeping the temperature at 20–30 °C throughout the addition. The resulting solution was stirred for 24 h at room temperature. The solvent was removed under reduced pressure and the residue diluted with warm water (10 mL). Diethyl ether (10 mL) was added to the two-phase mixture. The aqueous layer was drawn off and extracted with ether (2×20 mL). The combined organic extracts were washed with 10% hydrochloric acid (2×10 mL) and dried over magnesium sulfate. The ether was removed under reduced pressure and the residue was chromatographed on silica, eluting with dichloromethane. Recrystallization from methanol gave the α-free pyrrole (1.78 g, 60%) as pale yellow crystals, mp 99–100 °C (lit. mp[69] 100–101 °C); ^1H NMR ($CDCl_3$): δ 1.18 (3H, t, J=7.5 Hz), 1.59 (9H, s), 2.28 (3H, s), 2.44 (2H, q, J=7.5 Hz), 6.64 (1H, d), 8.96 (1H, s, NH); ^{13}C NMR ($CDCl_3$): δ 10.4, 14.8, 18.4, 28.7, 80.5, 118.6, 120.8, 125.0, 127.5, 161.7.

4.2.16. Benzyl 6-(5-*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-ethylcyclopenta[*b*]pyrrole-2-carboxylate (37b). Lead tetraacetate (3.46 g) was added in several portions to a stirred solution of **5b** (2.00 g) in acetic acid (38 mL) and acetic anhydride (2 mL) and the resulting mixture was stirred for an additional 2 h. The mixture was diluted with dichloromethane and washed with water, 5% sodium bicarbonate solution, and water. The solution was dried over sodium sulfate and evaporated under reduced pressure to give the crude acetoxy derivative as a yellow oil that solidified on standing. The residue and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (1.48 g) were dissolved in glacial acetic acid (52 mL). *p*-Toluenesulfonic acid (85 mg) was added and the resulting mixture stirred at room temperature for 2 h. The dark solution was diluted with chloroform, washed with water (240 mL), and the aqueous solutions back-extracted with chloroform. The combined organic phases were washed with 10% sodium bicarbonate solution and evaporated under reduced pressure. The dark residue was chromatographed on silica, eluting with dichloromethane. Recrystallization from ethanol gave

the dipyrrole (2.99 g; 85%) as an off-white solid, mp 150–151 °C; IR (Nujol mull): ν 3300 (s, sh, NH), 1652 cm^{-1} (s, sh, C=O); ^1H NMR ($CDCl_3$): δ 1.07 (3H, t, J=7.5 Hz), 1.20 (3H, t, J=7.5 Hz), 1.54 (9H, s), 2.25 (3H, s), 2.25–2.34 (1H, m), 2.41 (2H, q, J=7.5 Hz), 2.60–2.79 (3H, m), 2.83 (2H, q, J=7.5 Hz), 4.32 (1H, t), 5.21–5.33 (2H, AB quartet), 7.30–7.42 (5H, m), 8.24 (1H, br s), 8.49 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.6, 14.7, 16.3, 17.3, 19.8, 24.1, 28.7, 35.8, 39.4, 65.7, 80.5, 119.2, 121.9, 123.9, 125.7, 128.2, 128.3, 128.7, 130.2, 130.7, 133.3, 136.6, 140.4, 161.3, 161.7. Anal. Calcd for $C_{29}H_{36}N_2O_4$: C, 73.08; H, 7.61; N, 5.88. Found: C, 73.21; H, 8.01; N, 5.77.

4.2.17. Benzyl 7-(*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydroindole-2-carboxylate (22a). Lead tetraacetate (0.91 g) was added in several portions to a stirred solution of benzyl 3-methyl-4,5,6,7-tetrahydroindole-2-carboxylate[31] (**19a**; 0.500 g) in acetic acid (10 mL) and acetic anhydride (0.5 mL) and the resulting mixture was stirred for a further 2 h at room temperature. The solution was diluted with dichloromethane and washed with water and the aqueous layer back-extracted with dichloromethane. The combined organic layers were washed with saturated sodium bicarbonate solution and then with water. The solution was dried over sodium sulfate and evaporated under reduced pressure to give the crude acetoxy derivative **20a** as a pale yellow solid. The residue and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (0.32 g) were dissolved in glacial acetic acid (17 mL). *p*-Toluenesulfonic acid (0.12 g) was added and the resulting mixture was stirred for 2.5 h at room temperature. The dark green mixture was diluted with chloroform, washed with water, and the aqueous solution was back-extracted with chloroform. The combined organic phases were washed with saturated sodium bicarbonate solution (35 mL) and evaporated under reduced pressure. The residue was chromatographed on silica, eluting with dichloromethane. The residue was further purified by chromatography on silica gel, eluting with petroleum ether, followed by gradually increasing proportions of an ethyl acetate–petroleum ether mixture. A pale yellow solid (0.65 g; 88%) was obtained, mp 159–161.5 °C. An analytical sample was obtained by recrystallization from ethanol as white crystals, mp 164.5–166 °C; ^1H NMR ($CDCl_3$): δ 1.09 (3H, t, J=7.6 Hz), 1.54 (9H, s), 1.69–1.81 (2H, m), 1.91–1.98 (1H, m), 2.07–2.14 (1H, m), 2.26 (3H, s), 2.27 (3H, s), 2.41 (2H, q, J=7.3 Hz), 2.45–2.49 (2H, m), 4.06 (1H, t, J=6.4 Hz), 5.21–5.33 (2H, AB quartet, J=12.4 Hz), 7.29–7.41 (5H, m), 8.29 (1H, br s), 8.33 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.6, 10.7, 16.2, 17.4, 21.2, 22.5, 28.7, 31.9, 32.6, 65.7, 80.6, 118.3, 119.6, 121.2, 124.3, 125.6, 126.3, 128.2 (2), 128.7, 131.9, 132.8, 136.8, 161.6. Anal. Calcd for $C_{29}H_{36}N_2O_4$: C, 73.08; H, 7.61; N, 5.88. Found: C, 73.04; H, 7.75; N, 5.79.

4.2.18. Benzyl 8-(*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclohepta[*b*]pyrrole-2-carboxylate (22b). The title compound was prepared from benzyl 8-acetoxy-3-methylcyclohepta[*b*]pyrrole-2-carboxylate[32] (**20b**; 1.20 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (0.74 g) by the procedure described above. The product was chromatographed on silica, eluting with a gradient of 0–80% methylene chloride and hexane to give a pale yellow powder (1.05 g; 61%). An analytical sample was obtained by recrystallization from ethanol as white crystals, mp 113.5–115 °C; ^1H NMR ($CDCl_3$): δ 1.03 (3H, t, J=7.4 Hz), 1.50–1.61 (1H, m), 1.55 (9H, s), 1.68–1.76 (1H, m), 1.79–1.88 (1H, m), 1.88–2.03 (3H, m), 2.27 (6H, s), 2.37 (2H, q, J=7.4 Hz), 2.45–2.52 (1H, ddd, J=2.4, 10.2, 15.4 Hz), 2.64–2.71 (1H, ddd, J=2.4, 8, 15.6 Hz), 4.10 (1H, m), 5.20–5.27 (2H, AB quartet, J=12.6 Hz), 7.27–7.36 (5H, m), 8.13 (1H, br s), 8.36 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.7, 15.7, 17.5, 25.1, 28.4, 28.7, 30.0, 34.0, 37.8, 65.6, 80.6, 116.2, 119.7, 123.7, 123.9, 126.2, 127.6, 128.0, 128.1, 128.7, 131.4, 135.7, 136.8, 149.9, 161.4 (2). Anal. Calcd for $C_{30}H_{38}N_2O_4$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.17; H, 7.81; N, 5.76.

4.2.19. Benzyl 9-(*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcycloocta[*b*]pyrrole-2-carboxylate (22c). Dipyrrole **22c** was synthesized from benzyl 3-methylcycloocta[*b*]pyrrole-2-carboxylate[32] (**19**; 3.00 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (2.12 g) by the method previously described for **22a**. The crude product was chromatographed on silica eluting with gradient of 0–80% dichloromethane and hexane to give the title dipyrrole (3.51 g; 69%) as yellow crystals. An analytical sample was obtained by recrystallization from hexane as white needles, mp 118–120 °C; ^1H NMR ($CDCl_3$): δ 0.86 (3H, t, J=7.6 Hz), 1.42–1.52 (4H, m), 1.53–1.60 (1H, m), 1.58 (9H, s), 1.61–1.68 (1H, m), 1.90–2.04 (2H, m), 2.18–2.31 (2H, m), 2.24 (3H, s), 2.26 (3H, s), 2.48–2.55 (1H, m), 2.72–2.78 (1H, m), 4.23 (1H, dd, J=4.2, 12.2 Hz), 5.25 (2H, s), 7.28–7.40 (5H, m), 8.10 (1H, br s), 8.63 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.6 (2), 15.2, 17.5, 22.7, 25.6, 25.7, 28.8, 30.1, 34.2, 34.4, 65.6, 80.7, 117.4, 119.5, 122.0, 124.2, 126.4, 126.9, 128.1, 128.2, 128.7, 132.0, 134.9, 136.9, 161.6, 161.7. Anal. Calcd for $C_{31}H_{40}N_2O_4$: C, 73.78; H, 7.99; N, 5.55. Found: C, 73.87; H, 7.72; N, 5.89.

4.2.20. Benzyl 5′-*tert*-butoxycarbonyl-3′,4-diethyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carboxylate (30a). Benzyl 5-acetoxymethyl-3-ethyl-4-methylpyrrole-2-carboxylate (**29a**; 3.00 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (1.99 g) were dissolved in dichloromethane (200 mL). After the pyrroles had completely dissolved, Montmorillonite clay (13.6 g) was added to the stirred solution. The mixture was stirred at room temperature while monitoring the reaction's progress by thin layer chromatography. The reaction was usually complete after 1 h. The catalyst clay was filtered off, washed with dichloromethane, and the excess solvent removed under reduced pressure to give the desired dipyrrylmethane (4.42 g; quantitative) as an orange gum which could not be induced to crystallize. ^1H NMR ($CDCl_3$): δ 1.02 (3H, t, J=7.5 Hz), 1.06 (3H, t, J=7.5 Hz), 1.53 (9H, s), 1.98 (3H, s), 2.25 (3H, s), 2.40 (2H, q, J=7.5 Hz), 2.73 (2H, q, J=7.5 Hz), 3.83 (2H, s), 5.29 (2H, s), 7.26–7.35 (5H, m), 9.29 (1H, s), 9.31 (1H, s); ^{13}C NMR ($CDCl_3$): δ 8.7, 10.7, 15.3, 15.5, 17.4, 18.8, 23.1, 28.7, 53.6, 65.9, 80.7, 116.8, 119.2, 124.0, 126.2, 128.0, 128.1, 128.6, 130.7, 134.8, 136.4, 162.0 (2).

