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Porphyrins with Exocyclic Rings. Part 10.[1] Synthesis of *meso*,β-Propanoporphyrins from 4,5,6,7-Tetrahydro-1*H*-indoles.

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Abstract: *Benzyl (**6**) and tert-butyl 3-methyl-4,5,6,7-tetrahydro-1H-indole-2-carboxylates (**28**) were easily prepared from cyclohexanone using a variation of the Knorr pyrrole condensation. Regioselective oxidation with lead tetraacetate gave the corresponding 7-acetoxy derivatives, or related solvolysis products, and subsequent reaction with 5-unsubstituted pyrrole-2-carboxylates in the presence of p-toluenesulfonic acid in acetic acid gave a series of 7-pyrrolyltetrahydroindoles **16** in excellent overall yields. Cleavage of the protective ester units, followed by acid-catalyzed condensation with diformyldipyrrylmethanes **19** under modified MacDonald "2 + 2" conditions gave good yields of meso,β-propanoporphyrins **26**. This chemistry was sufficiently versatile that a porphyrin with two six-membered exocyclic rings (**34**) could be prepared by the same methodology. On the other hand, attempts to cyclize an a,c-biladiene **37** incorporating a six-membered carbocyclic ring gave moderate to poor yields of the required meso,β-propanoporphyrin **26a**, probably due to a deleterious steric interaction between the carbocyclic ring and an adjacent alkyl substituent. Nonetheless, the results described below demonstrate the value of this approach for the synthesis of sedimentary cycloalkanoporphyrins*

INTRODUCTION

Although the presence of metalloporphyrins in organic-rich sediments such as oil shales, petroleum and coal had been demonstrated over sixty years ago,[2] it was only with the advent of mass spectrometry that the structural complexity of these species was recognized.[3] Advances in high performance liquid chromatography and Fourier transform NMR spectroscopy in the early 1980's allowed the isolation and structure determination of individual sedimentary porphyrins (petroporphyrins) and by the end of the decade over fifty porphyrin structures had been identified, primarily from oil shales.[4] The porphyrins from oil shales and petroleum are mostly present as the nickel or vanadyl complexes, although they are often demetallated during isolation and structures are commonly determined for the corresponding free bases. Although the origins of these porphyrins are not always clear, they appear to be mostly derived from the chlorophylls and, to a far lesser extent, the hemes.[5] Porphyrins with exocyclic rings (cycloalkanoporphyrins or CAPs) are particularly common in sedimentary materials. Five-membered exocyclic rings are the most common structural motif, but porphyrins with six-, seven- and more complex exocyclic ring systems have also been discovered.[6]

Petroporphyrins with six-membered exocyclic rings were first described in 1984 by Maxwell and coworkers.[7,8] Vanadyl methylpropanoporphyrins (**1a** and **1b**) of uncertain origin were isolated from the Serpiano oil shale[7] and *meso*,β-propanoporphyrin **2** was tentatively identified in Gilsonite bitumen.[8] The latter porphyrin was subsequently shown to have been misidentified and the correct structure was shown to be **3**.[9] Nonetheless, these reports stimulated our initial interests in this area.[10] It is also noteworthy that the alcoholic

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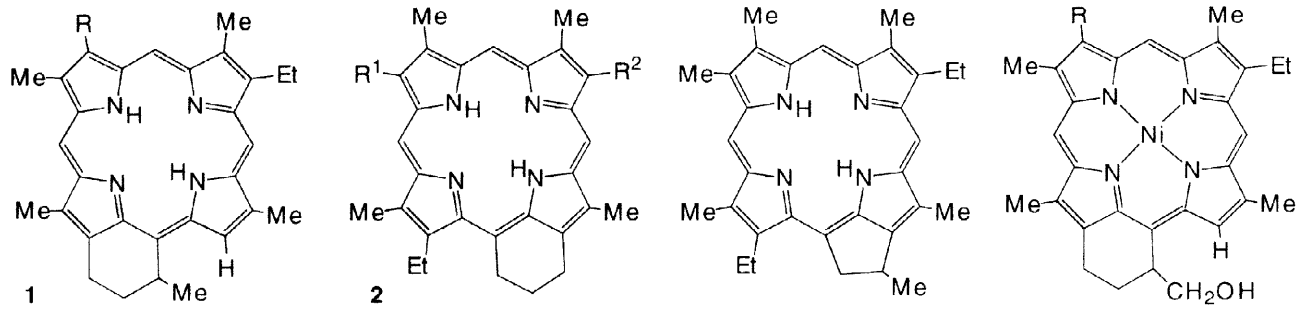
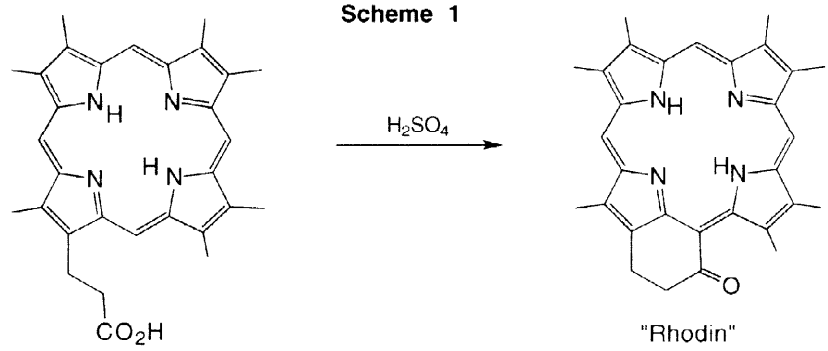
nickel chelates **4a** and **4b** were subsequently isolated from Messel oil shale[11] and it seems likely that these unusual petroporphyrins share a common origin with **1a** and **1b**.[12]



As part of a program to design new synthetic routes to cycloalkanoporphyrins, syntheses of *meso*,β-propanoporphyrins have been developed.[13,14] These studies provide the foundations for the synthesis of naturally occurring petroporphyrins, as well as a range of synthetic analogs.[10,15-20] Synthetic samples of CAPs are of value as standards in the isolation and identification of geoporphyrins, and allow the chemistry and spectroscopic properties of these systems to be explored.[21]

Scheme 1



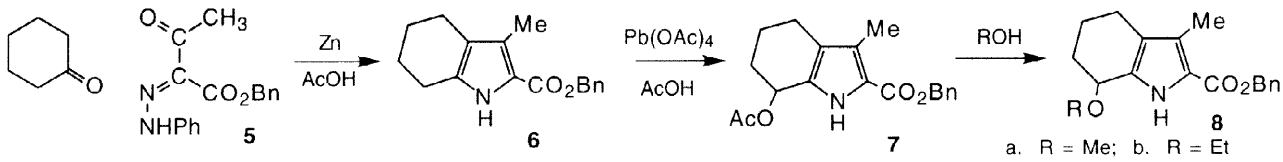
When these studies were initiated, little work had been carried out on the synthesis of porphyrins with six-membered or larger exocyclic rings. Porphyrins with β-propionic acid side-chains were known to cyclize in the presence of fuming sulfuric acid to give rhodins (Scheme 1),[22] and this chemistry has been adapted to the synthesis of methylpropanoporphyrin **1a**.[23] However, multistep synthetic modification of preformed synthetic porphyrins requires careful manipulations by skilled synthetic chemists and may result in relatively poor overall yields. Hence, we chose to introduce the six-membered ring system at an early stage in the synthesis by using 4,5,6,7-tetrahydro-1*H*-indoles as building blocks. The synthesis and chemistry of 4,5,6,7-tetrahydro-1*H*-indoles has been described in an earlier paper in this series.[24] The adaptation of those studies to the synthesis of *meso*,β-propanoporphyrins is described below.

RESULTS AND DISCUSSION

Phenylhydrazone **5** (Scheme 2) was prepared in excellent yield by treating benzyl acetoacetate with benzenediazonium chloride. Condensation of **5** with cyclohexanone in the presence of zinc dust and buffered acetic acid gave the required 4,5,6,7-tetrahydroindole benzyl ester **6**. In order to produce the dipyrrolic intermediates needed for this work, it was necessary to selectively derivatize the 7-position of the 4,5,6,7-tetrahydro-1*H*-indole system. Lead tetraacetate was found to regioselectively oxidize **6** and gave the 7-acetoxy derivative **7** in high yield. Attempts to crystallize **7** from methanol or ethanol gave the corresponding ethers **8a**

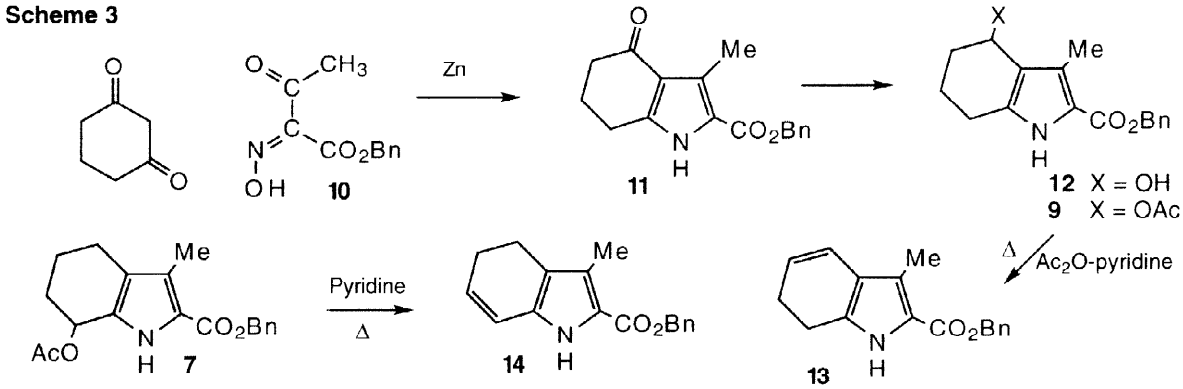
and **8b**, respectively, and this observation indicates that the labile 7-acetoxy derivative must be handled with care. However, crystallization from petroleum ether afforded **7** as a white powder.

Scheme 2



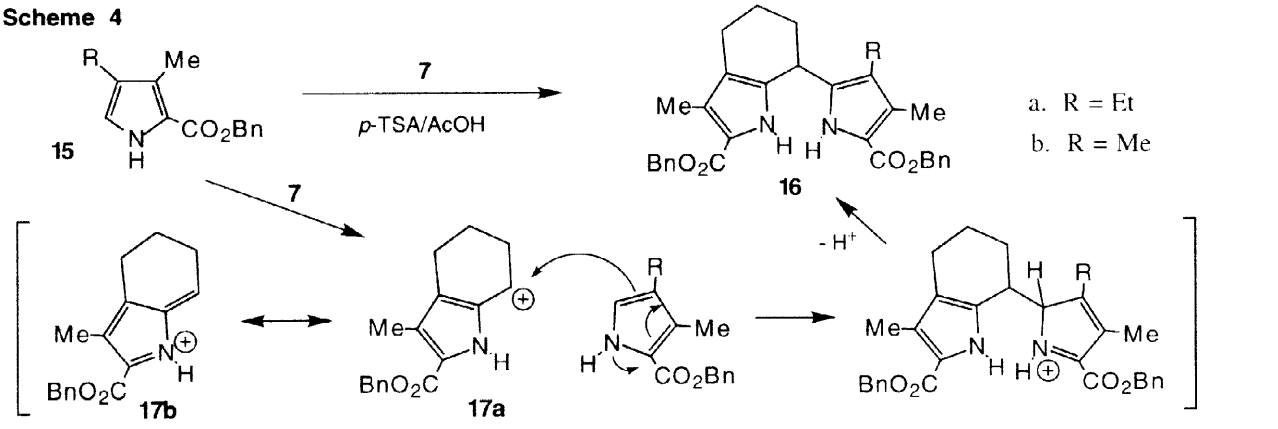
When these early studies were carried out, relatively poor spectroscopic facilities were available to us and the structure of **7** could not be unambiguously assigned. Mechanistic considerations suggested that **7** should be the favored product of this chemistry. However, the data available at that time did not allow this structure to be easily distinguished from the 4-substitution product. In order to confirm the regioselectivity of this reaction, the 4-acetoxy derivative **9** was prepared by the chemistry shown in Scheme 3. Similar studies were carried out independently with several related compounds.[24]

Scheme 3

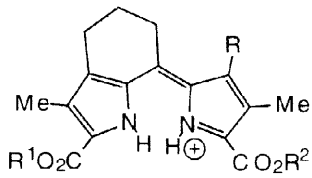


Knorr condensation of 1,3-cyclohexanedione with oxime **10** in the presence of zinc dust, sodium acetate and acetic acid gave the 4-oxo-4,5,6,7-tetrahydroindole **11** (Scheme 3). Reduction with sodium borohydride afforded the corresponding alcohol **12** and subsequent reaction with acetic anhydride in pyridine at room temperature yielded the required acetate **9**. Comparisons of **7** and **9** by mp, IR, ^{1}H NMR and ^{13}C NMR demonstrated that these were indeed different compounds and confirmed the earlier structure assignments. Treatment of **9** or **12** with refluxing acetic anhydride-pyridine gave the dihydroindole **13**. Similarly, **7** eliminated acetic acid under the same conditions to give the isomeric 4,5-dihydroindole **14**.

