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Porphyrins with Exocyclic Rings. Part 3.[1] A Reassessment on the Utility of Cyclopenta[b]pyrroles in the Synthesis of Porphyrin Molecular Fossils. Preparation of Three Type II Porphyrins Related to Deoxophylloerythroetioporphyrin (DPEP).[2]

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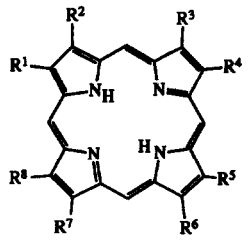
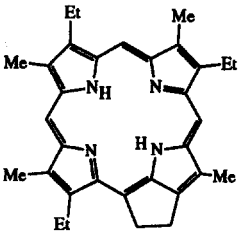
Abstract: *The utility of cyclopenta[b]pyrroles in porphyrin synthesis has been reinvestigated. A 6-oxocyclopenta[b]pyrrole* ***18*** *was prepared by cyclization of the propanoyl chloride sidechain of an α-unsubstituted pyrrole* ***17d*** *in the presence of tin(IV) chloride. Subsequent reduction with sodium borohydride afforded the corresponding 6-hydroxy compound* ***10*** *and further acid catalyzed condensation with α-unsubstituted pyrroles* ***11a*** *and* ***11b*** *gave the novel 6-pyrrolylcyclopenta[b]pyrroles* ***22a*** *and* ***22b*** *in excellent yields. Attempts to prepare deoxophylloerythroetioporphyrin (DPEP;* ***2****), a widespread sedimentary porphyrin molecular fossil, from these dipyrrolic intermediates using the tripyrrene-a,c-biladiene route were unsuccessful. However, the synthesis of three related meso,β-ethanoporphyrins using the MacDonald condensation was successfully carried out in moderate to good yields. Retention of an* sp^3 *hybridized carbon bridge at the cyclopentene ring fusion site of the intermediary open chain tetrapyrroles appears to be crucial during macrocycle formation, as this diminishes the steric repulsion between the peripheral substituents and the carbocyclic ring.*

Alfred Treibs first noted the presence of metalloporphyrins in petroleum, oil shales, coal and other organic-rich sedimentary materials nearly sixty years ago.[3,4] He tentatively identified two major metalloporphyrins, the vanadyl chelates of etioporphyrin-III (**1a**) and deoxophylloerythroetioporphyrin (DPEP; **2**), and proposed[5] that these geological pigments were degradation products from heme and chlorophyll-a, respectively. In the 1960's, mass spectrometric studies revealed[6] that complex mixtures of metalloporphyrins were in fact present in organic sediments, although two major series of porphyrins apparently related to etioporphyrin-III and DPEP were evident. Both DPEP[7] and etioporphyrin-III[8] have now been isolated from oil shales and unambiguously characterized by nOe difference proton NMR spectroscopy, but many other structures including **3-6** have also been identified.[9-11] It should be noted that all naturally occurring tetrapyrroles, including all of the fully characterized sedimentary porphyrins, are structurally related to etioporphyrin-III and the type I, II and IV isomers of etioporphyrin (**1b**, **1c** and **1d**, respectively) have not been identified in any geological samples. This lends considerable support to the notion that sedimentary porphyrins are the remnants of biological pigments.



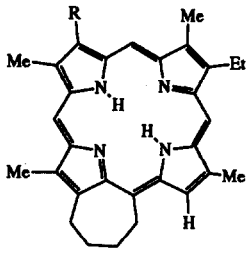
1

a. $R^{1,3,5,8}$ = Me; $R^{2,4,6,7}$ = Et (Etioporphyrin-III)
b. $R^{1,3,5,7}$ = Me; $R^{2,4,6,8}$ = Et (Etioporphyrin-I)
c. $R^{1,4,5,8}$ = Me; $R^{2,3,6,7}$ = Et (Etioporphyrin-II)
d. $R^{2,3,5,8}$ = Me; $R^{1,4,6,7}$ = Et (Etioporphyrin-IV)

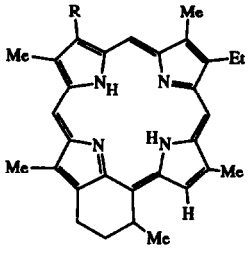


2

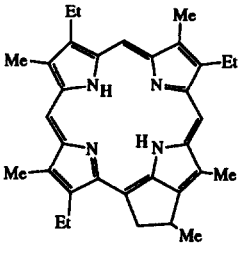
Deoxophylloerythroetioporphyrin



3 a. R = Et; b. R = Me



4 a. R = Et; b. R = Me



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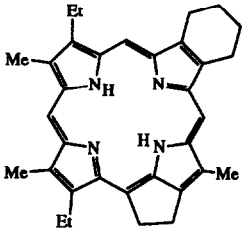