4.2.21. Benzyl 5′-*tert*-butoxycarbonyl-3′-ethyl-3,4′-dimethyl-3-propyl-2,2′-dipyrrylmethane-5-carboxylate (30b). The title dipyrrole was synthesized from benzyl 5-acetoxymethyl-4-methyl-3-propylpyrrole-2-carboxylate (**29b**;

3.00 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (1.91 g) using Montmorillonite clay catalyst (13.0 g) by the procedure detailed above. The dipyrrylmethane was obtained as an orange gum (4.36 g) in quantitative yield, but could not be induced to crystallize. ^{1}H NMR ($CDCl_3$): δ 0.87 (3H, t, J=7.3 Hz), 1.03 (3H, t, J=7.5 Hz), 1.46–1.58 (2H, m), 1.54 (9H, s), 1.99 (3H, s), 2.26 (3H, s), 2.40 (2H, q, J=7.5 Hz), 2.67 (2H, t, J=7.7 Hz), 3.86 (2H, s), 5.27 (2H, s), 7.3–7.4 (5H, s), 8.68 (1H, br s), 8.92 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.0, 10.7, 14.3, 15.6, 17.4, 23.3, 24.2, 27.5, 28.7, 66.0, 80.5, 117.3, 119.4, 124.2, 126.2, 128.0, 128.2, 128.7, 130.2, 133.3, 136.5, 161.5, 161.7.

4.2.22. Benzyl 5′-*tert*-butoxycarbonyl-3′-ethyl-4-isobutyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carboxylate (30c). The title dipyrrole was prepared from the clay catalyzed condensation of benzyl 5-acetoxymethyl-3-isobutyl-4-methylpyrrole-2-carboxylate (**29c**; 3.00 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (1.83 g) in the presence of Montmorillonite clay (12.5 g) by the procedure described above for **30a**. The dipyrrole was obtained in quantitative yield as an orange gum (4.30 g) that could not be induced to crystallize. ^{1}H NMR ($CDCl_3$): δ 0.81 (6H, d, J=6.6 Hz), 1.01 (3H, t, J=7.5 Hz), 1.53 (9H, s), 1.73–1.84 (1H, m), 1.96 (3H, s), 2.24 (3H, s), 2.39 (2H, q, J=7.5 Hz), 2.55 (2H, d, J=7.2 Hz), 3.84 (2H, s), 5.25 (2H, s), 7.30–7.40 (5H, m), 8.81 (1H, br s), 8.89 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.3, 10.7, 15.7, 17.4, 22.6, 23.2, 28.7, 30.3, 34.4, 66.1, 80.6, 117.5, 119.2, 124.0, 126.2, 128.2, 128.4, 128.6, 128.8, 130.7, 132.5, 136.4, 162.0 (2).

4.2.23. Benzyl 5′-*tert*-butoxycarbonyl-4-ethyl-3,3′,4′-trimethyl-2,2′-dipyrrylmethane-5-carboxylate (30d). The title dipyrrole was prepared from the clay catalyzed condensation of benzyl 5-acetoxymethyl-3-ethyl-4-methylpyrrole-2-carboxylate (**29a**; 1.00 g) and *tert*-butyl 3,4-dimethylpyrrole-2-carboxylate[69] (0.62 g) in the presence of Montmorillonite clay (4.2 g) by the procedure described above for **30a**. The dipyrrole was obtained as an orange gum (1.29 g; 90%) that could not be induced to crystallize. ^{1}H NMR ($CDCl_3$): δ 1.07 (3H, t, J=7.4 Hz), 1.51 (9H, s), 1.93 (3H, s), 1.96 (3H, s), 2.21 (3H, s), 2.71 (2H, q, J=7.6 Hz), 3.80 (2H, s), 5.26 (2H, s), 7.28–7.33 (5H, m), 9.02 (1H, br s), 9.18 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.8, 9.1, 10.9, 15.4, 18.8, 23.3, 28.7, 65.9, 80.6, 116.8, 117.3, 119.1, 126.8, 128.1, 128.2, 128.7, 128.8, 130.5, 134.8, 136.6, 161.8.

4.2.24. 6-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-ethylcyclopenta[*b*]pyrrole-2-carboxylic acid (38b). Benzyl 6-(5-*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-ethylcyclopenta[*b*]pyrrole-2-carboxylate (**37b**; 3.00 g) was taken up in ethanol (200 mL) and shaken with triethylamine (30 drops) and 10% palladium–charcoal (0.20 g) under an atmosphere of hydrogen at room temperature and 40 psi overnight. The catalyst was filtered off and the solution removed under reduced pressure. The residue was taken up in 5% ammonia solution and cooled to 0 °C. Acidification with glacial acetic acid, maintaining the temperature below 5 °C, gave a precipitate that was washed well with water and dried in vacuo. The title compound was obtained as an off-white powder (2.40 g; 99%), mp 105–114 °C, dec; IR (Nujol mull): ν 1654 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 1.07 (3H, t, J=7.5 Hz), 1.20 (3H, t, J=7.5 Hz), 1.53 (9H, s), 2.24 (3H, s), 2.40 (2H, q, J=7.5 Hz), 2.60–2.70 (4H, m), 2.84 (2H, q, J=7.5 Hz), 4.34 (1H, t, J=7.5 Hz), 8.47 (1H, br s), 8.74 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.5, 14.5, 16.1, 17.2, 19.7, 24.1, 28.7, 36.0, 39.2, 80.7, 119.4, 122.0, 124.1, 126.1, 130.5, 131.8, 133.4, 141.4, 162.0, 165.8. Anal. Calcd for $C_{22}H_{30}N_2O_4$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.41; H, 8.08; N, 7.14.

4.2.25. 7-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydroindole-2-carboxylic acid (23a). The title dipyrrole carboxylic acid was prepared from benzyl ester **22a** (1.00 g) by the same method used for preparing **38b**. The product (0.77 g; 93%) was obtained as an off-white solid, mp 134–160 °C, dec; ^{1}H NMR ($CDCl_3$): δ 1.08 (3H, t, J=7.5 Hz), 1.54 (9H, s), 1.72–1.79 (2H, m), 1.97–2.02 (1H, m), 2.07–2.12 (1H, m), 2.23 (3H, s), 2.25 (3H, s), 2.40 (2H, q, J=7.5 Hz), 2.44–2.51 (2H, m), 4.02–4.07 (1H, m), 8.27 (1H, br s), 8.76 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.4, 10.6, 16.2, 17.3, 21.1, 22.8, 28.7, 31.9, 32.9, 80.9, 117.7, 119.8, 121.4, 124.6, 126.0, 128.2, 133.0, 133.2, 162.3, 165.9. Anal. Calcd for $C_{22}H_{30}N_2O_4$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.13; H, 7.82; N, 7.47.

4.2.26. 8-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-cyclohepta[*b*]pyrrole-2-carboxylic acid (23b). The title dipyrrolic carboxylic acid was prepared from benzyl ester **22b** (1.00 g) as described for **38b**. The desired product (0.79 g; 95%) was obtained as a pale pink solid, mp 103–140 °C, dec; ^{1}H NMR ($CDCl_3$): δ 1.03 (3H, t, J=7.4 Hz), 1.56 (9H, s), 1.50–2.04 (6H, m), 2.18 (3H, s), 2.28 (3H, s), 2.38 (2H, q, J=7.6 Hz), 2.35–2.43 (1H, m), 2.67–2.75 (1H, m), 4.07 (1H, dd, J=2.2, 10.4 Hz), 8.11 (1H, br s), 9.68 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.5, 10.8, 15.9, 17.5, 25.2, 28.1, 28.8, 30.8, 34.8, 37.8, 81.2, 115.2, 119.9, 123.8, 124.1, 126.2, 129.4, 132.8, 136.7, 162.7, 164.8. Anal. Calcd for $C_{23}H_{32}N_2O_4$: C, 68.97; H, 8.05; N, 6.99. Found: C, 68.63; H, 8.09; N, 6.88.

4.2.27. 9-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-cycloocta[*b*]pyrrole-2-carboxylic acid (23c). The title carboxylic acid (0.78 g; 93%) was similarly obtained from **22c** (1.00 g) as a pale pink solid, mp 194–196 °C; ^{1}H NMR ($CDCl_3$): δ 0.85 (3H, t, J=7.5 Hz), 1.4–1.5 (2H, m), 1.58 (9H, s), 1.50–1.64 (1H, m), 1.74–1.80 (1H, m), 1.94–1.99 (2H, m), 2.23 (3H, s), 2.26 (3H, s), 2.22–2.26 (2H, m), 2.47–2.53 (1H, m), 2.73–2.78 (1H, m), 4.26 (1H, dd, J=4, 10.8 Hz), 8.44 (1H, br s), 9.19 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 10.4, 10.7, 15.3, 17.5, 22.9, 25.6, 25.9, 28.8, 30.4, 34.1, 34.3, 80.9, 116.8, 119.5, 122.5, 124.2, 126.5, 128.6, 132.5, 136.1, 162.2, 165.8. Anal. Calcd for $C_{24}H_{34}N_2O_4$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.68; H, 7.91; N, 6.62.

4.2.28. 5′-*tert*-Butoxycarbonyl-3′,4-diethyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carboxylic acid (31a). The title dipyrrole carboxylic acid was prepared from the hydrogenolysis of **30a** (5.77 g) over 10% palladium–charcoal (0.57 g) using the method described above. The dipyrrylmethane carboxylic acid (4.19 g; 90%) was obtained as a pale pink powder, mp 100–118 °C, dec; IR (Nujol mull): ν 1658 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 1.08–1.18 (6H, two overlapping triplets), 1.59 (9H, s), 2.07 (3H, s),

2.26 (3H, s), 2.58 (2H, q, J=7.5 Hz), 2.80 (2H, q, J=7.5 Hz), 3.88 (2H, s), 10.96 (1H, br s), 11.52 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.0, 11.2, 15.4, 16.2, 17.6, 18.8, 22.7, 25.7, 81.7, 116.4, 117.0, 119.5, 123.5, 126.3, 130.9, 132.5, 135.1, 163.8, 166.3. Anal. Calcd for $C_{21}H_{30}N_2O_4$: C, 67.35; H, 8.07; N, 7.48. Found: C, 67.03; H, 8.22; N, 7.64.