Scheme 4



Acetoxytetrahydroindole **7** condensed with 5-unsubstituted pyrroles **15a** and **15b** in the presence of *p*-toluenesulfonic acid in acetic acid to give the 7-pyrrolyltetrahydroindoles **16a** and **16b**, respectively, in good yields (Scheme 4). Protonation of **7**, followed by loss of acetic acid, would give the stabilized carbocation **17** and subsequent electrophilic substitution of **15a** or **15b** affords the dipyrroles **16**. In common with dipyrrylmethanes,[25] these dipyrroles can easily be detected on a tlc plate by developing it in the presence of bromine vapor. A red spot forms immediately, presumably due to the formation of the oxidized, fully conjugated species **18**. Dipyrroles incorporating five-membered, seven-membered or larger exocyclic rings may also be detected in this way.



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The NMR properties of these dipyrroles were fairly straightforward, but it is noteworthy that the single chiral center linking the two pyrrole moieties has far ranging effects. For pyrrolyltetrahydroindole **16a**, the methylene units of both terminal benzyl esters were sufficiently diastereotopic to produce two overlapping AB quartets near 5.2 ppm (Fig. 1), although the degree of resolution and coupling was somewhat concentration and solvent dependent. This feature has been less commonly observed for dipyrroles incorporating other ring sizes.

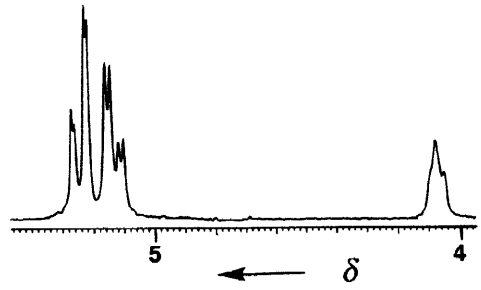
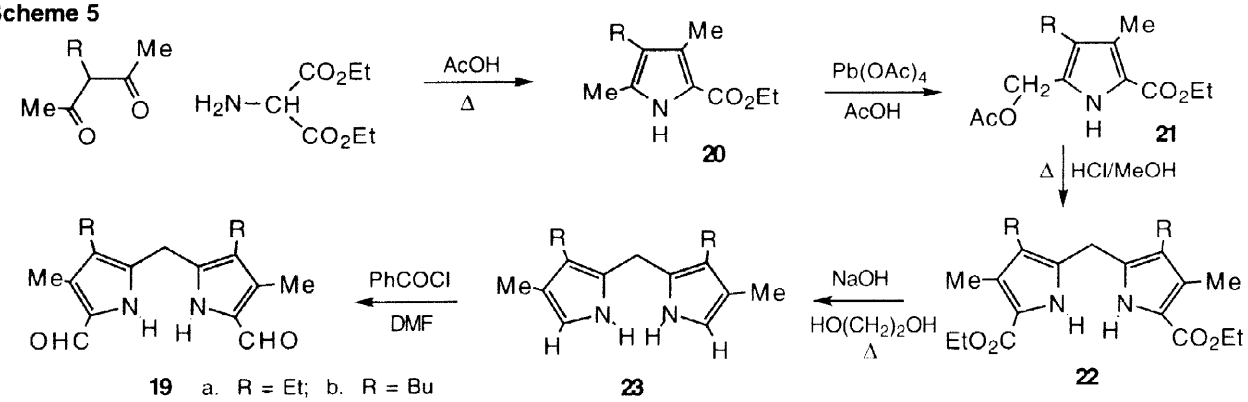


Figure 1: Partial 300 MHz Proton NMR Spectrum of **16a** in $CDCl_3$.

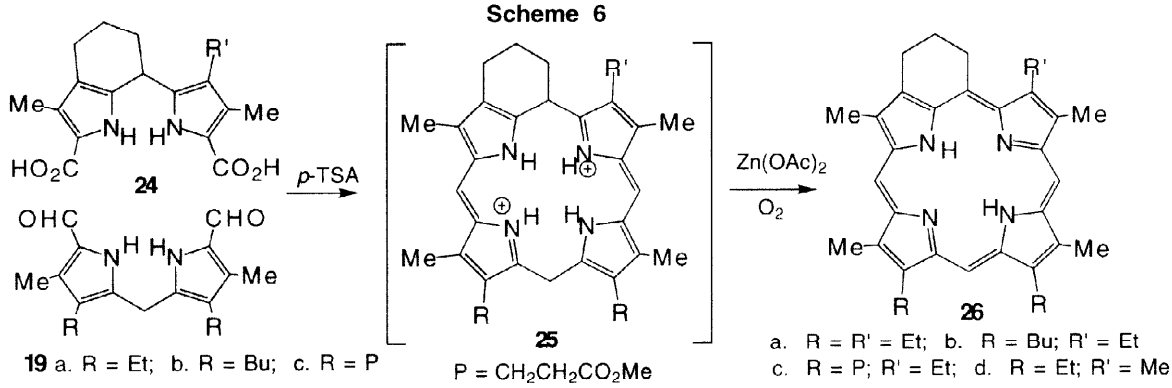
Scheme 5



In order to complete the synthesis of *meso*,β-propanoporphyrins, other pyrrolic intermediates were required. Diformyldipyrrylmethanes **19** are important intermediates in the synthesis of porphyrins by the MacDonald "2 + 2" condensation. Over the years, we have fine tuned the synthetic methodology for preparing these valuable compounds. Pyrrole esters **20** (Scheme 5) are readily available from the condensation of diethyl aminomalonate with β-diketones in refluxing acetic acid.[26] Reaction with lead tetraacetate affords the related acetoxymethylpyrroles **21** and subsequent self-condensation with concentrated hydrochloric acid in refluxing methanol affords the dipyrrylmethane diethyl esters **22** in excellent yields. Treatment with sodium hydroxide in ethylene glycol at 180°C under nitrogen saponifies and decarboxylates the ethyl ester moieties to give the α,α'-diunsubstituted dipyrrylmethanes **23**. Using a modification of the Vilsmeier formylation,[27] dipyrrylmethanes **23** were treated with benzoyl chloride and DMF, and the resulting diimine salts were collected after precipitation with toluene. Hydrolysis with sodium carbonate in ethanol-water then afforded the required dialdehydes **19**.

Hydrogenolysis of the benzyl esters of **16a** or **16b** over 10% palladium-charcoal gave the corresponding dicarboxylic acids **24** (Scheme 6). Dipyrrole **24a** condensed with diformyldipyrrylmethanes **19a-c** in the presence of *p*-toluenesulfonic acid in methanol-dichloromethane, followed by air oxidation. Under these modified conditions for the MacDonald condensation, porphodimethenes **25** appear to be formed initially (as judged by uv-vis spectrophotometry, e.g. Fig. 2) and little of the cycloalkanoporphyrins **26** seem to be present prior to the addition of zinc acetate. The dication resists oxidation due to the crowding in the internal cavity which is exacerbated on formation of the more planar porphyrin system. The zinc acetate acts in part as a buffer, but it may also be that the corresponding zinc porphodimethene complex undergoes air oxidation more easily than the free base. In MacDonald condensations where the carbocyclic ring is absent, 3 hr is usually sufficient for oxidation to be complete.[28] In the reactions under discussion, longer oxidation times are necessary (as indicated by the growth of the diagnostic Soret band near 400 nm, see Fig. 2), almost certainly due to the increase in steric congestion at the periphery between the exocyclic ring and substituent R in the near planar porphyrin system. The zinc porphyrins that result can easily be demetallated with TFA or 5% sulfuric acid/methanol. Following chromatography on alumina and recrystallization, overall yields of porphyrin were consistently in the range of 20-28%. Dipyrrole **24b** similarly condensed with **19a** to give *meso*,β-propanoporphyrin **26d** in 21% yield. The electronic spectra of porphyrins **26a-d** were similar to those for *meso*-alkylporphyrins, exhibited a strong Soret band near 402 nm and phyllo-type Q band region (Fig. 3A; band IV>II>III>I). The proton NMR spectra for **26a-d** were also highly diagnostic, showing 3 singlets for the *meso*-protons near 10 ppm and the internal NH's upfield at -3 to -4 ppm. The propano unit afforded two 2H triplets at 3.8 and 5.1 ppm for the β- and *meso*-CH_2's, respectively, and the middle methylene unit produced an ill resolved quintet near 2.9 ppm.

Scheme 6



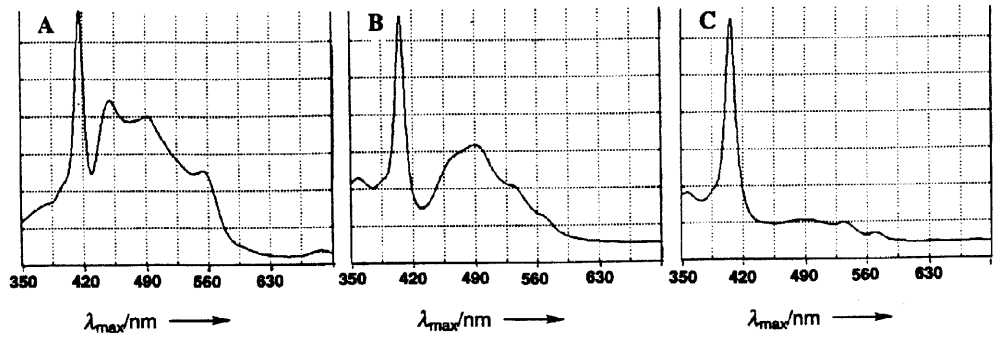


Figure 2: Uv-vis spectra for aliquots from a typical MacDonald condensation for porphyrins **26**: A. after reacting with *p*-TSA for 24 hr. B. 3 hr after addition of $Zn(OAc)_2$. C. 48 hr after addition of $Zn(OAc)_2$; note development of the Soret band near 400 nm.