4.2.29. 5′-*tert*-Butoxycarbonyl-3′-ethyl-3,4′-dimethyl-4-propyl-2,2′-dipyrrylmethane-5-carboxylic acid (31b). The dipyrrole carboxylic acid was synthesized from **30b** (3.67 g) and 10% palladium–charcoal (0.35 g) by the preceding method. The title carboxylic acid (2.42 g; 81%) was isolated as a pale pink powder, mp 95–110 °C, dec; IR (Nujol mull): ν 1657 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 0.94 (3H, t, J=7.2 Hz), 1.09 (3H, t, J=7.4 Hz), 1.54 (9H, s), 1.5–1.6 (2H, m), 2.01 (3H, s), 2.22 (3H, s), 2.53 (2H, q, J=7.5 Hz), 2.71 (2H, t, J=7.4 Hz), 3.85 (2H, s), 10.91 (1H, br s), 11.07 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.2, 11.1, 14.3, 16.0, 17.6, 22.8, 24.2, 27.5, 28.7, 81.4, 116.9, 117.5, 119.4, 123.5, 126.2, 130.7, 132.3, 133.6, 163.4, 166.3. Anal. Calcd for $C_{22}H_{32}N_2O_4$: C, 68.01; H, 8.30; N, 7.21. Found: C, 68.47; H, 8.17; N, 6.70.

4.2.30. 5′-*tert*-Butoxycarbonyl-3′-ethyl-4-isobutyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carboxylic acid (31c). The title dipyrrylmethane carboxylic acid was synthesized from **30c** (1.30 g) and 10% palladium–charcoal (0.12 g) using the procedure detailed above. The product (0.904 g, 85%) was obtained as a pale pink powder, mp 129–151 °C, dec; IR (Nujol mull): ν 1657 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 0.91 (6H, d, J=6.8 Hz), 1.09 (3H, t, J=7.4 Hz), 1.55 (9H, s), 1.87 (1H, nonet, J=6.7 Hz), 2.01 (3H, s), 2.22 (3H, s), 2.53 (2H, q, J=7.5 Hz), 2.61 (2H, d, J=7 Hz), 3.86 (2H, s), 10.92 (1H, br s), 11.27 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.6, 11.1, 16.1, 17.6, 22.8, 28.7, 30.4, 34.5, 81.5, 117.3, 117.9, 119.5, 123.6, 126.3, 130.9, 132.2, 132.8, 163.7, 166.3. Anal. Calcd for $C_{23}H_{34}N_2O_4$: C, 68.63; H, 8.51; N, 6.96. Found: C, 68.85; H, 8.40; N, 6.47.

4.2.31. 5′-*tert*-Butoxycarbonyl-3′,4-diethyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carbaldehyde (24a). A solution of dipyrrylmethane-5-carboxylic acid **31a** (2.00 g) in dichloromethane (120 mL) was stirred with *p*-toluenesulfonic acid (2.32 g) in methanol (36 mL) at room temperature for 30 min. The orange-red solution was washed with 5% sodium bicarbonate solution, dried over sodium sulfate, and evaporated under reduced pressure to give an orange oil. The residue was taken up in DMF (6 mL) and cooled to 0 °C in an ice–salt bath. Benzoyl chloride (2 mL) was added dropwise, maintaining the temperature at 0 °C throughout. Once the addition was complete, the ice bath was removed and the mixture stirred for 15 min. Toluene (40 mL) was added, but no precipitate formed. Sodium carbonate (4.0 g) was added and the mixture evaporated to dryness on a rotary evaporator. Water (20 mL) and ethanol (20 mL) were added and the mixture heated on a boiling water bath for 15 min. An additional amount of water (40 mL) was added and the mixture cooled in an ice bath. The precipitate was filtered and recrystallized from ethanol to give the aldehyde (1.32 g; 69%) as a yellow powder, mp 194.5–195.5 °C; IR (Nujol mull): ν 3284 (NH), 1676, 1614 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 1.02 (3H, t, J=7.3 Hz), 1.19 (3H, t, J=7.5 Hz), 1.51 (9H, s), 2.02 (3H, s), 2.24 (3H, s), 2.43 (2H, q, J=7.3 Hz), 2.70 (2H, q, J=7.4 Hz), 3.90 (2H, s), 9.49 (1H, s), 9.65 (1H, br s), 10.53 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.7, 10.7, 15.7, 16.7, 17.5, 28.8, 80.3, 117.5, 119.7, 124.1, 125.9, 127.6, 127.9, 137.1, 140.5, 161.6, 176.8. Anal. Calcd for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.43; N, 7.81. Found: C, 70.36; H, 8.49; N, 7.88.

4.2.32. 5′-*tert*-Butoxycarbonyl-3′-ethyl-3,4′-dimethyl-4-propyl-2,2′-dipyrrylmethane-5-carbaldehyde (24b). The title dipyrrylmethane aldehyde was prepared from the reaction of **31b** (2.00 g) and *p*-toluenesulfonic acid (2.24 g), followed by formylation with benzoyl chloride (2 mL) in DMF (5.6 mL) and hydrolysis with sodium carbonate in ethanol–water, as described in the previous procedure. Recrystallization from ethanol gave the dipyrrylmethane aldehyde (1.229 g; 64%) as a pale yellow solid (1.23 g; 64%). The residues were chromatographed on silica, eluting with toluene, followed by gradually increasing proportions of ethyl acetate–toluene mixtures. Recrystallization of the aldehyde fractions gave a pale yellow solid (38 mg, 66% overall), mp 138–139 °C; IR (Nujol mull): ν 3268 (NH), 1682, 1614 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 0.96 (3H, t, J=7.4 Hz), 1.02 (3H, t, J=7.5 Hz), 1.52 (9H, s), 1.59–1.69 (2H, m), 2.01 (3H, s), 2.25 (3H, s), 2.43 (2H, q, J=7.5 Hz), 2.66 (2H, t, J=7.4 Hz), 3.90 (2H, s), 9.43 (1H, br s), 9.49 (1H, s), 10.20 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.9, 10.7, 14.1, 15.7, 17.6, 23.1, 25.1, 26.2, 28.7, 80.3, 117.8, 119.7, 124.1, 125.9, 127.7, 128.5, 136.9, 138.7, 161.6, 177.0. Anal. Calcd for $C_{22}H_{32}N_2O_3$: C, 70.94; H, 8.66; N, 7.52. Found: C, 70.83; H, 8.45; N, 7.63.

4.2.33. 5′-*tert*-Butoxycarbonyl-3′-ethyl-4-isobutyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carbaldehyde (24c). The title dipyrrylmethane aldehyde was synthesized from **31c** (2.00 g) by treatment with *p*-toluenesulfonic acid (2.17 g) in dichloromethane (113 mL), followed by formylation with benzoyl chloride (2.0 mL) in DMF (5.2 mL) and hydrolysis with sodium carbonate in ethanol–water using the procedure detailed above for **24a**. After recrystallization from ethanol and column chromatography of the residues, a yellow powder (0.927 g; 48%) was obtained, mp 144–145 °C; IR (Nujol mull): ν 3275 (br, NH), 1679, 1611 cm^{-1} (s, sh, C=O); ^{1}H NMR ($CDCl_3$): δ 0.95 (6H, d, J=6.5 Hz), 1.01 (3H, t, J=7.5 Hz), 1.53 (9H, s), 1.79–1.90 (1H, m), 2.00 (3H, s), 2.25 (3H, s), 2.42 (2H, q, J=7.5 Hz), 2.55 (2H, d, J=7.2 Hz), 3.90 (2H, s), 9.36 (1H, br s), 9.46 (1H, s), 10.10 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 9.2, 10.8, 15.8, 17.6, 22.8, 23.1, 28.7, 30.8, 33.4, 80.2, 118.1, 119.7, 123.9, 125.8, 127.8, 129.0, 137.2, 137.9, 161.5, 177.3. Anal. Calcd for $C_{23}H_{34}N_2O_3$: C, 71.47; H, 8.87; N, 7.25. Found: C, 71.32; H, 8.65; N, 7.23.

4.2.34. 5′-*tert*-Butoxycarbonyl-4-ethyl-3,3′,4′-trimethyl-2,2′-dipyrrylmethane-5-carbaldehyde (24d). Benzyl ester **30d** (1.00 g) was hydrogenolyzed over 10% palladium–charcoal (0.10 g) under the conditions described for **38b**. The resulting carboxylic acid was obtained as a pink powder (0.80 g; quantitative). The crude carboxylic acid was decarboxylated and formylated under the conditions described for **24a**. Following recrystallization from ethanol, the title aldehyde (0.53 g; 69%) was obtained as pale yellow crystals, mp 210–211 °C; ^{1}H NMR ($CDCl_3$): δ 1.20 (3H, t, J=7.4 Hz), 1.52 (9H, s), 1.96 (3H, s), 2.01 (3H, s), 2.22 (3H, s), 2.70

(2H, q, J=7.4 Hz), 3.87 (2H, s), 9.17 (1H, br s), 9.49 (1H, s), 9.77 (1H, br s); ^{13}C NMR ($CDCl_3$): δ 8.8, 9.2, 10.9, 16.7, 17.6, 23.1, 28.7, 80.2, 117.1, 117.5, 119.6, 126.4, 127.8, 128.2, 137.5, 140.7, 161.5, 176.8. Anal. Calcd for $C_{20}H_{28}N_2O_3$: C, 69.74; H, 8.19; N, 8.13. Found: C, 69.83; H, 8.25; N, 8.37.

4.2.35. 3,5-Propano-7,13,18-triethyl-2,8,12,17-tetramethylporphyrin (35a). In a 100 mL round-bottomed flask, 7-(5-*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydroindole-2-carboxylic acid (**23a**; 300 mg) and 5′-*tert*-butoxycarbonyl-3′,4-diethyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carbaldehyde (**24a**; 278 mg) were dissolved in dichloromethane (45 mL). After the solid had dissolved, a solution of *p*-toluenesulfonic acid (591 mg) in methanol (7.2 mL) was added to the stirred solution. The resulting mixture was stirred under nitrogen protection and at room temperature for 30 min. The dark red solution was washed with 5% sodium carbonate solution, water and then dried over sodium sulfate. Evaporation of the solvent under reduced pressure afforded the tetrapyrrolic intermediate **34a** (*b*-bilene). The dark residue was then dissolved in dichloromethane (10 mL) and hydrogen chloride gas was bubbled through the solution for 5 s to form the hydrochloride salt. Immediately, the solvent was evaporated on a rotary evaporator and the residue taken up twice in toluene and evaporated in order to remove traces of water and HCl. The resulting crude *b*-bilene (558 mg; quantitative) was isolated as a dark red solid, which decomposed slowly and needed to be used within 4 weeks. This intermediate was used without further purification in the following reaction.

Trifluoroacetic acid (1 mL) was added to the crude *b*-bilene (100 mg) to cleave the *tert*-butyl esters and the mixture was stirred under nitrogen for 10 min. The mixture was diluted with dichloromethane (20 mL) and trimethyl orthoformate (32.5 μL) was added to the stirred solution. The mixture was then stirred in the dark and under nitrogen for 2 h. Triethylamine was added dropwise to neutralize the trifluoroacetic acid, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (31.6 mg) was added immediately and the resulting solution stirred in the dark and under nitrogen for an additional 1 h. The solution was washed with water, the solvent removed under reduced pressure, and the residue chromatographed on a grade III alumina column, eluting with dichloromethane. Evaporation of the solvent and recrystallization from chloroform–methanol afforded the title porphyrin as violet-red crystals (21 mg; 31%), mp 284–286 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 404 (5.22), 503 (4.16), 537 (3.71), 571 (3.79), 623 nm (3.41); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 412 (5.51), 556 (4.23), 598 nm (3.88); ^{1}H NMR ($CDCl_3$): δ −3.28 (2H, br s), 1.80 (3H, t, J=7.6 Hz), 1.81–1.90 (6H, two overlapping triplets), 2.88 (2H, quintet, J=6 Hz), 3.57 (3H, s), 3.58 (3H, s), 3.63 (3H, s), 3.65 (3H, s), 3.85 (2H, t, J=6 Hz), 4.03 (2H, q, J=7.6 Hz), 4.07–4.14 (4H, two overlapping quartets), 5.10 (2H, t, J=5.8 Hz), 9.89 (1H, s), 10.03 (1H, s), 10.08 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −3.64 (1H, br s), −3.37 (2H, br s), −2.85 (1H, br s), 1.68–1.74 (9H, three overlapping triplets), 2.87 (2H, quintet, J=6 Hz), 3.48 (3H, s), 3.53 (3H, s), 3.59 (3H, s), 3.60 (3H, s), 3.89 (2H, q, J=7.6 Hz), 3.94 (2H, t, J=6 Hz), 4.02–4.10 (4H, two overlapping quartets), 5.24 (2H, t, J=6.2 Hz), 10.33 (1H, s), 10.40 (1H, s), 10.50 (1H, s); ^{13}C NMR (TFA–$CDCl_3$): δ 11.7, 11.9 (2), 15.7, 16.4 (2), 20.2, 20.3, 21.6, 24.3, 27.1, 31.1, 96.3, 97.2, 99.6, 120.4, 134.8, 137.4, 137.7, 138.6, 140.5, 140.6, 140.8, 141.7, 142.9, 143.0, 143.4, 144.6; HRMS (EI): m/z calcd for $C_{33}H_{38}N_4$: 490.3096; found: 490.3096. Anal. Calcd for $C_{33}H_{38}N_4\cdot 1/10CHCl_3$: C, 79.10; H, 7.64; N, 11.15. Found: C, 78.96; H, 7.69; N, 11.14. *Nickel(II) complex **36a***. The nickel(II) complex was prepared from crude free base porphyrin which was obtained after chromatography but before recrystallization. Chloroform (10 mL) and a saturated solution of nickel(II) acetate in methanol (5 mL) were added to the crude porphyrin (prepared from 100 mg of crude *b*-bilene **34a**) and the mixture was refluxed overnight. The deep red solution was washed with water (×2) to remove the excess nickel acetate and the solvent removed under reduced pressure. The red solid was chromatagraphed on a grade III alumina column, eluting with dichloromethane. A bright red band was collected and the solvent evaporated. Recrystallization from chloroform–methanol afforded the nickel(II) complex (29 mg; 38%) as red-violet crystals, mp 242.5–244.5 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 400 (5.06), 522 (3.87), 557 nm (4.07); ^{1}H NMR ($CDCl_3$): δ 1.65 (3H, t, J=7.4 Hz), 1.71–1.76 (6H, two overlapping triplets), 2.50 (2H, quintet, J=6 Hz), 3.39 (3H, s), 3.41 (3H, s), 3.42 (6H, s), 3.74 (2H, t, J=6 Hz), 3.86 (2H, q), 3.83–3.90 (4H, two overlapping quartets), 3.94 (2H, q, J=7.6 Hz), 4.76 (2H, t, J=6 Hz), 9.53 (1H, s), 9.57 (1H, s), 9.60 (1H, s); ^{13}C NMR ($CDCl_3$): δ 11.3, 11.5, 16.4, 17.5 (2), 19.8, 22.7, 25.4, 26.4, 30.7, 95.6, 96.3, 97.1, 113.9, 133.1, 136.2, 136.5, 138.4, 138.7, 140.1, 140.2, 140.6, 140.9, 141.5, 142.2, 143.2, 143.6, 143.8.

4.2.36. 3,5-Butano-7,13,18-triethyl-2,8,12,17-tetramethylporphyrin (35b). This porphyrin was prepared in the same manner as the analogue above from **23b** (100 mg) and **24a** (90 mg). The crude *b*-bilene **34b** (which appeared to be less stable than **34a**, and should not be stored for more than 2 weeks at room temperature) was obtained as a red solid. Cyclization with TFA–trimethyl orthoformate, followed by purification and recrystallization from chloroform–methanol gave porphyrin **35b** (22 mg; 32%) as dark violet crystals, mp 280–282 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 406 (5.26), 506 (4.14), 541 (3.75), 575 (3.77), 628 nm (3.24); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 414 (5.50), 558 (4.21), 601 nm (3.84); ^{1}H NMR ($CDCl_3$): δ −3.16 (2H, br s), 1.81–1.89 (9H, three overlapping triplets), 2.32–2.39 (2H, m), 2.78 (2H, quintet, J=6.6 Hz), 3.58 (6H, s), 3.62 (3H, s), 3.66 (3H, s), 3.88 (2H, t, J=6 Hz), 4.01 (2H, q, J=7.6 Hz), 4.08–4.16 (4H, two overlapping quartets), 4.84 (2H, t, J=6 Hz), 9.87 (1H, s), 10.05 (1H, s), 10.07 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −3.71 (1H, br s), −3.65 (1H, br s), −3.04 (1H, br s), −2.72 (1H, br s), 1.66–1.76 (9H, three overlapping triplets), 1.87–1.93 (2H, m), 2.82 (2H, quintet, J=6 Hz), 3.39 (3H, s), 3.40 (3H, s), 3.53 (3H, s), 3.55 (3H, s), 3.67–3.77 (4H, m), 3.97–4.06 (4H, two overlapping quartets), 5.10 (2H, t, J=6 Hz), 10.20 (1H, s), 10.34 (1H, s), 10.35 (1H, s); ^{13}C NMR (TFA–$CDCl_3$): δ 11.7, 11.8 (2), 15.9, 16.2, 16.3, 20.1, 20.2, 22.0, 25.3, 25.4, 29.8, 30.7, 95.5, 98.2, 98.3, 124.4, 134.7, 137.3, 137.4, 138.7, 140.3, 140.8, 140.9, 141.0, 141.4, 141.5, 142.5, 143.3, 143.8, 144.7, 145.1; HRMS (EI): m/z calcd for $C_{34}H_{40}N_4$: 504.3255; found: 504.3253. Anal. Calcd for $C_{35}H_{42}N_4\cdot 1/20CHCl_3$: C,

80.08; H, 7.91; N, 10.97. Found: C, 80.10; H, 8.11; N, 10.76. *Nickel(II) complex* ***36b***. This was obtained from 100 mg of crude *b*-bilene, as described for the previous example. Recrystallization from chloroform–methanol gave the complex (23 mg, 30%) as red-violet crystals, mp 215–217 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 404 (5.23), 528 (4.06), 563 nm (4.19); ^{1}H NMR ($CDCl_3$): δ 1.60 (3H, t, J=7.4 Hz) 1.68–1.75 (6H, two overlapping triplets), 2.30–2.37 (4H, m), 3.37 (12H, s), 3.79–3.87 (6H, m), 3.95 (2H, q, J=7.2 Hz), 4.26 (2H, br t), 9.43 (1H, s), 9.45 (1H, s), 9.47 (1H, s); ^{13}C NMR ($CDCl_3$): δ 11.3, 11.5, 16.4, 17.4, 17.5, 19.8, 22.2, 25.6, 28.7, 30.6, 95.5, 96.5, 95.7, 116.7, 136.2, 136.4, 136.5, 139.2, 139.5, 139.9, 140.0, 140.7, 141.0, 141.7, 142.2, 143.7 (2), 144.4, 144.6.

4.2.37. 3,5-Pentano-7,13,18-triethyl-2,8,12,17-tetramethylporphyrin (35c). The title porphyrin was synthesized from **23c** (100 mg) and **24a** (87 mg) by the same method detailed above. Recrystallization from chloroform–methanol gave the desired porphyrin (63 mg; 50%) as dark violet crystals, mp 252.5–254 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 406 (5.26), 505 (4.16), 540 (3.76), 573 (3.80), 626 nm (3.27); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 415 (5.48), 559 (4.23), 602 nm (3.87); ^{1}H NMR ($CDCl_3$): δ −2.93 (2H, br s), 1.50–1.57 (2H, m), 1.80 (3H, t, J=7.6 Hz), 1.83–1.90 (6H, two overlapping triplets), 2.14–2.28 (2H, br m), 2.59–2.67 (2H, m), 3.60 (3H, s), 3.61 (3H, s), 3.64 (3H, s), 3.67 (3H, s), 4.02 (2H, q, J=7.6 Hz), 4.11 (4H, q, J=7.6 Hz), 4.28 (2H, t, J=7 Hz), 5.27 (2H, t, J=6.8 Hz), 9.86 (1H, s), 10.12 (1H, s), 10.16 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −3.56 (1H, br s), −3.55 (1H, br s), −2.80 (1H, br s), −2.62 (1H, br s), 1.24–1.34 (2H, m), 1.60–1.70 (9H, two overlapping triplets), 2.09–2.16 (2H, br m), 2.60 (2H, quintet, J=6 Hz), 3.33 (3H, s), 3.44 (3H, s), 3.52 (3H, s), 3.54 (3H, s), 3.63 (2H, q, J=7.6 Hz), 3.95–4.04 (4H, two overlapping quartets), 4.09 (2H, t, J=6.8 Hz), 5.25 (2H, t, J=7 Hz), 10.17 (1H, s), 10.29 (1H, s), 10.38 (1H, s); ^{13}C NMR (TFA–$CDCl_3$): δ 11.7, 11.8, 12.0, 15.8, 16.2, 16.3, 20.0, 20.2, 21.7, 26.1, 27.1, 30.8, 32.5, 95.5, 96.5, 99.6, 123.2, 136.8, 137.6, 138.5, 138.8, 140.4, 140.6, 140.7, 141.4, 142.0, 142.4, 143.4, 143.9, 144.9; HRMS (EI): *m/z* calcd for $C_{35}H_{42}N_4$: 518.3400; found: 518.3409. Anal. Calcd for $C_{35}H_{42}N_4$: C, 81.04; H, 8.16; N, 11.08. Found: C, 81.00; H, 7.70; N, 11.12. *Nickel(II) complex* ***36c***. Prepared from crude free base porphyrin obtained from *b*-bilene **34c** (180 mg), chloroform (20 mL), and a saturated solution of nickel acetate in methanol (9 mL) by the procedure given above. Recrystallization from chloroform–methanol gave the title porphyrin as red-violet crystals (71 mg, 51%), mp 219–221 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 405 (5.21), 529 (4.05), 563 nm (4.18); ^{1}H NMR ($CDCl_3$): δ 1.28–1.40 (2H, m), 1.56 (3H, t, J=7.5 Hz), 1.61–1.73 (6H, two overlapping triplets), 2.05–2.17 (2H, m), 3.36 (12H, s), 3.77–3.92 (6H, three overlapping quartets), 4.06 (2H, t, J=6.9 Hz), 4.70 (2H, t, J=6.9 Hz), 9.38 (1H, s), 9.42 (2H, s); ^{13}C NMR ($CDCl_3$): δ 11.3, 11.4, 11.6, 11.7, 16.5, 17.4, 17.5, 19.7, 22.6, 23.1, 27.9, 28.3, 30.2, 30.9, 95.4, 96.2, 96.5, 115.1, 136.4, 136.6, 137.9, 139.2, 139.3, 139.6, 140.6, 140.7, 141.0, 141.8, 143.1, 143.2, 143.9, 144.2.