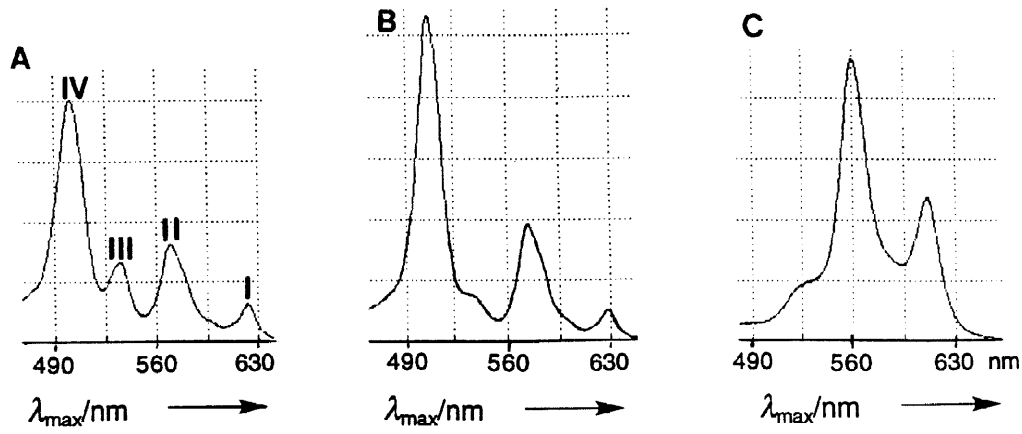
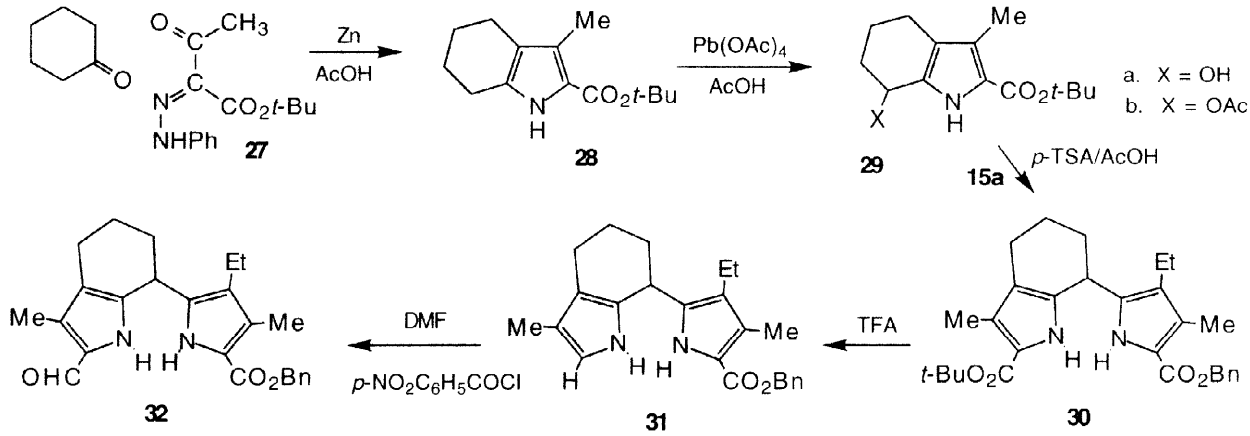


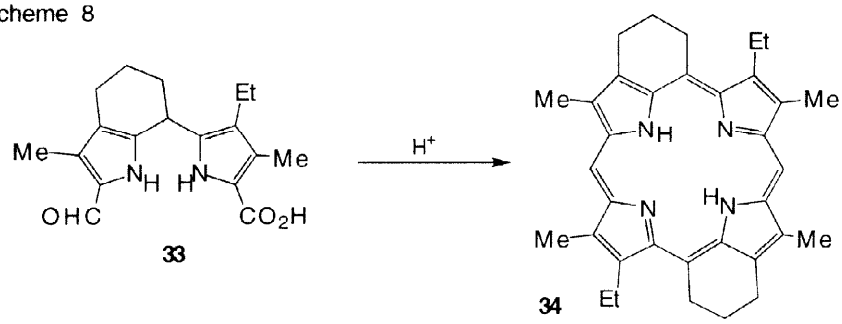
Figure 3: Selected electronic spectra (Soret bands excluded) for *meso*,β-propanoporphyrins. A. Porphyrin **26a** in CH_2Cl_2; B. Dipropanoporphyrin **34** in CH_2Cl_2; C. Dication of **34** in 5% TFA-CH_2Cl_2.

The yields obtained in the MacDonald condensations described above demonstrate that the six-membered carbocyclic ring does not significantly impede this chemistry. Therefore, this study was extended to investigate the synthesis of a centrosymmetric porphyrin with two exocyclic rings. *tert*-Butyl acetoacetate reacted with benzenediazonium chloride to give phenylhydrazone **27** (Scheme 7). Subsequent reaction with cyclohexanone and zinc dust in acetic acid yielded the pyrrole *tert*-butyl ester **28**. A solution of tetrahydroindole **28** in acetic acid was stirred with lead tetraacetate at room temperature for 3 hr and the reaction mixture was poured into ice-water. The resulting precipitate was recrystallized to give the 7-hydroxy derivative **29a** and this species was presumably formed by hydrolysis of the related acetate **29b**. When the reaction was carried out using dichloromethane as the solvent, the acetate **29b** could be isolated in excellent yields. In any case, the alcohol **29a** reacted smoothly with α-free pyrrole **15a** in the presence of *p*-toluenesulfonic acid to give the dipyrrolic mixed ester **30**. Cleavage of the *tert*-butyl ester with TFA afforded the α-unsubstituted dipyrrole **31**, and subsequent formylation with *p*-nitrobenzoyl chloride-DMF gave the aldehyde **32** in good overall yield.

Scheme 7



Scheme 8



Benzyl ester **32** was hydrogenolysed over 10% palladium-charcoal to give the corresponding carboxylic acid **33** (Scheme 8). Head-to-tail self-condensation occurred under modified MacDonald conditions and following air oxidation and work-up, porphyrin **34** was isolated in 25% yield. In common with many other symmetrical porphyrin systems, **34** was rather insoluble in organic solvents. The visible region of the electronic spectrum for **34** was somewhat unusual showing small bathochromic shifts for the major absorptions and essentially only three Q bands (Fig. 2B). In the presence of trifluoroacetic acid, an inky blue colored dication was generated (Fig. 2C). This species also gave slightly red shifted absorption bands compared to the the dication for propanoporphyrin **26a**. The carbon-13 NMR for diprotonated **34** in TFA-$CDCl_3$ showed the expected degree of symmetry with 7 aliphatic resonances in the range of 11-30 ppm and 9 signals in the downfield region (Figure 4). The unsubstituted *meso*-carbons appeared at 98.3 ppm, as expected for systems of this type,[29] while the ring *meso*-carbons were shifted downfield by nearly 20 ppm to 118 ppm. The latter downfield shift is comparible to those seen for alkyl substituents on simple benzene systems.

In a previously published paper on the synthesis of porphyrins with five-membered exocyclic rings,[18] far poorer yields of porphyrin products were obtained when *tert*-butyl ester **35a** was used in place of dicarboxylic acid **35b** in the MacDonald "2 + 2" condensation. The *tert*-butyl ester **35b** was initially treated with TFA to cleave the ester moiety, and subsequently extracted prior to use in the "2 + 2" condensation. Initial data suggested that the *tert*-butyl ester had been incompletely cleaved and that this resulted in the low yields observed.[18] However, further observations indicated that the primary problem involved decomposition during extraction and isolation. The five-membered carbocyclic ring appears to significantly decrease the stability of these intermediates and the additional handling takes a heavy toll (proton NMR spectroscopy shows considerable decomposition). With this in mind, the robustness of the six-membered ring system was briefly considered. Hydrogenolysis of the benzyl ester **30** over 10% palladium-charcoal afforded the corresponding

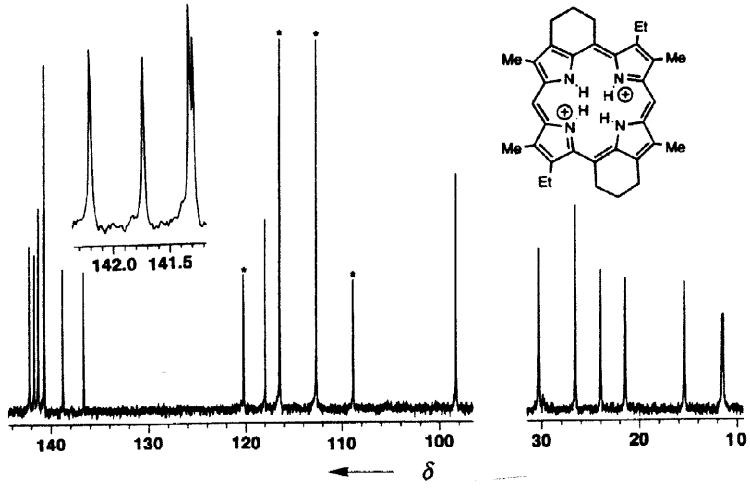
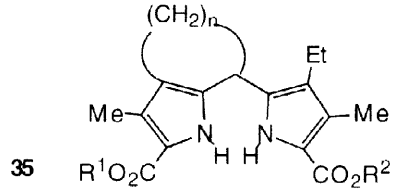


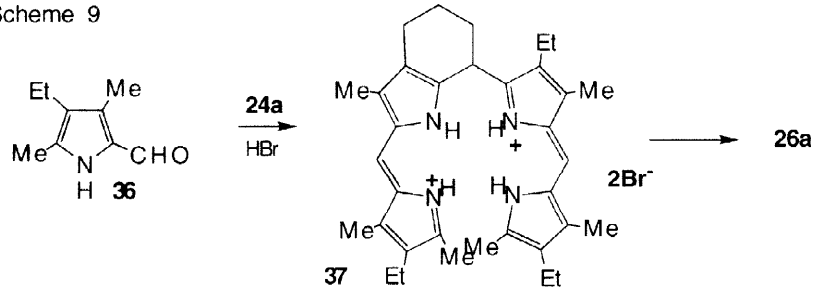
Figure 4: Carbon-13 NMR of dipropanoporphyrin **34** in TFA-$CDCl_3$. Peaks labeled with an asterisk correspond to the TFA.

carboxylic acid **35c**. This intermediate was treated with TFA for 10 min at room temperature, extracted and evaporated to give **35d** as an yellow oil. Condensation of **35d** with diformyldipyrrylmethane **19a** under the standard conditions given above gave the propanoporphyrin **26a** in comparible yields (>20%) to those obtained using dicarboxylic acid **24a**. This result suggests that cyclopenta[*b*]pyrrole intermediates such as **35a** and **35b** are considerably less stable than their ring homologs (e.g. **35c**), and this insight needs to be kept in mind when designing syntheses of petroporphyrins with five-membered exocyclic rings.

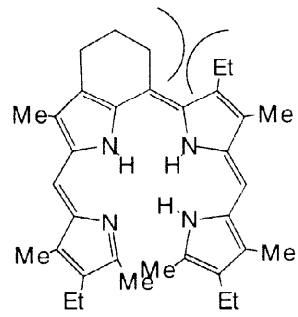


a. n = 2; $R^1 = R^2 = CO_2H$
b. n = 2; $R^1 = CO_2H$; $R^2 = CO_2t$-Bu
c. n = 3; $R^1 = CO_2t$-Bu; $R^2 = CO_2H$
d. n = 3; $R^1 = R^2 = H$

Scheme 9



One of the most versatile methods for preparing porphyrins involves the oxidative cyclization of a,c-biladienes.[30] The possible utility of this approach in the synthesis of *meso*,β-propanoporphyrins was also investigated. Dipyrrole dicarboxylic acid **24a** was decarboxylated with TFA and further reacted with two equivalents of formylpyrrole **36** and hydrobromic acid (Scheme 9). Precipitation with diethyl ether afforded the tetrapyrrolic a,c-biladiene **37** as a brick red powder. a,c-Biladienes are commonly cyclized with copper(II) chloride in DMF. However, **37** gave only trace amounts of impure porphyrin (< 2%) under these conditions. Treatment of **37** with copper(II) acetate in pyridine gave slightly improved yields (3% of **26a** after demetallation and purification), but this approach is greatly inferior to the results obtained for the MacDonald condensation. Smith and Minnetian reported[31] several alternative methods for the cyclization of a,c-biladienes, including the use of silver iodate-zinc acetate in DMF, and this latter procedure increased yields of **26a** to 12%. It should be noted, however, that longer reaction times were required for our system compared to the literature procedure. The improvement in yield may be due to the less harsh conditions involved, which possibly slows down the rate at which **37** undergoes decomposition and thereby allows more time for cyclization to occur. Even so, this result is only marginally useful. Cyclizations of a,c-biladienes are known to occur via bilatrienes[32] (in this case structure **38**) and this conversion would vastly increase the amount of steric congestion between the exocyclic ring and the alkyl substituent. This steric interaction is likely to twist the conformation of the tetracyclic intermediate so that the geometry is less well suited for cyclization to occur, and this presumably leads to the poor yields observed. This is not a problem for the MacDonald condensation because the bridging carbon atom bearing the propano unit is sp^3 hybridized during the critical cyclization step (Scheme 6) and this relieves most of the deleterious steric interactions involved.