4.2.38. Deoxophylloerythroetioporphyrin (DPEP) (2a). 6-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-cyclopenta[*b*]pyrrole-2-carboxylic acid[33,34] (**38a**; 100 mg) and 5′-*tert*-butoxycarbonyl-3′,4-diethyl-3,4′-dimethyl-2,2′-dipyrrylmethane-5-carbaldehyde (**24a**; 100 mg) were dissolved in dichloromethane (15 mL). A solution of *p*-toluenesulfonic acid (53 mg) in methanol (0.7 mL) was added and the resulting mixture was stirred under nitrogen protection in the dark overnight to form *b*-bilene **39a**. The solvent was removed under reduced pressure and the residue was dissolved in trifluoroacetic acid (2 mL) to cleave the ester protective groups. The dark red solution was allowed to stir at room temperature for 10 min under nitrogen and then diluted with dichloromethane (40 mL). Trimethyl orthoformate (32.5 μL) was immediately added and the mixture was stirred under nitrogen in the dark for a further 4 h. A saturated solution of zinc acetate in methanol (20 mL) was added and the resulting solution was stirred in the dark and open air for 2 days. The resulting metalated porphyrin solution was washed with water (×3) and the solvent was evaporated to give a red solid. Sufficient trifluoroacetic acid (about 4 mL) was added to dissolve the solid and ensure demetalation of the zinc porphyrin. The solution was diluted with dichloromethane, and washed with water and 5% aqueous sodium bicarbonate solution. The solvent was removed under reduced pressure and the crude free base porphyrin was chromatographed on a grade III alumina column, eluting with dichloromethane. After the solvent was evaporated, the residue was dissolved in chloroform (30 mL). A saturated solution of nickel(II) acetate in methanol (10 mL) was added and the mixture was allowed to reflux overnight. The resulting solution was washed with water to remove the excess nickel(II) acetate. The solvent was removed under reduced pressure and the compound was chromatographed on silica gel, eluting with dichloromethane. The crude porphyrin, which was contaminated with nickel(II) etioporphyrin by-products, was flash chromatographed twice on silica gel, eluting with a 75:25 mixture of hexane and toluene. The nickel(II) DPEP fraction was recrystallized from chloroform–methanol to yield nickel(II) DPEP (40 mg; 28%) as bright red crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 394 (5.33), 515 (4.16), 553 nm (4.42); ^{1}H NMR ($CDCl_3$): δ 1.58 (3H, t, J=7.6 Hz), 1.76–1.81 (6H, two overlapping triplets), 3.39 (6H, s), 3.46 (3H, s), 3.49 (3H, s), 3.69 (2H, q, J=7.6 Hz), 3.78–3.82 (2H, m), 3.88–3.95 (4H, two overlapping quartets), 4.94 (2H, t, J=4 Hz), 9.68 (2H, s), 9.73 (1H, s); ^{13}C NMR ($CDCl_3$): δ 11.5, 11.7, 12.4, 16.7, 17.7, 17.8, 20.0 (2), 20.9, 24.4, 37.2, 96.0, 97.2, 97.3, 118.0, 127.6, 135.1, 136.1, 137.1, 139.1, 141.3, 141.5, 141.7, 142.3, 142.6, 143.1, 146.5, 149.3, 149.5. *Free base DPEP* ***2a***. The foregoing nickel(II) complex (20 mg) was dissolved in 15% sulfuric acid–TFA (15 mL) and stirred at room temperature for 2 h. The mixture was poured into ice water, extracted with chloroform, and the organic solutions washed with 5% sodium bicarbonate. Following evaporation of the solvent under reduced pressure, the residue was chromatographed on a grade III alumina column eluting with dichloromethane. The porphyrin fraction was recrystallized from chloroform–methanol to give DPEP (16 mg; 72%) as purple crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.29), 500 (4.17), 534 (3.70), 564 (3.81), 616 nm (3.76); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 407 (5.58), 551 (4.24), 595 nm (3.86); ^{1}H NMR ($CDCl_3$): δ −3.72 (1H, br s), −2.93 (1H, br s), 1.78 (3H, t, J=7.6 Hz), 1.86 (3H, t, J=7.6 Hz), 1.90 (3H, t, J=7.6 Hz), 2.02 (3H, t, J=7.5 Hz),

3.58 (3H, s), 3.69 (3H, s), 3.70 (3H, s), 4.02 (2H, q, J=7.6 Hz), 4.08–4.20 (6H, m), 5.41–5.47 (2H, m), 10.01 (2H, s), 10.07 (1H, s); HRMS (FAB): *m/z* calcd for $C_{32}H_{36}N_4$+H: 477.3018; found: 477.3018.

4.2.39. 13,15-Ethano-3,17-diethyl-2,7,12,18-tetramethyl-8-propylporphyrin (18b). The nickel(II) porphyrin was synthesized from dipyrrole carboxylic acid **38a** (100 mg) and dipyrrole aldehyde **24b** (100 mg) as described above. Recrystallization from chloroform–methanol gave the nickel(II) porphyrin **40b** (33 mg; 12%) as red crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 394 (5.32), 515 (4.10), 553 nm (4.39); ^{1}H NMR ($CDCl_3$; 40 °C): δ 1.27 (3H, t, J=7.4 Hz), 1.63 (3H, t, J=7.4 Hz), 1.79 (3H, t, J=7.8 Hz), 2.25 (2H, sextet, J=7.4 Hz), 3.44 (3H, s), 3.45 (3H, s), 3.48 (3H, s), 3.50 (3H, s), 3.80 (2H, q, J=7.6 Hz), 3.87–3.96 (6H, m), 5.09 (2H, t, J=5 Hz), 9.73 (1H, s), 9.74 (1H, s), 9.76 (1H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.5, 11.7, 11.9, 12.4, 14.7, 16.7, 17.6, 20.0, 21.0, 24.5, 26.4, 28.8, 37.4, 96.1, 97.4, 97.5, 118.1, 127.7, 135.9, 136.2, 139.3, 141.6, 141.7, 141.9, 142.4, 142.7, 146.6, 149.5, 149.7. *Free base porphyrin **18b***: purple crystals from chloroform–methanol, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.29), 501 (4.14), 535 (3.54), 564 (3.74), 616 nm (3.72); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 407 (5.65), 552 (4.15), 596 nm (3.66); ^{1}H NMR ($CDCl_3$): δ −3.72 (1H, br s), −2.92 (1H, br s), 1.29 (3H, t, J=7.2 Hz), 1.78 (3H, t, J=7.6 Hz), 1.85 (3H, t, J=7.4 Hz), 2.35 (2H, sextet, J=7.4 Hz), 3.57 (3H, s), 3.59 (3H, s), 3.69 (6H, s), 4.02 (2H, q, J=7.6 Hz), 4.07–4.17 (6H, m), 5.42–5.46 (2H, m), 9.98 (1H, s), 10.01 (1H, s), 10.06 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −4.81 (1H, s), −4.17 (1H, br s), −3.49 (1H, s), −2.7 (1H, v br s), 1.25 (3H, t, J=7.4 Hz), 1.73 (3H, t, J=7.6 Hz), 1.78 (3H, t, J=7.8 Hz), 2.24 (2H, sextet, J=7.5 Hz), 3.66 (3H, s), 3.67 (3H, s), 3.68 (6H, s), 4.08–4.19 (6H, m), 4.36–4.40 (2H, m), 5.71–5.76 (2H, m), 10.51 (1H, s), 10.54 (1H, s), 10.64 (1H, s); HRMS (ESI): *m/z* calcd for $C_{33}H_{38}N_4$+H: 491.3175; found: 491.3178.

4.2.40. 3,13-Diethyl-2,7,12,17-tetramethyl-8,18-dipropylporphyrinatonickel(II) (41b). This by-product was obtained from the previous procedure, and after recrystallization from chloroform–methanol was isolated as bright red crystals, mp 218–219 °C, dec. NMR spectroscopy indicated that this nickel(II) porphyrin consisted primarily of the type I isomer. UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 393 (5.20), 517 (4.02), 553 nm (4.49); ^{1}H NMR ($CDCl_3$; 40 °C): δ 1.28 (6H, t, J=7.4 Hz), 1.80 (6H, t, J=7.6 Hz), 2.25 (4H, sextet, J=7.4 Hz), 3.48 (8H, m), 9.75 (2H, s), 9.76 (2H, s); ^{13}C NMR ($CDCl_3$; 50 °C): δ 11.6, 11.9, 14.7, 17.6, 20.0, 26.4, 28.8, 97.0, 97.2, 136.0, 136.7, 141.0, 141.5, 141.7, 141.9, 143.3. Anal. Calcd for $C_{34}H_{40}N_4Ni$: C, 72.48; H, 7.15; N, 9.94. Found: C, 72.39; H, 7.12; N, 9.92.

4.2.41. 13,15-Ethano-3,17-diethyl-8-isobutyl-2,7,12,18-tetramethylporphyrin (18d). The nickel(II) porphyrin was prepared from dipyrrole carboxylic acid **38a** (100 mg) and dipyrrole aldehyde **24c** (110 mg) by the procedure described above for **2a**. Recrystallization from chloroform–methanol gave the nickel(II) porphyrin **40d** (20 mg; 13%), as red crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 394 (5.31), 515 (4.12), 553 nm (4.40); ^{1}H NMR ($CDCl_3$; 40 °C): δ 1.26 (6H, d, J=6.4 Hz), 1.62 (3H, t, J=7.6 Hz), 1.79 (3H, t, J=7.8 Hz), 2.61 (1H, nonet, J=7 Hz), 3.42 (3H, s), 3.43 (3H, s), 3.47 (3H, s), 3.49 (3H, s), 3.73–3.79 (4H, overlapping doublet and quartet), 3.86–3.90 (2H, m), 3.92 (2H, q, J=7.8 Hz), 5.05 (2H, m), 9.69 (1H, s), 9.72 (1H, s), 9.76 (1H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.5, 11.7, 12.2, 12.4, 16.7, 17.6, 20.0, 21.0, 23.5, 24.5, 32.5, 36.1, 37.4, 96.1, 97.3, 97.8, 118.1, 127.7, 136.2, 136.4, 137.2, 139.3, 140.9, 141.6, 141.7, 142.3, 142.7, 146.6, 149.4, 149.7. *Free base porphyrin **18d***: purple crystals from chloroform–methanol, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.37), 501 (4.19), 535 (3.59), 564 (3.80), 616 nm (3.78); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 408 (5.72), 552 (4.21), 596 nm (3.73); ^{1}H NMR ($CDCl_3$): δ −3.73 (1H, br s), −2.91 (1H, br s), 1.29 (6H, d, J=6.8 Hz), 1.77 (3H, t, J=7.6 Hz), 1.85 (3H, t, J=7.6 Hz), 2.72 (1H, nonet, J=6.8 Hz), 3.57 (3H, s), 3.59 (3H, s), 3.68 (3H, s), 3.69 (3H, s), 3.98–4.12 (8H, m), 5.40–5.44 (2H, m), 9.96 (1H, s), 10.01 (1H, s), 10.06 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −4.67 (1H, s), −4.04 (1H, br s), −3.35 (1H, s), −2.5 (1H, v br s), 1.22 (6H, d, J=6.8 Hz), 1.71–1.75 (6H, two overlapping triplets), 2.59 (1H, nonet, J=7 Hz), 3.65 (3H, s), 3.67 (3H, s), 3.68 (6H, s), 3.99 (2H, d, J=7.2 Hz), 4.09–4.18 (4H, two overlapping quartets), 4.36–4.40 (2H, m), 5.70–5.74 (2H, m), 10.47 (1H, s), 10.53 (1H, s), 10.62 (1H, s); HRMS (ESI): *m/z* calcd for $C_{34}H_{40}N_4$+H: 505.3331; found: 505.3332.

4.2.42. 3,13-Diethyl-8,18-diisobutyl-2,7,12,17-tetramethylporphyrinatonickel(II) (41c). This by-product was obtained from the previous procedure, and after recrystallization from chloroform–methanol was isolated as bright red crystals, mp 265 °C, dec; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 393 (5.21), 517 (4.01), 553 nm (4.48); ^{1}H NMR ($CDCl_3$; 25 °C): δ 1.25 (12H, d, J=6.8 Hz), 1.78 (6H, t, J=7.8 Hz), 2.59 (2H, nonet, J=6.7 Hz), 3.47 (12H, s), 3.76 (4H, d, J=7.2 Hz), 3.92 (4H, q, J=7.6 Hz), 9.72 (2H, s), 9.75 (2H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.6, 12.2, 17.7, 20.0, 23.5, 32.5, 36.1, 97.0, 97.5, 136.0, 137.2, 140.9, 141.0, 141.8, 143.3. Anal. Calcd for $C_{36}H_{44}N_4Ni$: C, 73.11; H, 7.50; N, 9.47. Found: C, 72.78; H, 7.53; N, 9.43.

4.2.43. 13,15-Ethano-3,8,12,17-tetraethyl-2,7,18-trimethylporphyrin (18a). The nickel(II) porphyrin complex was prepared from the corresponding dipyrrole carboxylic acid **38b** (300 mg) and dipyrrole aldehyde **24a** (290 mg) in the same manner as described above. Recrystallization from chloroform–methanol gave the nickel(II) porphyrin **40a** (97 mg; 23%) as bright red crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 394 (5.27), 515 (4.10), 553 nm (4.38); ^{1}H NMR ($CDCl_3$; 40 °C): δ 1.62 (3H, t, J=7.6 Hz), 1.77–1.82 (6H, two overlapping triplets), 1.90 (3H, t, J=7.6 Hz), 3.43 (3H, s), 3.47 (3H, s), 3.50 (3H, s), 3.77 (2H, q, J=7.6 Hz), 3.89–4.04 (8H, m), 5.06 (2H, t, J=4.6 Hz), 9.72 (1H, s), 9.74 (2H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.5, 11.7, 15.3, 16.7, 17.6, 17.7, 20.0, 20.1, 21.0, 21.1, 25.3, 37.6, 96.0, 97.3 (2), 118.0, 134.3, 135.2, 136.2, 137.2, 139.3, 141.4, 141.6, 141.7, 141.9, 142.4, 142.7, 143.2, 145.9, 148.5, 149.8. *Free base porphyrin **18a***: purple crystals from chloroform–methanol, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.37), 501 (4.21), 535 (3.65), 564 (3.82), 616 nm (3.77); UV–vis (1%

TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 408 (5.69), 552 (4.26), 596 nm (3.80); ^{1}H NMR ($CDCl_3$): δ −3.72 (1H, br s), −2.93 (1H, br s), 1.78 (3H, t, J=7.6 Hz), 1.86 (3H, t, J=7.6 Hz), 1.90 (3H, t, J=7.6 Hz), 2.02 (3H, t, J=7.5 Hz), 3.58 (3H, s), 3.69 (3H, s), 3.70 (3H, s), 4.02 (2H, q, J=7.6 Hz), 4.08–4.20 (6H, m), 5.41–5.47 (2H, m), 10.01 (2H, s), 10.07 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −4.73 (1H, s), −4.16 (1H, br s), −3.51 (1H, s), −2.7 (1H, v br s), 1.73 (3H, t, J=7.6 Hz), 1.78 (3H, t, J=7.6 Hz), 1.80 (3H, t, J=7.6 Hz), 1.98 (3H, t, J=7.6 Hz), 3.67 (3H, s), 3.68 (6H, s), 4.01–4.22 (8H, four overlapping quartets), 4.43–4.47 (2H, m), 5.71–5.76 (2H, m), 10.52 (1H, s), 10.53 (1H, s), 10.63 (1H, s); HRMS (ESI): *m/z* calcd for $C_{33}H_{38}N_4$+H: 491.3175; found: 491.3180.

4.2.44. 13,15-Ethano-3,12,17-triethyl-2,7,18-trimethyl-8-propylporphyrin (18c). The nickel(II) porphyrin was synthesized from the corresponding dipyrrole carboxylic acid **38b** (300 mg) and dipyrrole aldehyde **24b** (290 mg) in the same manner as the analogues described above. Recrystallization from chloroform–methanol afforded the porphyrin complex **40c** (58 mg; 14%) as red-violet crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 395 (5.32), 515 (4.14), 553 nm (4.41); ^{1}H NMR ($CDCl_3$; 50 °C): δ 1.27 (3H, t, J=7.2 Hz), 1.68 (3H, t, J=7.6 Hz), 1.79 (3H, t, J=7.6 Hz), 1.94 (3H, t, J=7.6 Hz), 2.26 (2H, sextet, J=7.4 Hz), 3.49 (6H, s), 3.50 (3H, s), 3.88–3.97 (6H, m), 4.03 (2H, q, J=7.6 Hz), 4.06–4.10 (2H, m), 5.23 (2H, t, J=5 Hz), 9.78 (1H, s), 9.792 (1H, s), 9.795 (1H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.5, 11.7, 11.9, 14.7, 15.3, 16.7, 17.6, 20.0, 21.0, 21.1, 25.3, 26.4, 28.8, 37.5, 96.0, 97.3, 97.5, 118.0, 134.3, 135.9, 136.2, 137.2, 139.2, 141.6, 141.7, 141.8, 142.4, 142.7, 145.9, 148.4, 149.8. *Free base porphyrin* ***18c***: purple crystals from chloroform–methanol, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.42), 501 (4.27), 535 (3.69), 564 (3.88), 616 nm (3.84); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 408 (5.73), 552 (4.29), 596 nm (3.83); ^{1}H NMR ($CDCl_3$): δ −3.73 (1H, br s), −2.94 (1H, br s), 1.28 (3H, t, J=7.2 Hz), 1.77 (3H, t, J=7.4 Hz), 1.85 (3H, t, J=7.6 Hz), 2.01 (3H, t, J=7.6 Hz), 2.35 (2H, sextet, J=7.6 Hz), 3.57 (3H, s), 3.68 (3H, s), 3.69 (3H, s), 4.02 (2H, q, J=7.6 Hz), 4.06–4.19 (8H, m), 5.41–5.46 (2H, m), 9.99 (1H, s), 10.00 (1H, s), 10.05 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −4.74 (1H, s), −4.13 (1H, br s), −3.49 (1H, s), −2.6 (1H, v br s), 1.25 (3H, t, J=7.4 Hz), 1.71–1.80 (6H, two overlapping triplets), 1.98 (3H, t, J=7.6 Hz), 2.23 (2H, sextet, J=7.5 Hz), 3.67 (3H, s), 3.68 (6H, s), 4.08–4.22 (8H, m), 4.44–4.48 (2H, m), 5.72–5.75 (2H, m), 10.51 (1H, s), 10.53 (1H, s), 10.63 (1H, s); HRMS (ESI): *m/z* calcd for $C_{34}H_{40}N_4$+H: 505.3331; found: 505.3330.