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CONCLUSIONS

Regioselective oxidation of 4,5,6,7-tetrahydro-1*H*-indole-2-carboxylates with lead tetraacetate gives high yields of 7-acetoxy derivatives, or the related solvolysis products, and these compounds undergo acid-catalyzed condensations with α-unsubstuted pyrroles to give 7-pyrrolyltetrahydroindoles. Using the MacDonald condensation, 5 examples of *meso*,β-propanoporphyrins, including a dipropanoporphyrin, have been prepared in excellent yields. Attempts to prepare *meso*,β-propanoporphyrins by the cyclization of an a,c-biladiene were only marginally successful, probably due to steric crowding between the carbocyclic ring and the adjacent alkyl substituent. While steric factors must be considered, these results provide the basic groundwork for synthesizing sedimentary porphyrins with six-membered or larger exocyclic rings, as well as more complex porphyrin systems.

EXPERIMENTAL

Hydrogenations were carried out using a Parr hydrogenator at 30-40 psi. Chromatography was performed using Grade 3 neutral alumina or 70-230 mesh silica gel. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 710B spectrometer or a Perkin-Elmer 1600 Series FT-IR Spectrometer. UV spectra were obtained on a Beckmann DU-40 spectrophotometer. NMR spectra were recorded on a Hitachi-Perkin Elmer R24B 60 MHz nmr spectrometer or a Varian Gemini-300 nmr spectrometer; partial funding for two 300 MHz NMR spectrometers was provided by the National Science Foundation under Grant Numbers CHE-9001175 and DUE-9452437. Mass spectral determinations were made at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln with partial support by the National Science Foundation, Biology Division (Grant No. DIR9017262), the Mass Spectral Laboratory, School of Chemical Sciences, University of Illinois at Urbana-Champaign, supported in part by a grant from the National Institute of General Medical Sciences (GM 27029) or at the Washington University Mass Spectrometry Resource, supported by a grant from the National Institutes of Health (RR00954). Elemental analyses were obtained from Micro-Analysis, Inc., Wilmington, DE 19808, or the School of Chemical Sciences Microanalysis Laboratory at the University of Illinois.

Benzyl 2,3-Dioxobutanoate-2-phenylhydrazone (5). Distilled aniline (100.0 g) was added to a mixture of concentrated hydrochloric acid (225 mL) and water (225 mL) in a 2L Erlenmeyer flask. Sodium nitrite (80.00 g) in water (350 mL) was added dropwise to the stirred aniline solution, while maintaining the temperature below 10°C with the aid of a salt/ice bath. Once the addition was complete, the diazonium salt solution was neutralized to congo red with a saturated sodium acetate solution.

In a 4L Erlenmeyer flask, a solution of sodium acetate (130.0 g) in water (225 mL) was added to a mixture of benzyl acetoacetate (127 mL) in 95% ethanol (800 mL). The mixture was cooled to 10°C in a salt-ice bath, and the diazonium salt solution was then added slowly over several minutes. After the addition was complete, the mixture was stirred at 0°C for 30 min and then allowed to stand at room temperature for an additional 1 hr. The resulting yellow precipitate was filtered and recrystallized from 95% ethanol to give a dull yellow powder (270.4 g, 91%), mp 95.5-96°C (lit. mp[33] 111.5-113.5°C); IR (nujol mull): ν 1708 (st, sh, C=O); 1691 (st, sh, C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): The presence of two isomers was evident: δ 2.50 (3H, s, $COCH_3$), 5.38 (2H, s, OCH_2), 7.15-7.21 (2H, m), 7.36-7.45 (8H, m) (2 x Ph), 12.74 (1H, br s, NH); 2.59 (3H, s, $COCH_3$), 5.34 (2H, s, OCH_2), 7.15-7.21 (2H, m), 7.36-7.45 (8H, m) (2 x Ph), 14.85 (1H, br s, NH). The syn and anti isomers were present in varying proportions. Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.89; H, 5.45; N, 9.45. Found: C, 68.71; H, 5.59; N, 9.71.

***tert*-Butyl 2,3-Dioxobutanoate-2-phenylhydrazone (27).** The title compound was prepared from *tert*-butyl acetoacetate (158.0 g) by the procedure described above. Recrystallization from ethanol gave the phenylhydrazone (241.4 g; 96%) as bright yellow crystals, mp 85-87°C; ^{1}H NMR ($CDCl_3$): δ 1.58 (6H, s), 1.60 (3H, s) (syn and anti *t*-Bu), 2.47 (2H, s), 2.55 (1H, s) (syn and anti $COCH_3$), 7.14 (2H, m), 7.3-7.4 (8H, m) (2 x Ph), 12.63 ($^2/_3$H, br s), 14.62 ($^1/_3$H, br s) (NH for syn and anti forms in ratio of 2:1). Anal. Calcd. for $C_{14}H_{18}N_2O_3$: C, 64.09; H, 6.93; N, 10.68. Found: C, 64.80; H, 7.09; N, 10.99.

Benzyl 3-Methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (6). Cyclohexanone (9.80 g), sodium acetate (25.0 g) and glacial acetic acid (150 mL) were placed in a 2 L Erlenmeyer flask and the stirred mixture heated on an oil bath to 100°C. A solution of phenylhydrazone **9a** (29.60 g) in acetic acid (150 mL) was added slowly to the foregoing mixture, whilst simultaneously adding small portions of zinc dust (30 g) and maintaining the temperature of the reaction mixture between 105-110°C. After the addition was complete, the reaction mixture was stirred at 110°C for 1 hr. The mixture was cooled to 70°C and the solution decanted from the excess zinc into an ice/water slurry (2 L). The residues were washed several times with acetone and the resulting solutions decanted into the ice/water mixture. A yellow precipitate formed which was filtered, washed well with water and recrystallized from

ethanol-water to give the pyrrole benzyl ester (11.92 g; 44%) as white crystals, mp 104-105°C; IR (nujol mull): ν 3296 (NH str.), 1660 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.74 (4H, m, 5,6-CH_2), 2.24 (3H, s, pyrrole-CH_3), 2.38 (2H, br t, 4-CH_2), 2.51 (2H, br t, 7-CH_2), 5.29 (2H, s, OCH_2Ph), 7.28-7.40 (5H, m, Ph), 8.8 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.55, 10.60, 21.22, 23.04, 23.43, 65.49, 116.92, 119.94, 126.59, 128.09, 128.44, 128.64, 133.01, 136.95, 161.85. Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.80; H, 7.12; N, 5.20. Found: C, 75.93; H, 7.27; N, 5.15.

***tert*-Butyl 3-Methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (28).** The title pyrrole was prepared from cyclohexanone (9.80 g) and phenylhydrazone **9b** (26.20 g) by the procedure described above. Recrystallization from ethanol gave the pyrrole (8.91 g; 38%) as white crystals, mp 149-150°C; IR (nujol mull): ν 3316 (NH str.), 1660 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.57 (9H, s, *t*-Bu), 1.77 (4H, m, 5,6-CH_2), 2.21 (3H, s, pyrrole-CH_3), 2.40 (2H, t, J = 5.4 Hz, 4-CH_2), 2.57 (2H, t, J = 5.4 Hz, 7-CH_2), 8.8 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.34, 21.23, 23.04, 23.14, 23.47, 28.71, 80.14, 118.79, 119.75, 125.25, 131.88, 161.98. Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.44; H, 9.01; N, 5.95. Found: C, 71.37; H, 8.95; N, 5.91.

Benzyl 7-Acetoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (7). Lead tetraacetate (3.46 g; 1.05 equivalents) was added in one portion to a stirred solution of benzyl 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (2.00 g) in acetic acid (20 mL)-acetic anhydride (1 mL). The mixture was stirred for 2 hr at room temperature, poured into ice/water and extracted with dichloromethane. The organic solutions were dried over sodium sulfate and evaporated under reduced pressure to give the desired acetoxy compound as a yellow oil (quantitative). Crystallization from dichloromethane-petroleum ether (60-90°) gave the 7-acetoxytetrahydroindole (2.08 g; 86%) as off-white crystals, mp 116.5-117.5°C; IR (nujol mull): ν 3306 (NH str.), 1724, 1678 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.86 (4H, m, 5,6-CH_2), 2.05 (3H, s, acetoxy-CH_3), 2.24 (3H, s, pyrrole-CH_3), 2.24-2.35 (1H, m), 2.5-2.6 (1H, m) (4-CH_2), 5.24-5.36 (2H, AB quartet, J = 12.6 Hz, OCH_2Ph), 5.65 (1H, br t, CHOAc), 7.28-7.40 (5H, m, Ph), 9.2 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.37, 19.36, 21.05, 29.21, 65.41, 65.74, 119.13, 122.82, 125.23, 128.18, 128.69, 129.39, 136.67, 161.49, 172.56. Anal. Calcd. for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.77; H, 6.29; N, 4.14.

Benzyl 7-Methoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (8a). Crystallization of the foregoing crude acetoxytetrahydroindole from methanol gave the corresponding methyl ether as white crystals, mp 102-104°C; IR (nujol mull): ν 3299 (NH str.), 1672 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.65-1.75 (1H, m), 1.78-1.88 (1H, m) (5-CH_2), 1.9-2.0 (2H, m, 6-CH_2), 2.24 (3H, s, pyrrole-CH_3), 2.3-2.48 (2H, m, 4-CH_2), 3.40 (3H, s, OCH_3), 4.32 (1H, m, CHOMe), 5.31 (2H, AB quartet, OCH_2Ph), 7.3-7.43 (5H, m, Ph), 8.78 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.43, 20.31, 21.12, 28.31, 55.92, 65.73, 72.52, 118.81, 121.87, 126.08, 128.34, 128.39, 128.83, 132.24, 136.96, 161.82. Anal. Calcd. for $C_{18}H_{21}NO_3$: C, 72.20; H, 7.08; N, 4.68. Found: C, 72.17; H, 6.93; N, 4.52.

Benzyl 7-Ethoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (8b). The crude acetoxytetrahydroindole was heated with ethanol for 15 min and recrystallized from ethanol-water to give the corresponding ethoxy derivative as off-white crystals, mp 72-73.5°C; IR (nujol mull): ν 3262 (NH str.), 1667 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.23 (3H, t, J = 7 Hz, CH_2CH_3), 1.7-2.05 (4H, m, CH_2CH_2), 2.23 (3H, s, pyrrole-CH_3), 2.3-2.5 (2H, m, pyrrole-CH_2), 3.52 (1H, m), 3.66 (1H, m) (OCH_2CH_3), 4.41 (1H, br t, CHOEt), 5.30 (2H, AB quartet, CH_2Ph), 7.3-7.42 (5H, m, Ph), 8.73 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.47, 15.72, 20.35, 21.09, 28.94, 63.75, 65.68, 71.03, 118.66, 121.75, 126.03, 128.30, 128.81, 132.63, 136.95, 161.96. Anal. Calcd. for $C_{19}H_{23}NO_3$: C, 72.80; H, 7.41; N, 4.47. Found: C, 73.02; H, 7.37; N, 4.47.