4.2.45. 13,15-Ethano-3,12,17-triethyl-8-isobutyl-2,7,18-trimethylporphyrin (18e). The nickel(II) porphyrin was prepared from the corresponding dipyrrole carboxylic acid **38b** (150 mg) and dipyrrole aldehyde **24c** (149 mg) using the same method described for **2a**. Recrystallization from chloroform–methanol afforded the nickel(II) porphyrin **40e** (29 mg; 12%) as bright red crystals, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 395 (5.33), 515 (4.16), 553 nm (4.42); ^{1}H NMR ($CDCl_3$; 50 °C): δ 1.26 (6H, d, J=6.4 Hz), 1.66 (3H, t, J=7.6 Hz), 1.80 (3H, t, J=7.6 Hz), 1.93 (3H, t, J=7.6 Hz), 2.61 (1H, nonet, J=6.8 Hz), 3.46 (3H, s), 3.48 (3H, s), 3.50 (3H, s), 3.79 (2H, d, J=7.2 Hz), 3.85 (2H, q, J=7.7 Hz), 3.93 (2H, q, J=7.7 Hz), 3.98–4.07 (4H, m), 5.16 (2H, t, J=4.8 Hz), 9.75 (1H, s), 9.76 (1H, s), 9.77 (1H, s); ^{13}C NMR ($CDCl_3$; 40 °C): δ 11.5, 11.7, 12.2, 15.3, 16.7, 17.6, 20.0, 21.1 (2), 23.5, 25.3, 32.5, 36.1, 37.6, 96.1, 97.3, 97.9, 118.0, 134.3, 136.2, 136.4, 137.2, 139.3, 140.9, 141.7, 141.8, 142.4, 142.7, 145.9, 148.5, 149.9. *Free base porphyrin* ***18e***: purple crystals from chloroform–methanol, mp >300 °C; UV–vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.36), 501 (4.20), 535 (3.61), 564 (3.81), 616 nm (3.77); UV–vis (1% TFA–$CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 408 (5.67), 552 (4.22), 596 nm (3.74); ^{1}H NMR ($CDCl_3$): δ ^{1}H NMR ($CDCl_3$): δ −3.72 (1H, br s), −2.93 (1H, br s), 1.29 (6H, d, J=6.8 Hz), 1.77 (3H, t, J=7.8 Hz), 1.86 (3H, t, J=7.8 Hz), 2.01 (3H, t, J=7.5 Hz), 2.709 (1H, nonet, J=6.8 Hz), 3.57 (3H, s), 3.68 (3H, s), 3.69 (3H, s), 3.98–4.18 (10H, m), 5.42–5.46 (2H, m), 9.98 (1H, s), 10.01 (1H, s), 10.05 (1H, s); ^{1}H NMR (TFA–$CDCl_3$): δ −4.70 (1H, s), −4.08 (1H, br s), −3.42 (1H, s), −2.6 (1H, v br s), 1.22 (6H, d, J=6.4 Hz), 1.71–1.79 (6H, two overlapping triplets), 1.97 (3H, t, J=7.6 Hz), 2.58 (1H, nonet, J=Hz), 3.67 (3H, s), 3.675 (3H, s), 3.68 (3H, s), 3.99 (2H, d, J=7.6 Hz), 4.01–4.21 (8H, three overlapping quartets), 4.43–4.47 (2H, m), 5.72–5.75 (2H, m), 10.49 (1H, s), 10.53 (1H, s), 10.63 (1H, s); HRMS (ESI): *m/z* calcd for $C_{35}H_{42}N_4$+H: 519.3488; found: 519.3499.

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References and notes

1. Treibs, A. *Justus Liebigs Ann. Chem.* **1934**, *510*, 42.
2. Baker, E. W.; Palmer, S. E. *The Porphyrins*; Dolphin, D., Ed.; Academic: New York, NY, 1978; Vol. 1, pp 486–552.
3. (a) Filby, R. H.; Van Berkel, G. J. *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing*; Filby, R. H., Branthaver, J. F., Eds.; American Chemical Society: Washington, DC, 1987; pp 2–37; (b) Callot, H. J. *The Chlorophylls*; Scheer, H., Ed.; CRC: Boca Raton, FL, 1991; pp 339–364; (c) Callot, H. J.; Ocampo, R. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: San Diego, CA, 2000; Vol. 1, pp 349–398; (d) Czernuszewicz, R. S. *J. Porphyrins Phthalocyanines* **2000**, *4*, 426.
4. (a) Baker, E. W. *J. Am. Chem. Soc.* **1966**, *88*, 2311; (b) Baker, E. W.; Yen, T. F.; Dickie, J. P.; Rhodes, R. E.; Clark, L. F. *J. Am. Chem. Soc.* **1967**, *89*, 3631.
5. (a) Quirke, J. M. E. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: San Diego, CA, 2000; Vol. 7, pp 371–422; (b) Quirke, J. M. E.; Cuesta, L. L.; Yost, R. A.; Johnson, J.; Britton, E. D. *Org. Geochem.* **1989**, *14*, 43; (c) Laycock, J. D.; Yost, R. A.; Wang, L.; Quirke, J. M. E. *Energy Fuels* **1995**, *9*, 1079; (d) Rodgers, R. P.; Hendrickson, C. L.; Emmett, M. R.; Marshall, A. G.; Greaney, M.; Qian, K. *Can. J. Chem.* **2001**, *79*, 546.
6. (a) Verne-Mismer, J.; Ocampo, R.; Bauder, C.; Callot, H. J.; Albrecht, P. *Energy Fuels* **1990**, *4*, 639; (b) Boreham, C. J.; Fookes, C. J. R. *J. Chromatogr.* **1989**, *467*, 195.

7. (a) Chicarelli, M. I.; Kaur, S.; Maxwell, J. R. *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing*; Filby, R. H., Branthaver, J. F., Eds.; American Chemical Society: Washington, DC, 1987; pp 40–67; (b) Ocampo, R.; Callot, H. J.; Albrecht, P. *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing*; Filby, R. H., Branthaver, J. F., Eds.; American Chemical Society: Washington, DC, 1987; pp 68–73; (c) For a review on the NMR properties of porphyrins, see: Medforth, C. J. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: San Diego CA, 2000; Vol. 5, pp 1–80.
8. (a) Quirke, J. M. E.; Maxwell, J. R. *Tetrahedron* **1980**, *36*, 3453; (b) Fookes, C. J. R. *J. Chem. Soc., Chem. Commun.* **1985**, 706; (c) Chicarelli, M. I.; Wolff, G. A.; Maxwell, J. R. *J. Chem. Soc., Chem. Commun.* **1985**, 723; (d) Krane, J.; Skjetne, T.; Telnaes, N.; Bjoroy, M.; Schou, L.; Solli, H. *Tetrahedron* **1983**, *39*, 4109; (e) Bonnett, R.; Burke, P. J. *Geochim. Cosmochim. Acta* **1985**, *49*, 1487; (f) Boreham, C. J.; Fookes, C. J. R.; Popp, B. N.; Hayes, J. M. *Geochim. Cosmochim. Acta* **1989**, *53*, 2451; (g) Huseby, B.; Barth, T.; Ocampo, R. *Org. Geochem.* **1996**, *25*, 273.
9. (a) Clewlow, P. J.; Jackson, A. H.; Roberts, I. *J. Chem. Soc., Chem. Commun.* **1985**, 724; (b) Clewlow, P. J.; Jackson, A. H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1925.
10. (a) Quirke, J. M. E.; Maxwell, J. R.; Eglinton, G.; Sanders, J. K. M. *Tetrahedron Lett.* **1980**, *21*, 2987; (b) Fookes, C. J. R. *J. Chem. Soc., Chem. Commun.* **1983**, 1472; (c) Ekstrom, A.; Fookes, C. J. R.; Hambley, T.; Loeh, H. J.; Miller, S. A.; Taylor, J. C. *Nature* **1983**, *306*, 173; (d) Shulga, A. M.; Serebrennikova, O. V.; Mozzhelina, T. K. *Neftekhimiya* **1986**, *26*, 309; (e) Verne-Mismer, J.; Ocampo, R.; Callot, H. J.; Albrecht, P. *J. Chem. Soc., Chem. Commun.* **1987**, 1581; (f) Kaur, S.; Chicarelli, M. I.; Maxwell, J. R. *J. Am. Chem. Soc.* **1986**, *108*, 1347; (g) Ocampo, R.; Callot, H. J.; Albrecht, P.; Kintzinger, J. P. *Tetrahedron Lett.* **1984**, *25*, 258; (h) Eckardt, C. B.; Keely, B. J.; Waring, J. R.; Chicarelli, M. I.; Maxwell, J. R. *Philos. Trans. R. Soc. London, Ser. B* **1991**, *333*, 339; (i) Ocampo, R.; Bauder, C.; Callot, H. J.; Albrecht, P. *Geochim. Cosmochim. Acta* **1992**, *56*, 745.
11. (a) Chicarelli, M. I.; Wolff, G. A.; Murray, M.; Maxwell, J. R. *Tetrahedron* **1984**, *40*, 4033; (b) Boreham, C. J.; Clezy, P. S.; Robertson, G. B. *Energy Fuels* **1990**, *4*, 661; (c) Prowse, W. G.; Maxwell, J. R. *Geochim. Cosmochim. Acta* **1989**, *53*, 3081.
12. (a) Wolff, G. A.; Murray, M.; Maxwell, J. R.; Hunter, B. K.; Sander, J. K. M. *J. Chem. Soc., Chem. Commun.* **1983**, 922; (b) Fookes, C. J. R. *J. Chem. Soc., Chem. Commun.* **1983**, 1474.
13. Boreham, C. J.; Fookes, C. J. R.; Popp, B. N.; Hayes, J. M. *Energy Fuels* **1990**, *4*, 658.
14. Quirke, J. M. E. *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing*; Filby, R. H., Branthaver, J. F., Eds.; American Chemical Society: Washington, DC, 1987; pp 74–83.
15. (a) Palmer, S. E.; Baker, E. W. *Science* **1978**, *201*, 49; (b) Baker, E. W.; Louda, J. W. *Org. Geochem.* **1984**, *6*, 183; (c) Chicarelli, M. I.; Eckardt, C. B.; Owen, C. R.; Maxwell, J. R.; Eglinton, G.; Hutton, R. C.; Eaton, A. N. *Org. Geochem.* **1990**, *15*, 267.
16. (a) Barwise, A. J. G. *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing*; Filby, R. H., Branthaver, J. F., Eds.; American Chemical Society: Washington, DC, 1987; pp 100–109; (b) Frakman, Z.; Ignasiak, T. M.; Montgomery, D. S.; Strausz, O. P. *AOSTRA J. Res.* **1988**, *4*, 171.
17. (a) Gosselink, J. W.; Stork, W. H. *J. Ind. Eng. Chem. Res.* **1997**, 3354; (b) Saitoh, K.; Tanji, H.; Zheng, Y. *Anal. Sci.* **2001**, *17*, i1511.
18. Cantú, R.; Stencel, J. R.; Czernuszewicz, R. S.; Jaffé, P. R.; Lash, T. D. *Environ. Sci. Technol.* **2000**, *34*, 192.
19. Ocampo, R.; Callot, H. J.; Albrecht, P. *J. Chem. Soc., Chem. Commun.* **1985**, 200.
20. (a) Smith, K. M. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: New York, NY, 2003; Vol. 13, Chapter 81; (b) Blankenship, R. E. *J. Bacteriol.* **2004**, *186*, 5187.
21. Callot, H. J.; Ocampo, R.; Albrecht, P. *Energy Fuels* **1990**, *4*, 635.
22. Fischer, H.; Hofmann, H. J. *Justus Liebigs Ann. Chem.* **1935**, *517*, 274.
23. Flaugh, M. E.; Rapoport, H. *J. Am. Chem. Soc.* **1968**, *90*, 6877.
24. (a) Chaudry, I. A.; Clezy, P. S.; Mirza, A. H. *Aust. J. Chem.* **1980**, *33*, 1095; (b) Smith, K. M.; Langry, K. C.; Minnetian, O. M. *J. Org. Chem.* **1984**, *49*, 4602; (c) Bauder, C.; Ocampo, R.; Callot, H. J. *Tetrahedron* **1992**, *48*, 5135.
25. (a) Clezy, P. S.; Fookes, C. J. R.; Prashar, J. K.; Salek, A. *Aust. J. Chem.* **1992**, *45*, 703; (b) Bong, I. C. C.; Clezy, P. S.; Fookes, C. J. R.; Prashar, J. K.; Salek, A. *Aust. J. Chem.* **1993**, *46*, 1193; (c) Clezy, P. S.; Leung, C. W. F. *Aust. J. Chem.* **1993**, *46*, 1705; (d) Atkinson, E. J.; Clezy, P. S.; Leung, C. W. F.; Ramadan, S.; Salek, A.; Zhuo, M. *Aust. J. Chem.* **1995**, *48*, 1873; (e) Clezy, P. S.; Salek, A. *Aust. J. Chem.* **1996**, *49*, 265.
26. Baker, E. W.; Corwin, A. H.; Klesper, E.; Wei, P. E. *J. Org. Chem.* **1968**, *33*, 3144.
27. Verne-Mismer, J.; Ocampo, R.; Callot, H. J.; Albrecht, P. *Tetrahedron Lett.* **1986**, *27*, 5257; Verne-Mismer, J.; Ocampo, R.; Callot, H. J.; Albrecht, P. *Tetrahedron Lett.* **1988**, *29*, 371; Bauder, C.; Ocampo, R.; Callot, H. J. *Synlett* **1990**, 335.
28. (a) Smith, N. W.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 188; (b) Smith, N. W.; Smith, K. M. *Energy Fuels* **1990**, *4*, 675.
29. Lash, T. D. *Advances in Nitrogen Heterocycles*; Moody, C. J., Ed.; JAI: Greenwich, CT, 1995; Vol. 1, pp 19–51.
30. (a) Lash, T. D. *Org. Geochem.* **1989**, *14*, 213; (b) Lash, T. D.; Balasubramaniam, R. P.; Catarello, J. J.; Johnson, M. C.; May, D. A., Jr.; Bladel, K. A.; Feeley, J. M.; Hoehner, M. C.; Marron, T. G.; Nguyen, T. H.; Perun, T. J., Jr.; Quizon, D. M.; Shiner, C. M.; Watson, A. *Energy Fuels* **1990**, *4*, 668.
31. (a) Lash, T. D.; Bladel, K. A.; Shiner, C. M.; Zajeski, D. L.; Balasubramaniam, R. P. *J. Org. Chem.* **1992**, *57*, 4809; (b) Lash, T. D.; Balasubramaniam, R. P. *Tetrahedron Lett.* **1990**, *31*, 7545; (c) Lash, T. D. *Tetrahedron Lett.* **1988**, *29*, 6877; (d) Lash, T. D. *Tetrahedron* **1998**, *54*, 359; (e) Shiner, C. M.; Lash, T. D. *Tetrahedron* **2005**, *61*, 11628.
32. (a) Lash, T. D.; Johnson, M. C. *Tetrahedron Lett.* **1989**, *30*, 5697; (b) Lash, T. D.; Perun, T. J., Jr. *Tetrahedron Lett.* **1987**, *28*, 6265; (c) Bastian, J. A.; Lash, T. D. *Tetrahedron* **1998**, *54*, 6299.
33. Lash, T. D.; Catarello, J. J. *Tetrahedron* **1993**, *49*, 4159.
34. Quizon-Colquitt, D. M.; Lash, T. D. *J. Heterocycl. Chem.* **1993**, *30*, 477.
35. Arsenault, G. P.; Bullock, E.; MacDonald, S. F. *J. Am. Chem. Soc.* **1960**, *82*, 4384.