***tert*-Butyl 7-Hydroxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (29a).** Lead tetraacetate (26.30 g; 1.05 equivalents) was added in one portion to a stirred solution of *tert*-butyl 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (13.30 g) in acetic acid (140 mL)-acetic anhydride (4 mL). The mixture was stirred for 16 hr at room temperature, poured into ice/water and the resulting precipitate collected by suction filtration. Recrystallization from ethanol gave the alcohol (7.95 g; 56%) as white crystals, mp 120-123°C; IR (nujol mull): ν 3506 (OH str.), 3277 (NH str.), 1673 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.55 (9H, s, *t*-Bu), 1.79 (2H, m, 5-CH_2), 1.92 (1H, m), 2.01 (1H, m) (6-CH_2), 2.19 (3H, s, pyrrole-CH_3), 2.3-2.45 (2H, m, 4-CH_2), 2.90 (1H, br s, OH), 4.74 (1H, m, CHOH), 9.32 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.41, 20.31, 21.19, 28.62, 33.27, 63.86, 80.61, 120.37, 121.14, 124.64, 133.19, 162.08. Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.89; H, 8.44; N, 5.57. Found: C, 66.44; H, 8.33; N, 5.51.

***tert*-Butyl 7-Acetoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (29b).** Lead tetraacetate (0.99 g; 1.05 equivalents) was added in one portion to *tert*-butyl 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (0.500 g) in dichloromethane (10 mL) and the resulting mixture was stirred for 16 hr at room temperature. The solution was washed with water and 5% sodium bicarbonate solution, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue recrystallized from hexanes to give the acetate (0.485 g; 91%) as off-white crystals, mp 98°C; IR (nujol mull): ν 3335 (NH str.), 1736 (acetate C=O str.), 1675 (pyrrole C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.55 (9H, s, *t*-Bu), 1.86 (2H, m, 5-CH_2), 2.05 (3H, s, acetoxy-CH_3), 2.20 (3H, s, pyrrole-CH_3), 2.24-2.35 (2H, m, 6-CH_2), 2.48 (1H, m), 2.54 (1H, m) (4-CH_2), 5.64 (1H, br t, CHOAc), 8.99 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.16, 19.31, 21.00, 21.35, 28.55, 29.17, 65.43, 80.67, 120.77, 122.67, 123.86, 128.43, 161.43, 172.75. Anal. Calcd. for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 64.85; H, 8.01; N, 4.34.

Benzyl 3-Methyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (11). Benzyl acetoacetate (19.2 g) and acetic acid (25 mL) were placed in a 1 l Erlenmeyer flask and the mixture was cooled in an ice-salt bath to 10°C. A solution of sodium nitrite (10.6 g) in water (25 mL) was added dropwise to the stirred mixture, maintaining the reaction temperature below 15°C throughout. The resulting oxime (**10**) solution was stirred for 3 hr at room temperature.

Sodium acetate (9.0 g), 1,3-cyclohexanedione (10.0 g) and acetic acid (90 mL) were placed in a 500 mL Erlenmeyer flask and heated on a water bath to 60°C. The foregoing oxime solution was added dropwise to the stirred mixture, whilst simultaneously adding zinc dust and maintaining the reaction temperature at 75-80°C. The mixture was heated on a boiling water bath for 1 hr, cooled to 70°C and poured into ice/water. The resulting precipitate was filtered, washed thoroughly with water to remove traces of acetic acid and recrystallized from ethanol to give the desired 4-oxotetrahydroindole (12.15 g; 43%) as shiny white crystals, mp 168.5-170°C (lit. mp[34] 169-170°C); IR (nujol mull): ν 3219 (NH str.), 1706, 1634 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.07 (2H, quintet, 6-CH_2), 2.45 (2H, t, J = 6.3 Hz, 7-CH_2), 2.62 (3H, s, pyrrole-CH_3), 2.75 (2H, t, J = 6.1 Hz, 5-CH_2), 5.33 (2H, s, OCH_2Ph), 7.3-7.4 (5H, m, Ph), 9.80 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 11.70, 23.05, 23.40, 38.94, 66.30, 119.54, 120.59, 128.21, 128.50, 128.86, 129.46, 136.23, 146.21, 162.28, 195.83.

Benzyl 4-Hydroxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (12). Sodium borohydride (0.50 g) was added in one portion to a stirred mixture of benzyl 3-methyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate **11** (0.60 g) in ethanol (8 mL). After stirring for 10 min at room temperature, the mixture was heated on a boiling water bath for 10 min. Water (8 mL) was added and the mixture heated on a boiling water bath for a further 15 min. An additional 20 mL of water was added, the mixture cooled in an ice bath and the resulting precipitate filtered off. Recrystallization from chloroform-petroleum ether (60-90°) gave **12** (0.54 g; 89%) as as white powder, mp 129-130°C; IR (nujol mull): ν 3350 (OH str.), 3318 (NH str.), 1669 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.44 (1H, d, J = 5.4 Hz, OH), 1.75-1.85 (2H, m, 6-CH_2), 1.93-2.0 (2H, m, 5-CH_2), 2.38 (3H, s, pyrrole-CH_3), 2.45-2.52 (1H, m), 2.57-2.65 (1H, m) (7-CH_2), 4.80 (1H, m, *CH*OH), 5.30 (2H, s, OCH_2Ph), 7.3-7.42 (5H, m, Ph), 8.58 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.46, 17.93, 22.87, 32.64, 62.36, 65.76, 118.09, 122.28, 127.37, 128.29, 128.35, 128.83, 134.30, 136.88, 161.92. Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.55; H, 6.72; N, 4.91. Found: C, 71.46; H, 6.54; N, 5.08.

Benzyl 4-Acetoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (9). Acetic anhydride (1.0 mL) was added to a solution of the foregoing hydroxytetrahydroindole (0.50 g) in pyridine (5 mL) and the mixture was allowed to stir at room temperature for 24 hr. The mixture was partitioned between water (15 mL) and dichloromethane (10 mL), the organic phase was separated, and the aqueous solution extracted with dichloromethane (2 x 10 mL). The combined organic solutions were dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was crystallized from hexanes to give the acetate (0.47 g; 82%) as a white powder, mp 96.5-97.5°C; IR (nujol mull): ν 3334 (NH str.), 1737 (acetate C=O str.), 1675 (pyrrole C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.86 (4H, m, $CHC*H*_2C*H*_2$), 2.06 (3H, s, $OCOCH_3$), 2.27 (3H, s, pyrrole-CH_3), 2.45-2.55 (1H, m), 2.3-2.7 (1H, m) (pyrrole-CH_2), 5.31 (2H, s, OCH_2Ph), 5.96 (1H, m, CHOAc), 7.3-7.4 (5H, m, Ph), 9.0 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.48, 18.58, 21.53, 22.78, 29.63, 65.30, 65.89, 118.02, 118.23, 127.28, 128.27, 128.33, 128.78, 135.20, 136.65, 161.65, 170.93. Anal. Calcd. for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.46; N, 4.28. Found: C, 69.52; H, 6.31; N, 4.31.

Benzyl 3-Methyl-6,7-dihydro-1*H*-indole-2-carboxylate (13). Acetic anhydride (1 mL) was added to a solution of benzyl 4-hydroxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (0.50 g) in pyridine (5mL) and the resulting mixture was stirred under reflux for 1 hr. The solution was cooled to room temperature, partitioned between dichloromethane (10 mL) and water (15 mL), the aqueous phase extracted with dichloromethane (2 x 10 mL), and the combined organic solutions dried over sodium sulfate. The solvent was evaporated under reduced pressure to give a light brown solid which was recrystallized from ethanol-water to give the dihydroindole (0.34 g; 72%) as white crystals, mp 104-106°C; IR (nujol mull): ν 3279 (NH str.), 1658 (C=O str.), 1618 (C=C str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (3H, s, pyrrole-CH_3), 2.35-2.40 (2H, m, 6-CH_2), 2.57 (2H, t, J = 8.6 Hz, 7-CH_2), 5.30 (2H, s, OCH_2Ph), 5.62 (1H, dt, J = 9.5 Hz, 4.3 Hz, =*CH*CH_2), 6.37 (1H, dt, ^3J = 9.5 Hz, ^4J = 2 Hz, pyrrole-CH=), 7.3-7.4 (5H, m, Ph), 9.0 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.40, 21.46, 23.73, 65.68, 117.23, 119.85, 120.81, 128.17, 128.51, 128.73, 133.20, 136.84, 161.80. Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.37; H, 6.42; N, 5.24. Found: C, 76.24; H, 6.37; N, 5.34.

Benzyl 3-Methyl-4,5-dihydro-1*H*-indole-2-carboxylate (14). Acetate **7** (0.50 g) was reacted with pyridine-acetic anhydride under the conditions described above. Crystallization from ethanol gave the dihydroindole (0.26 g; 65%) as off-white crystals, mp 113-114°C; IR (nujol mull): ν 3296 (NH str.), 1650 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.27 (3H, s, pyrrole-CH_3), 2.35-2.41 (2H, m, 5-CH_2), 2.57 (2H, t, J = 8.5 Hz, 4-CH_2), 5.31 (2H, s, OCH_2Ph), 5.93 (1H, dt, J = 9.5 Hz, 4.3 Hz, =*CH*CH_2), 6.30 (1H, dt, ^3J = 9.5 Hz, ^4J = 2 Hz, pyrrole-CH=), 7.3-7.4 (5H, m, Ph), 8.76 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.49, 18.92, 24.24, 65.66, 117.63, 118.01, 119.40, 126.40, 128.31, 128.33, 128.83, 129.23, 131.96, 137.06, 161.84. Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.37; H, 6.42; N, 5.24. Found: C, 74.74; H, 6.01; N, 5.18.

Benzyl 7-(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (16a). Benzyl 7-acetoxy-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (**7**; 2.00 g) and benzyl 4-ethyl-3-methylpyrrole-2-carboxylate[35] (**15a**; 1.40 g) were dissolved in glacial acetic acid (40 mL). *p*-Toluenesulfonic acid (80 mg) was added and the resulting mixture stirred at room temperature for 2 hr. The brown solution was diluted with chloroform, washed with water (500 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 residue was recrystallized from ethanol to give the dipyrrole (2.28g; 73%) as a white powder, mp 145-146.5°C; IR (nujol mull): ν 3264 (NH str.), 1657 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.10 (3H, t, J = 7.5 Hz, pyrrole-CH_2CH_3), 1.76 (2H, m, $CH_2CH_2CH_2$), 2.03 (1H, m), 2.10 (1H, m) ($CHCH_2$), 2.24 (3H, s), 2.27 (3H, s) (2 x pyrrole-CH_3), 2.46 (2H, q, J = 7.5 Hz, pyrrole-CH_2CH_3), 2.50 (2H, m, pyrrole-CH_2CH_2), 4.09 (1H, m, bridge-CH), 5.05 (1H, d, 12.7 Hz), 5.07 (1H, d, 12.7 Hz), 5.26 (2H, d, 12.7 Hz) (2 x OCH_2Ph), 7.23-7.40 (10H, m, 2 x Ph), 9.55 (1H, br s), 9.65 (1H, br s) (2 x NH); ^{13}C NMR ($CDCl_3$): δ 10.91, 10.99, 16.46, 17.57, 21.46, 23.13, 32.58, 33.20, 65.69, 117.70, 118.14, 120.88, 124.37, 125.68, 126.70, 127.97, 128.06, 128.64, 132.80, 134.94, 136.75, 161.95, 162.10; ei ms: m/z (% relative abundance) 510 (80%; M^+), 91 (100%). Anal. Calcd. for $C_{32}H_{34}N_2O_4$: C, 75.26; H, 6.72; N, 5.49. Found: C, 74.86; H, 6.61; N, 5.32.

Benzyl 7-(5-Benzyloxycarbonyl-3,4-dimethyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (16b). Prepared from benzyl 3,4-dimethylpyrrole-2-carboxylate[35] (**15b**; 2.00 g) by the procedure detailed above. Recrystallization from ethanol gave the title dipyrrole (3.91 g; 90%) as a white powder, mp 154.5-155.5°C; IR (nujol mull): ν 3254 (NH str.), 1651 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.73 (2H, m, $CH_2CH_2CH_2$), 1.99 (3H, s, 3'-CH_3), 2.0 (1H, m), 2.11 (1H, m) ($CHCH_2$), 2.25 (6H, s, 2 x pyrrole-CH_3), 2.50 (2H, m, pyrrole-CH_2CH_2), 4.09 (1H, m, bridge-CH), 5.09 (1H, d, 12.4 Hz), 5.11 (1H, d, 12.6 Hz), 5.26 (2H, d, 12.7 Hz) (2 x OCH_2Ph), 7.27-7.40 (10H, m, 2 x Ph), 9.35 (1H, br s), 9.45 (1H, br s) (2 x NH); ^{13}C NMR ($CDCl_3$): δ 9.05, 10.96, 11.18, 21.56, 23.11, 31.59, 33.40, 65.68, 117.10, 117.31, 118.08, 120.80, 125.50, 127.14, 127.93, 128.02, 128.63, 132.94, 135.76, 136.74, 162.05, 162.24; ei ms: m/z (% relative abundance) 496 (74%; M^+), 91 (100%). Anal. Calcd. for $C_{31}H_{32}N_2O_4$: C, 74.98; H, 6.49; N, 5.64. Found: C, 74.64; H, 6.34; N, 5.70.

***tert*-Butyl 7-(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (30).** Prepared by the same procedure from **29a** (4.00 g) and benzyl 4-ethyl-3-methylpyrrole-2-carboxylate[35] (**15a**; 3.87 g). Crystallization from chloroform-petroleum ether (60-90°) gave the required dipyrrole (5.92 g; 78%) as a white powder, mp 120.5-121.5°C; IR (nujol mull): ν 3449, 3346 (NH str.), 1698 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.09 (3H, t, J = 7.5 Hz, pyrrole-CH_2CH_3), 1.53 (9H, s, *t*-Bu), 1.75 (2H, m, $CH_2CH_2CH_2$), 1.93 (1H, m), 2.08 (1H, m) ($CHCH_2$), 2.21 (3H, s), 2.30 (3H, s) (2 x pyrrole-CH_3), 2.42 (2H, q, J = 7.5 Hz, pyrrole-CH_2CH_3), 2.46 (2H, m, pyrrole-CH_2CH_2), 4.07 (1H, br t, bridge-CH), 5.22-5.32 (2H, AB quartet, OCH_2Ph), 7.3-7.4 (5H, m, Ph), 8.20 (1H, br s), 8.35 (1H, br s) (2 x NH); ^{13}C NMR ($CDCl_3$): δ 10.41, 10.60, 16.09, 17.14, 21.06, 22.44, 28.56, 31.73, 32.32, 65.57, 80.43, 117.74, 119.81, 120.78, 12.42, 124.53, 127.11, 128.54, 130.45, 133.95, 136.61, 161.50. Anal. Calcd. for $C_{29}H_{36}N_2O_4$: C, 73.08; H, 7.61; N, 5.88. Found: C, 73.31; H, 7.64; N, 5.71.

7-(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxaldehyde (32). Dipyrrole *tert*-butyl ester **30** (2.00 g) was dissolved in trifluoroacetic acid (25 mL) and stirred at 35°C for 10 min. The mixture was poured into dilute aqueous ammonia (300 mL), extracted with chloroform, washed water, and dried over sodium sulfate. Upon evaporation, the 2-unsubstituted dipyrrole **31** was obtained as a pale yellow oil in quantitative yield. ^1H NMR ($CDCl_3$): δ 1.13 (3H, t, CH_2CH_3), 1.7-2.1 (4H, m, CH_2CH_2), 2.05 (3H, s), 2.34 (3H, s) (2 x pyrrole-CH_3), 2.3-2.7 (4H, m, 2 x pyrrole-CH_2), 4.12 (1H, m, bridge-CH), 5.29 (2H, s, CH_2Ph), 6.43 (1H, s, pyrrole-H), 7.3-7.5 (6H, m, Ph and NH), 8.4 (1H, br s, NH). The residue was dissolved in DMF (7.6 mL) and cooled to 0°C. A solution of *p*-nitrobenzoyl chloride (1.12 g) in N,N-dimethylformamide (1.2 mL) was added dropwise to the stirred solution, maintaining the temperature of the reaction mixture below 5°C throughout. Once the addition was complete, the mixture was stirred for 15 min. Anhydrous ether (12 mL) was added and the mixture was allowed to stand for 15 min. The resulting yellow precipitate was filtered off and washed well with ether. The solid was taken up in ethanol (12 mL) and stirred with sodium carbonate (1.16 g) in water (12 mL) at 70°C for 15 min. The resulting solution was poured onto a slurry of crushed ice and water (70 mL) and the precipitate suction filtered. Recrystallization from ethanol gave the title aldehyde (1.31; 77%) as off-white microneedles, mp 158-159.5°C; IR (nujol mull): ν 3255, 3200 (NH str.), 1665 (ester C=O str.), 1636 (aldehyde C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.14 (3H, t, J = 7.5 Hz, pyrrole-CH_2CH_3), 1.7-1.86 (2H, m, $CH_2CH_2CH_2$), 2.0-2.14 (2H, m, $CHCH_2$), 2.22 (3H, s), 2.29 (3H, s) (2 x pyrrole-CH_3), 2.47 (2H, q, J = 7.5 Hz, pyrrole-CH_2CH_3), 2.50 (2H, m, pyrrole-CH_2CH_2), 4.07 (1H, m, bridge-CH), 5.04 (1H, d, 12.7 Hz), 5.25 (1H, d, 12.7 Hz) (OCH_2Ph), 7.3-7.4 (5H, m, Ph), 9.07 (1H, s, CHO), 9.82 (1H, br s), 10.36 (1H, br s) (2 x NH); ^{13}C NMR ($CDCl_3$): δ 8.86, 10.89, 15.98, 17.41, 21.06, 22.96, 32.11, 33.24, 65.78, 117.99, 121.99, 124.76, 126.39, 128.12, 128.22, 128.77, 129.03, 130.80, 135.04, 136.76, 138.67, 162.29, 175.77. Anal. Calcd. for $C_{25}H_{28}N_2O_3$: C, 74.22; H, 6.99; N, 6.93. Found: C, 74.13; H, 7.02; N, 6.72.

7-(5-Carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylic acid (24a). Benzyl 7-(5-benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate (**16a**; 1.00 g) and triethylamine (20 drops) were dissolved in methanol (200 mL) and placed in a hydrogenation vessel. The air was flushed out with nitrogen and 10% palladium/charcoal (100 mg) was added. The mixture was shaken under an atmosphere of hydrogen at room temperature and 30 psi for 16 hr. The catalyst was filtered off and the solvent removed under reduced pressure. The residue was taken up in 3% aqueous ammonia solution. The catalyst was washed with 3% aqueous ammonia and the aqueous solutions combined. The mixture was cooled to 0°C in an ice/salt bath and neutralized with glacial acetic acid, maintaining the temperature below 5°C throughout. The resulting precipitate was filtered, washed with liberal quantities of water to remove all traces of acetic acid and dried *in vacuo* overnight to give the dipyrrole dicarboxylic acid (645 mg; quantitative) as a pale pink powder, mp 161-162°C, dec.; ^1H NMR (d_6-DMSO-$CDCl_3$): δ 0.90 (3H, t, pyrrole-CH_2CH_3), 1.5-1.69 (2H, m, $CH_2CH_2CH_2$), 1.77-1.79 (1H, m),

1.86-1.94 (1H, m) ($CHCH_2$), 2.07 (3H, s), 2.11 (3H, s) (2 x pyrrole-CH_3), 2.24 (2H, q, pyrrole-CH_2CH_3), 2.29 (2H, m, pyrrole-CH_2CH_2), 3.91 (1H, br t, bridge-CH), 8.57 (2H, br s, 2 x NH). Anal. Calcd. for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.52; H, 6.74; N, 8.37.

7-(5-Carboxy-3,4-dimethyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylic acid (24b). Using the previous procedure, **16b** (500 mg) afforded the title dicarboxylic acid (300 mg; 94%) as an off-white powder, mp 143-144°C, dec; ^{1}H NMR (d_6-DMSO-$CDCl_3$): δ 1.5-2.1 (4H, m, $CHCH_2CH_2CH_2$), 1.92 (3H, s), 2.27 (6H, s) (3 x pyrrole-CH_3), 2.25 (2H, m, pyrrole-CH_2CH_3), 2.47 (2H, m, pyrrole-CH_2CH_2), 3.91 (1H, br t, bridge-CH), 8.61 (2H, br s, 2 x NH). Anal. Calcd. for $C_{17}H_{20}N_2O_4$: C, 64.54; H, 6.37; N, 8.85. Found: C, 64.04; H, 6.52; N, 8.47.

3-Ethyl-4-methyl-5-(2-formyl-3-methyl-4,5,6,7-tetrahydro-7-indolyl)-pyrrole-2-carboxylic acid (33). Using the previous procedure, **32** (907 mg) afforded the title carboxylic acid (635 mg; 90%) as a pale yellow powder, mp 183-185°C, dec.; ^{1}H NMR (d_6-DMSO-$CDCl_3$): δ 0.96 (3H, t, pyrrole-CH_2CH_3), 1.6-1.72 (2H, m, $CH_2CH_2CH_2$), 1.78-1.9 (1H, m), 1.9-2.0 (1H, m) ($CHCH_2$), 2.13 (3H, s), 2.18 (3H, s) (2 x pyrrole-CH_3), 2.24-2.4 (4H, m, pyrrole-CH_2CH_3 and pyrrole-CH_2CH_2), 3.97 (1H, m, bridge-CH_2), 8.68 (1H, br s), 9.26 (1H, br s) (2 x NH), 9.33 (1H, s, CHO); ^{1}H NMR ($CDCl_3$): The carboxylic acid was only sparingly soluble in deuteriochloroform. Downfield resonances were observed at δ 8.56 (1H, br s, NH), 9.37 (1H, s, CHO), 9.62 (1H, br s, NH). Anal. Calcd. for $C_{18}H_{22}N_2O_4$: C, 68.76; H, 7.07; N, 8.91. Found: C, 69.30; H, 7.34; N, 8.72.

Ethyl 4-Butyl-3,5-dimethylpyrrole-2-carboxylate (20b). 1-Iodobutane (114 mL), 2,4-pentanedione (100.0 g), acetone (250 mL) and potassium carbonate (168.0 g) were placed in a 1 L three-necked flask fitted with a mechanical stirrer and a condenser. The mixture was vigorously stirred under reflux for 20 h. The flask was cooled, and the inorganic solids were removed by suction filtration and washed well with acetone. The combined solutions were evaporated under reduced pressure and the residue distilled to give 3-butyl-2,4-pentanedione (100.6 g; 64.5%) as a pale yellow oil, bp 98-103°C at 20 torr (lit. bp[36] 98-102°C at 16-17 torr).