36. Smith, K. M. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: San Diego, CA, 2000; Vol. 1, pp 119–148.
37. (a) Dolphin, D.; Harris, R. L. N.; Huppatz, J. L.; Johnson, A. W.; Kay, I. T.; Leng, J. *J. Chem. Soc.* **1966**, 98; (b) Grigg, R.; Johnson, A. W.; Kenyon, R.; Math, V. B.; Richardson, K. *J. Chem. Soc. C* **1969**, 176; (c) Smith, K. M.; Minnetian, O. M. *J. Org. Chem.* **1985**, *50*, 2073.
38. Preliminary communication: Li, W.; Lash, T. D. *Tetrahedron Lett.* **1998**, *39*, 8571.
39. These results were presented, in part, at the following meetings: (a) Quizon-Colquitt, D. M.; Lash, T. D. *Book of Abstracts*, 203rd National American Chemical Society Meeting, San Francisco, CA, April 1992; ORGN 28; (b) Lash, T. D.; Li, W. *Symposium on the Role of Nickel in Catalytic and Biological Chemistry*, 5th Chemical Congress of North America, Cancun, Mexico, November 1997; Abstract No. 1384. (c) Lash, T. D. *Symposium on the Geochemistry of Porphyrins*, 1st International Conference on Porphyrins and Phthalocyanines (ICPP-1), Dijon, France, June 2000; Abstract No. SYM 123.
40. Jackson, A. H.; Kenner, G. W.; Smith, K. M. *J. Chem. Soc. C* **1971**, 502.
41. Milton, C.; Dwornik, E. J.; Estep-Barnes, P. A.; Finkelman, R. B.; Pabst, A.; Palmer, S. E. *Am. Mineral.* **1978**, *63*, 930; Storm, C. B.; Krane, J.; Skjetne, T.; Telnaes, N.; Branthaver, J. F.; Baker, E. W. *Science* **1984**, *223*, 1075.
42. Unfortunately, cyclizations using trimethyl orthoacetate were not successful in our hands, and the synthesis of *meso*-methyl petroporphyrins by this approach has not been further investigated.
43. Gribble, G. W. Knorr and Paal–Knorr Pyrrole Syntheses. In *Name Reactions in Heterocyclic Chemistry*; Li, J. J., Ed.; Wiley: Hoboken, NJ, 2005; pp 79–88.
44. Novak, B. H.; Lash, T. D. *J. Org. Chem.* **1998**, *63*, 3998.
45. Gribble, G. W. Barton–Zard Reaction. In *Name Reactions in Heterocyclic Chemistry*; Li, J. J., Ed.; Wiley: Hoboken, NJ, 2005; pp 70–78.
46. (a) Paine, J. B., III; Dolphin, D. *J. Org. Chem.* **1985**, *50*, 5598; (b) May, D. A., Jr.; Lash, T. D. *J. Org. Chem.* **1992**, *57*, 4820.
47. Jackson, A. H.; Pandey, R. K.; Rao, K. R. N.; Roberts, E. *Tetrahedron Lett.* **1985**, *26*, 793.
48. Burns, D. H.; Burden, M. W.; Li, Y. H. *J. Porphyrins Phthalocyanines* **1998**, *2*, 295.
49. Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. *Aust. J. Chem.* **1969**, *22*, 229.
50. Lash, T. D. *Chem.—Eur. J.* **1996**, *2*, 1197.
51. (a) Lin, Y.; Lash, T. D. *Tetrahedron Lett.* **1995**, *36*, 9441; (b) Lash, T. D.; Chandrasekar, P.; Osuma, A. T.; Chaney, S. T.; Spence, J. D. *J. Org. Chem.* **1998**, *63*, 8455; (c) Lash, T. D.; Lin, Y.; Novak, B. H.; Parikh, M. D. *Tetrahedron* **2005**, *61*, 11601.
52. (a) Lash, T. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2533; (b) Lash, T. D.; Richter, D. T.; Shiner, C. M. *J. Org. Chem.* **1999**, *64*, 7973; (c) Lash, T. D.; Colby, D. A.; Graham, S. R.; Chaney, S. T. *J. Org. Chem.* **2004**, *69*, 8851.
53. Czernuszewicz, R. S.; Maes, E. M.; Rankin, J. G. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: San Diego, CA, 2000; Vol. 7, pp 293–337.
54. Rankin, J. G.; Czernuszewicz, R. S.; Lash, T. D. *Org. Geochem.* **1995**, *23*, 419.
55. (a) Rankin, J. G.; Czernuszewicz, R. S.; Lash, T. D. *Inorg. Chem.* **1995**, *34*, 3025; (b) Czernuszewicz, R. S.; Rankin, J. G.; Lash, T. D. *Inorg. Chem.* **1996**, *35*, 199; (c) Rankin, J. G.; Cantú, R.; Czernuszewicz, R. S.; Lash, T. D. *Org. Geochem.* **1999**, *30*, 201; (d) Boggess, J. M.; Czernuszewicz, R. S.; Lash, T. D. *Org. Geochem.* **2002**, *33*, 1111.
56. For related studies on coal porphyrins, see: (a) Xu, K.; Rankin, J. G.; Lash, T. D. *Vib. Spectrosc.* **1998**, *18*, 157; (b) Xu, K.; Rankin, J. G.; Lash, T. D. *Vib. Spectrosc.* **1998**, *18*, 175.
57. (a) Rankin, J. G. Ph.D. Dissertation, University of Houston, 1993; (b) Meloni, P. A. Ph.D. Dissertation, University of Houston, 1997; (c) Cantú, R. Ph.D. Dissertation, University of Houston, 1999.
58. Lash, T. D.; Quizon-Colquitt, D. M.; Shiner, C. M.; Nguyen, T. H.; Hu, Z. *Energy Fuels* **1993**, *4*, 668.
59. Cavaleiro, J. A. S.; Rocha Gonsalves, A. M. d'A.; Kenner, G. W.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1771.
60. (a) Krane, J.; Skjetne, T.; Telnaes, N.; Bjoroy, M.; Schou, L.; Solli, H. *Org. Geochem.* **1984**, *6*, 193; (b) Clezy, P. S.; Mirza, A. H.; Prashar, J. K. *Aust. J. Chem.* **1990**, *43*, 857; (c) Hu, Z.; Lash, T. D. *Synlett* **1994**, 909.
61. Zhang, B.; Lash, T. D. *Tetrahedron Lett.* **2003**, *44*, 7253.
62. Lash, T. D. *J. Porphyrins Phthalocyanines* **1997**, *1*, 29.
63. The initial low yielding synthesis of **18a**, reported in Ref. 58, was therefore completed several years before this natural product was discovered in Kupferschiefer.[65]
64. Keely, B. J.; Maxwell, J. R. *Org. Geochem.* **1993**, *20*, 1217.
65. Gibbison, R.; Peakman, T. M.; Maxwell, J. R. *Tetrahedron Lett.* **1995**, *36*, 9057.
66. See also: Squier, A. H.; Hodgson, D. A.; Keely, B. J. *Org. Geochem.* **2002**, *33*, 1655.
67. Ellis, J.; Jackson, A. H.; Jain, A. C.; Kenner, G. W. *J. Chem. Soc.* **1964**, 1935.
68. Baptista de Almeida, J. A. P.; Kenner, G. W.; Rimmer, J.; Smith, K. M. *Tetrahedron* **1976**, *32*, 1793.
69. Barton, D. H. R.; Kervagoret, J.; Zard, S. Z. *Tetrahedron* **1990**, *46*, 7587.