A mixture of diethyl aminomalonate[26] (109.88 g) and 3-butyl-2,4-pentanedione (97.95 g) were added in a steady stream to gently boiling acetic acid (230 mL) in a 1 L flask. After the vigorous reaction had subsided, gentle boiling was continued for a further 2 h. The clear light brown solution was diluted with 2 L of ice water. After the product had precipitated out overnight, the solids were collected by suction filtration and washed with a small amount of 60% ethanol-water. Recrystallization from 95% ethanol gave the pyrrole (110.5 g; 79%) as a white powder, mp 99-101°C (lit mp[37] 102°C); IR (nujol mull): ν 3303 (NH str.), 1671 (C=O str.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.91 (3H, t, J = 7 Hz, $(CH_2)_3CH_3$), 1.26-1.45 (7H, m, $CH_2CH_2CH_2CH_3$ and OCH_2CH_3), 2.19 (3H, s), 2.26 (3H, s) (2 x pyrrole-CH_3), 2.35 (3H, t, J = 7.2 Hz, pyrrole-CH_2), 4.29 (2H, q, J = 7 Hz, OCH_2), 8.74 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.66, 11.56, 14.06, 14.69, 22.61, 23.88, 33.21, 59.69, 117.08, 122.70, 127.40, 129.70, 162.13.

Ethyl 5-Acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate (21a). Ethyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate[26] (**20a**; 5.00 g) was dissolved in a mixture of glacial acetic acid (80 mL) and acetic anhydride (4 mL), and lead tetraacetate (11.95 g) was added in portions to the stirred solution. The mixture was stirred at room temperature for 3 hr and then poured into 400 mL of ice-water. The resulting precipitate was collected by suction filtration and washed with cold water until the eluents were neutral. Recrystallization from chloroform-petrolum ether (60-80°) afforded the acetoxymethylpyrrole (5.24 g; 81%) as fluffy white needles, mp 128-129.5°C (lit. mp[38] 128°C); ^{1}H NMR ($CDCl_3$): δ 1.08 (3H, t, J = 7.5 Hz, pyrrole-CH_2CH_3), 1.35 (3H, t, J = 7.1 Hz, OCH_2CH_3), 2.06 (3H, s, $COCH_3$), 2.28 (3H, s, pyrrole-CH_3), 2.46 (2H, q, J = 7.5 Hz, pyrrole-CH_2CH_3), 4.31 (2H, q, J = 7.1 Hz, OCH_2CH_3), 5.02 (2H, s, pyrrole-CH_2O), 9.01 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.28, 14.64, 16.04, 17.20, 21.05, 57.17, 60.13, 119.59, 126.31, 126.75, 127.22, 161.82, 171.92.

Ethyl 5-Acetoxymethyl-4-butyl-3-methylpyrrole-2-carboxylate (21b). The acetoxypyrrole was prepared by the previous procedure from ethyl 5-methyl-4-butyl-3-methylpyrrole-2-carboxylate (**20b**; 5.00 g). Recrystallization from chloroform-petrolum ether gave the acetoxymethylpyrrole (4.91 g; 78%) as fluffy white needles, mp 104-105°C; IR (Nujol Mull): ν 3305 (NH str.), 1736 (acetate C=O str.), 1674 (pyrrole C=O str.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.94 (3H, t, J = 7 Hz, pyrrole-$(CH_2)_3CH_3$), 1.27-1.46 (7H, m, pyrrole-$CH_2CH_2CH_2CH_3$ and OCH_2CH_3), 2.06 (3H, s, $OCOCH_3$), 2.27 (3H, s, pyrrole-CH_3), 2.42 (2H, t, J = 7 Hz, pyrrole-CH_2CH_2), 4.31 (2H, q, J = 7 Hz, OCH_2CH_3), 5.01 (2H, s, pyrrole-CH_2O), 9.05 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): δ 10.42, 14.01, 14.61, 20.97, 22.56, 23.69, 33.65, 57.29, 60.09, 119.60, 125.66, 126.55, 127.15, 161.84, 171.87. Anal. Calcd. for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 63.97; H, 8.26; N, 5.18.

Diethyl 3,3'-Diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxylate (22a). Concentrated hydrochloric acid (3.1 mL) was added to ethyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate (**21a**; 3.94 g) and methanol (46 mL), and the resulting mixture was refluxed for 3 h. The mixture was cooled and stored in the freezer overnight. Yellowish needle shaped crystals formed and were collected by suction filtration. Recrystallization from absolute ethanol gave the title compound as white needles (2.53 g; 87%), mp 126.5-127.5°C (lit. mp[38] 126°C). ^{1}H NMR ($CDCl_3$): δ 1.09 (6H, t, J = 7.7 Hz, 2 x pyrrole-CH_2CH_3), 1.37 (6H, t, J = 7.7 Hz, 2 x OCH_2CH_3), 2.35 (6H, s, 2 x pyrrole-CH_3), 2.45 (4H, q, J = 7.7 Hz, 2 x pyrrole-CH_2), 3.90 (2H, s, bridge-CH_2), 4.31 (4H, q, J = 7.7 Hz, 2 x OCH_2), 8.44 (2H, br s, 2 x NH); ^{13}C NMR ($CDCl_3$): δ 10.52, 14.60, 15.45, 17.34, 23.17, 59.97, 118.34, 124.57, 127.24, 128.98, 162.17.

Diethyl 3,3'-Dibutyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxylate (22b). Using the previous procedure, ethyl 5-acetoxymethyl-4-butyl-3-methylpyrrole-2-carboxylate (**21b**; 20.00 g) was self-condensed to give the title dipyrrylmethane

(13.45 g; 88%) as white needles, mp 106-107°C (from ethanol); IR (nujol mull): ν 3316 (NH str.), 1692, 1647 (C=O str.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.90 (6H, t, J = 7 Hz, 2 x $(CH_2)_3CH_3$), 1.31 (14H, m, 2 x $CH_2CH_2CH_3$ and 2 x OCH_2CH_3), 2.27 (6H, s, 2 x pyrrole-CH_3), 2.37 (4H, t, J = 7 Hz, 2 x pyrrole-CH_2), 3.85 (2H, s, bridge-CH_2), 4.26 (4H, q, J = 7.2 Hz, 2 x OCH_2), 8.67 (2H, br s, 2 x NH); ^{13}C NMR ($CDCl_3$): δ 10.69, 14.03, 14.58, 22.77, 23.34, 23.98, 33.32, 59.95, 118.24, 123.08, 127.48, 129.60, 162.27. Anal. Calcd. for $C_{25}H_{38}N_2O_4$: C, 69.74; H, 8.89; N, 6.50. Found: C, 69.35; H, 8.83; N, 6.68.

3,3'-Diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (19a). Diethyl 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxylate (**22a**; 1.94 g) was heated under reflux with sodium hydroxide (2.0 g) and ethylene glycol (20 mL) for 1 hr. The mixture was diluted with water and extracted with hexanes. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure to give **23a** an a pale yellow oil. The oil was dissolved in DMF (6.0 mL), and the resulting solution was cooled to 0°C in an ice-salt bath. Benzoyl chloride (2.0 mL) was added dropwise, maintaining the temperature below 0°C. When the addition was complete, the temperature dropped to - 5°C. The ice bath was removed, and the mixture was stirred for 15 min allowing the temperature to rise to room temperature. Toluene (20 mL) was added, and the resulting mixture was cooled in an ice-salt bath and stirred for 1 h. The imine salt was filtered and washed with cold toluene (20 mL). The solid was taken up with sodium carbonate (2.0 g) dissolved in a 50/50 mixture of ethanol/water (32 mL), and the resulting mixture stirred on a boiling water bath for 15 min. Water (40 mL) was added and the solution was allowed to stand overnight at room temperature. The precipitate was filtered off and recrystallized from chloroform/petroleum ether (60-90°) to give the desired dialdehyde as pale yellow crystals (1.26 g; 85%), mp 219-220.5°C (lit. mp[27] 218-222°C). ^{1}H NMR ($CDCl_3$): δ 1.08 (6H, t, J = 8 Hz, 2 x CH_2CH_3), 2.29 (6H, s, 2 x pyrrole-CH_3), 2.45 (4H, q, J = 8 Hz, 2 x pyrrole-CH_2), 3.92 (2H, s, bridge-CH_2), 9.50 (2H, s, 2 x CHO), 9.98 (2H, br s, 2 x NH); ^{13}C NMR ($CDCl_3$): δ 8.87, 15.29, 17.18, 22.90, 125.27, 129.22, 132.54, 134.98, 177.12.

3,3'-Dibutyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (19b). Using the previous procedure, dipyrrylmethane **22b** (5.00 g) afforded the title dialdehyde (3.30 g; 83%) as pale yellow microneedles, mp 168-169°C (from ethanol); IR (nujol mull): ν 3242 (NH str.), 1615 (C=O str.) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.93 (6H, t, 2 x $(CH_2)_3CH_3$), 1.37 (8H, m, 2 x $CH_2CH_2CH_3$), 2.26 (6H, s, 2 x pyrrole-CH_3), 2.41 (4H, m, 2 x pyrrole-CH_2), 3.94 (2H, s, bridge-CH_2), 9.47 (2H, s, 2 x CHO), 10.95 (2H, br s, 2 x NH); ^{13}C NMR ($CDCl_3$): δ 9.15, 14.18, 22.97, 23.15, 23.96, 33.26, 123.77, 129.05, 132.71, 135.34, 176.92. Anal. Calcd. for $C_{21}H_{30}N_2O_2$: C, 73.65; H, 8.83; N, 8.18. Found: C, 73.26; H, 9.02; N, 8.16.

3,12,18-Triethyl-1,2,7,13,17,19-hexamethyl-8,10-propano-10,23-dihydrobilin Dihydrobromide (37). Dicarboxylic acid **24a** (106 mg) was dissolved in trifluoroacetic acid (0.7 mL) and stirred for 10 min at room temperature. A solution of 4-ethyl-3,5-dimethylpyrrole-2-carboxaldehyde (**36**; 120 mg) in methanol (3 mL) was added, immediately followed by 30% HBr-acetic acid (0.6 mL), and the resulting deep red mixture was stirred at room temperature for 30 min. Anhydrous ether (13 mL) was added dropwise, and the resulting mixture stirred for an additional 2 hr. The precipitate was filtered off and washed well with ether. Upon vacuum drying overnight, the title compound (163 mg; 72%) was obtained as a brick red powder, mp 190-192°C, dec.; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 462 (4.98), 517 (4.98) nm; ^{1}H NMR ($CDCl_3$): δ 0.99-1.1 (9H, 3 overlapping triplets, 3 x CH_2CH_3), 1.5-1.8 (4H, m, $CHCH_2CH_2$), 2.23 (6H, s), 2.29 (3H, s), 2.31 (3H, s) (2,7,13,17-CH_3), 2.33-2.42 (8H, m, 4 x pyrrole-CH_2), 4.90 (1H, m, bridge CH), 7.13 (1H, s), 7.19 (1H, s) (2 x methine bridge), 12.36 (1H, br s), 12.40 (1H, br s), 13.16 (1H, br s), 13.40 (1H, br s) (4 x NH). Anal. Calcd. for $C_{34}H_{46}N_4Br_2$: C, 60.89; H, 6.93; N, 8.36. Found: C, 60.08; H, 7.08; N, 8.04.

7,13,17-Triethyl-2,8,12,18-tetramethyl-3,5-propanoporphyrin (26a).

Method A: A solution of *p*-toluenesulfonic acid monohydrate (370 mg) in methanol (6 mL) was added to a stirred mixture of 7-(5-carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylic acid (**24a**; 215 mg) and 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (**19a**; 176 mg) in dichloromethane (60 mL) and methanol (6 mL). After a few minutes, a deep orange-red solution was formed. The mixture was stirred overnight in the dark at room temperature; at this point spectral examination showed absorptions at λ_{max} 416, 450, 492, 553 nm. A saturated solution of zinc acetate in methanol (7 mL) was added and the resulting mixture stirred at room temperature for 2 days. Spectral examination showed the development of an intense Soret band at λ_{max} 406 nm. The mixture was evaporated to dryness under reduced pressure and taken up in 5% sulfuric acid-methanol. The resulting mixture was partitioned between chloroform and water. The two layers were separated and the aqueous phase was reextracted with chloroform. The combined organic solutions were washed with water, 3% aqueous ammonia solution and water, and evaporated to dryness on a rotary evaporator. The residue was chromatographed on grade 3 alumina, eluting with CH_2Cl_2. The colored fractions were evaporated and further purified by chromatography on a grade 3 alumina column, eluting with CH_2Cl_2, and the major red band was collected and recrystallized from chloroform-methanol to give the title porphyrin (63 mg; 21%) as purple crystals, mp > 300°C; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 402 (5.27), 501 (4.18), 535 (3.69), 570 (3.78), 623 (3.37) nm; UV/Vis (5% TFA-CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 406 (5.52), 552 (4.09), 597 (3.40) nm; ^{1}H NMR ($CDCl_3$): δ -3.26 (2H, br s, 2 x NH), 1.8-2.0 (9H, 3 overlapping triplets, 3 x CH_2CH_3), 2.88 (2H, quintet, $CH_2CH_2CH_2$), 3.56 (3H, s), 3.58 (3H, s), 3.64 (3H, s), 3.66 (3H, s) (4 x porphyrin-CH_3), 3.85 (2H, t, J = 6 Hz, 3-CH_2), 4.01 (2H, q), 4.02-4.16 (4H, 2 overlapping quartets) (3 x CH_2CH_3), 5.12 (2H, t, J = 5.8 Hz, *meso*-CH_2), 9.89 (1H, s), 10.03 (1H, s), 10.09 (1H, s) (3 x *meso*-H); ^{1}H NMR (TFA-$CDCl_3$): δ -3.71 (1H, br s), -3.44 (2H, br s), -2.88 (1H, br s) (4 x NH), 1.68-1.77 (9H, 3 overlapping triplets, 3 x CH_2CH_3), 2.87 (2H, quintet, $CH_2CH_2CH_2$), 3.48 (3H, s), 3.53 (3H, s), 3.60 (6H, s) (4 x porphyrin-CH_3), 3.86-3.95 (4H, m), 4.02-4.12 (4H, 2 overlapping quartets) (3 x CH_2CH_3

and 3-CH_2), 5.24 (2H, t, J = 5.7 Hz, *meso*-CH_2), 10.33 (1H, s), 10.41 (1H, s), 10.50 (1H, s) (3 x *meso*-H). EI MS: m/z (% rel. int.) 490 (100, M^+), 475 (6, $[M - CH_3]^+$), 245 (10, M^{2+}); HR MS calcd. for $C_{33}H_{38}N_4$: 490.30994. Found: 490.30755.

Method B: a,c-Biladiene **37** (100 mg) was added to a solution of zinc acetate (713 mg) and silver iodate (918 mg) in DMF (54 mL), and the stirred mixture was heated under reflux for 40 min. The mixture was cooled to room temperature, diluted with dichloromethane and filtered through Celite. The filtrate was washed with water (3 x 100 mL) and the solvent removed under reduced pressure. The residue was chromatographed on alumina eluting with dichloromethane. The product was recrystallized from chloroform-methanol to give the required porphyrin (9 mg; 12%) as purple crystals, mp > 300°C.

13,17-Diethyl-2,7,8,12,18-pentamethyl-3,5-propanoporphyrin (26d). Dicarboxylic acid **24b** (250 mg) and dialdehyde **19a** (215 mg) were reacted under the conditions described above. Recrystallization from chloroform-methanol gave the pentamethylporphyrin (79 mg; 22%) as purple crystals, mp > 300°C; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 402 (5.27), 500 (4.19), 534 (3.74), 569 (3.81), 623 (3.35) nm; ^{1}H NMR ($CDCl_3$): δ -3.35 (2H, br s, 2 x NH), 1.86 (3H, t), 1.87 (3H, t) (2 x CH_2CH_3), 2.87 (2H, quintet, $CH_2CH_2CH_2$), 3.57 (3H, s), 3.60 (3H, s), 3.61 (3H, s), 3.64 (6H, s) (5 x porphyrin-CH_3), 3.85 (2H, t, 3-CH_2), 4.0-4.11 (4H, 2 overlapping quartets, 2 x CH_2CH_3), 5.06 (2H, t, *meso*-CH_2), 9.90 (1H, s), 10.04 (1H, s), 10.08 (1H, s) (3 x *meso*-H); HR MS calcd. for $C_{32}H_{36}N_4$: 476.293997. Found: 476.294082.

13,17-Dibutyl-7-ethyl-2,8,12,18-tetramethyl-3,5-propanoporphyrin (26b). Dicarboxylic acid **24a** (200 mg) and dialdehyde **19b** (196 mg) were reacted under the conditions described above. Recrystallization from chloroform-methanol gave the propanoporphyrin (63 mg; 20%) as flaky purple crystals, mp > 300°C; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 402 (5.25), 502 (4.17), 535 (3.71), 570 (3.79), 623 (3.40) nm; ^{1}H NMR ($CDCl_3$): δ -3.28 (2H, br s, 2 x NH), 1.12 (6H, t, J = 7.2 Hz, 2 x $(CH_2)_3CH_3$), 1.80 (7H, m, 2 x $CH_2CH_2CH_2CH_3$ and CH_2CH_3), 2.27 (4H, sextet, 2 x $CH_2CH_2CH_2CH_3$), 2.88 (2H, quintet, ring $CH_2CH_2CH_2$), 3.56 (3H, s), 3.58 (3H, s), 3.64 (3H, s), 3.66 (3H, s) (4 x porphyrin-CH_3), 3.85 (2H, t, 3-CH_2), 3.98 (2H, t), 4.06 (2H, t) (2 x $CH_2CH_2CH_2CH_3$), 4.12 (2H, q, porphyrin-CH_2CH_3), 5.12 (2H, t, J = 6 Hz, *meso*-CH_2), 9.89 (1H, s), 10.02 (1H, s), 10.08 (1H, s) (3 x *meso*-H); ^{1}H NMR (TFA-$CDCl_3$): δ -3.59 (1H, br s), -3.31 (2H, br s), -2.75 (1H, br s) (4 x NH), 1.05 (3H, t), 1.07 (3H, t) (2 x $(CH_2)_3CH_3$), 1.59-1.74 (7H, m, 2 x $CH_2CH_2CH_2CH_3$ and CH_2CH_3), 2.0-2.2 (4H, m, 2 x $CH_2CH_2CH_2CH_3$), 2.86 (2H, quintet, ring $CH_2CH_2CH_2$), 3.47 (3H, s), 3.52 (3H, s), 3.59 (6H, s) (4 x porphyrin-CH_3), 3.85-3.93 (4H, m), 3.99-4.06 (4H, m), (3-CH_2, 2 x $CH_2CH_2CH_2CH_3$ and porphyrin-CH_2CH_3), 5.23 (2H, br t, *meso*-CH_2), 10.31 (1H, s), 10.39 (1H, s), 10.48 (1H, s) (3 x *meso*-H); HR MS calcd. for $C_{37}H_{46}N_4$: 546.372248. Found: 546.371906.

7-Ethyl-13,17-bis-(2-methoxycarbonylethyl)-2,8,12,18-tetramethyl-3,5-propanoporphyrin (26c). Prepared from dicarboxylic acid **24a** (250 mg) and 3,3'-bis(2-methoxycarbonylethyl)-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde[39] (**19c**; 288 mg) by the procedure given above, except that the crude porphyrin was treated with 5% sulfuric acid-methanol overnight to allow reesterification of the propionate sidechains. Recrystallization from chloroform-methanol gave the title porphyrin (122 mg; 28%) as lustrous purple crystals, mp 246-246.5°C; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 404 (5.22), 503 (4.17), 537 (3.65), 572 (3.77), 625 (3.31) nm. ^{1}H NMR ($CDCl_3$): δ -3.26 (2H, br s, 2 x NH), 1.79 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.87 (2H, quintet, $CH_2CH_2CH_2$), 3.27 (2H, t), 3.29 (2H, t) (2 x CH_2CO), 3.55 (3H, s), 3.60 (3H, s), 3.65 (3H, s), 3.67 (6H, s), 3.68 (3H, s) (4 x porphyrin-CH_3 and 2 x OCH_3), 3.84 (2H, t, J = 6 Hz, 3-CH_2), 4.11 (2H, q, CH_2CH_3), 4.34 (2H, t), 4.42 (2H, t) (2 x CH_2CH_2CO), 5.10 (2H, t, J = 5.7 Hz, *meso*-CH_2), 9.89 (1H, s), 10.03 (1H, s), 10.09 (1H, s) (3 x *meso*-H); ^{1}H NMR (TFA-$CDCl_3$): δ -4.05 (1H, br s), -3.90 (1H, br s), -3.80 (1H, br s), -3.37 (1H, br s) (4 x NH), 1.74 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.89 (2H, m, $CH_2CH_2CH_2$), 3.13 (2H, t), 3.18 (2H, t) (2 x CH_2CO), 3.51 (3H, s), 3.56 (3H, s), 3.64 (6H, s), 3.68 (3H, s), 3.69 (3H, s) (4 x porphyrin-CH_3 and 2 x OCH_3), 3.9-4.0 (4H, m, 3-CH_2 and CH_2CH_3), 4.47 (4H, 2 overlapping triplets, 2 x CH_2CH_2CO), 5.28 (2H, br t, *meso*-CH_2), 10.54 (1H, s), 10.62 (1H, s), 10.64 (1H, s) (3 x *meso*-H). FAB MS: m/z 607 ($[M+H]^+$); HR MS (EI) calcd. for $C_{37}H_{42}N_4O_4$: 606.320606. Found: 606.320934.

7,17-Diethyl-2,8,12,18-tetramethyl-3,5:13,15-dipropanoporphyrin (34). Formyldipyrrole **33** (362 mg) was self-condensed using the standard conditions given above. Recrystallization from chloroform-methanol afforded the title porphyrin (72 mg; 25%) as purple crystals, mp > 300°C; UV/Vis (CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 408 (5.33), 508 (4.17), 574 (3.75), 627 (3.17) nm; UV/Vis (5% TFA-CH_2Cl_2): λ_{max} ($\log_{10}\varepsilon$) 412 (5.61), 524 (3.45, infl.), 560 (4.15), 610 (3.86) nm; ^{1}H NMR ($CDCl_3$): δ -2.7 (2H, br s, 2 x NH), 1.80 (6H, t, J = 7.5 Hz, 2 x CH_2CH_3), 2.87 (4H, quintet, $CH_2CH_2CH_2$), 3.54 (6H, s), 3.67 (6H, s) (4 x porphyrin-CH_3), 3.81 (4H, t, J = 5.8 Hz, 3-CH_2), 4.13 (4H, q, J = 7.5 Hz, 2 x CH_2CH_3), 5.05 (4H, t, J = 5.7 Hz, *meso*-CH_2), 10.05 (2H, s) (2 x *meso*-H); ^{1}H NMR (TFA-$CDCl_3$): δ -4.24 (2H, br s), -3.51 (2H, br s) (4 x NH), 1.74 (6H, t, J = 7.2 Hz, 2 x CH_2CH_3), 2.84 (4H, quintet, $CH_2CH_2CH_2$), 3.48 (6H, s), 3.53 (6H, s) (4 x porphyrin-CH_3), 3.9-4.0 (8H, m, 2 x CH_2CH_3 and 3,13-CH_2), 5.18 (4H, br t, *meso*-CH_2), 10.44 (2H, s) (2 x *meso*-H); ^{13}C NMR (TFA-$CDCl_3$): δ 11.44, 11.64, 15.46, 21.53, 24.06, 26.65, 30.32, 98.35, 117.97, 136.66, 138.79, 140.70, 141.28, 141.31, 141.72, 142.19; EI MS: m/z 502 (M^+); HR MS calcd. for $C_{34}H_{38}N_4$: 502.30994. Found: 502.30926. Anal. Calcd. for $C_{34}H_{38}N_4$: C, 81.23; H, 7.62; N, 11.14. Found: C, 81.41; H, 7.68; N, 11.10.

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