6

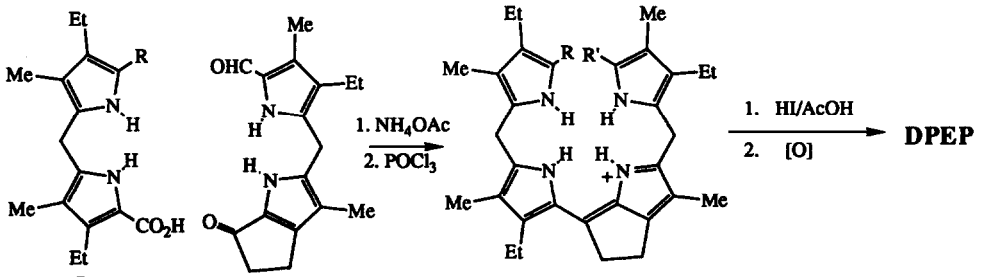
Sedimentary porphyrins are generally known as geoporphyrins or petroporphyrins. In oil shales and petroleum, they occur almost exclusively as the nickel or vanadyl complexes, although metal-free porphyrins,[12] iron porphyrins[13] and copper(II) porphyrins[14] have also been noted. Complex mixtures of etioporphyrins and cycloalkanoporphyrins of diverse structural types (e.g., **2**-**6**) are found in these deposits and the vast majority of these tetrapyrroles appear to be derived from plant, algal, or bacterial chlorophylls. In contrast, immature coals and lignites contain mostly polyalkyl- or etio-type porphyrins[15] and this suggests that coal porphyrins originated primarily from bacterial hemes, rather than the chlorophylls. Iron,[15] gallium,[15-17] manganese,[17] and metal-free porphyrins have all been detected in these materials.

Synthetic samples of petroporphyrins are of value in the unambiguous identification of these natural products, and in the development of new analytical techniques (spectrophotometric, mass spectral, HPLC, etc.). We have investigated the synthesis of cycloalkanoporphyrins of geochemical significance.[18-24] Our early studies were directed towards the synthesis of porphyrins with six-, seven- and eight- membered exocyclic rings and this work led to the total synthesis of petroporphyrins **3a**, **3b**,[21,22] **4a** and **4b**.[23] We have now extended these investigations to the synthesis of porphyrins with five-membered exocyclic rings and in this paper we report our initial studies in this area.

The first synthesis of DPEP was reported by Fischer and Hofmann in 1935[25a] and involved the fusion of two pyrromethene units in a succinic acid melt. Very low yields of the meso,β-ethanoporphyrin system were obtained in these and related[25b] early studies. In subsequent work, three different strategies were investigated for the synthesis of DPEP: (1) Partial synthesis from naturally occurring chlorophylls;[26] (2) Total synthesis, where the exocyclic ring is introduced subsequent to porphyrin formation;[27,28] and (3) formation of the porphyrin macrocycle from tetrapyrrolic intermediates that already incorporate the carbocyclic ring.[18-24,29] The first approach is limited by the structure, and availability, of the initial chlorophyll. Overall yields in many of

these studies were also low, but this was primarily due to the difficulties encountered in carrying out the decarboxylation of the propionic acid sidechain. The recent introduction of 1,5,7-triazabicyclo[4.4.0]dec-5-ene as a reaction medium for this transformation[30] appears to have overcome this problem. None-the-less, partial synthesis remains a relatively inflexible approach that can only be applied to a limited number of porphyrin molecular fossils.

The introduction of the exocyclic ring subsequent to porphyrin formation has been the subject of many investigations[27,28] but multiple synthetic steps are usually necessary and this approach tends to be rather inefficient. The most effective version of the second strategy involves the cyclization of vinylic porphyrins.[28] However, when one considers that the vinyl moiety must be introduced subsequent to porphyrin formation, and that yields in the cyclization step are typically in the range of 25-40%, overall yields are far from ideal. Adaptation of this method to the synthesis of molecular fossils derived from chlorophyll-c required the use of protective groups and this further lowered the overall yields to 6% from the first formed porphyrin.[28b]



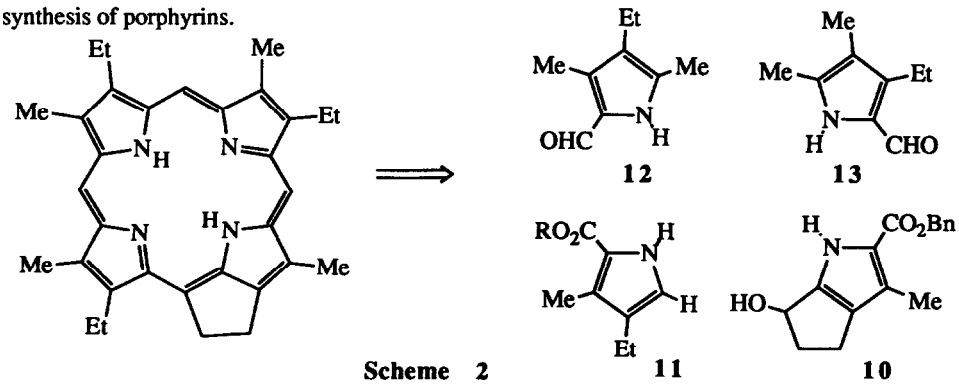
7 R = $CO_2C_6H_4OMe$

8

9 a. R = $CO_2C_6H_4OMe$; R' = CH=NH.HCl
b. R = $CO_2C_6H_4OMe$; R' = CHO

Scheme 1

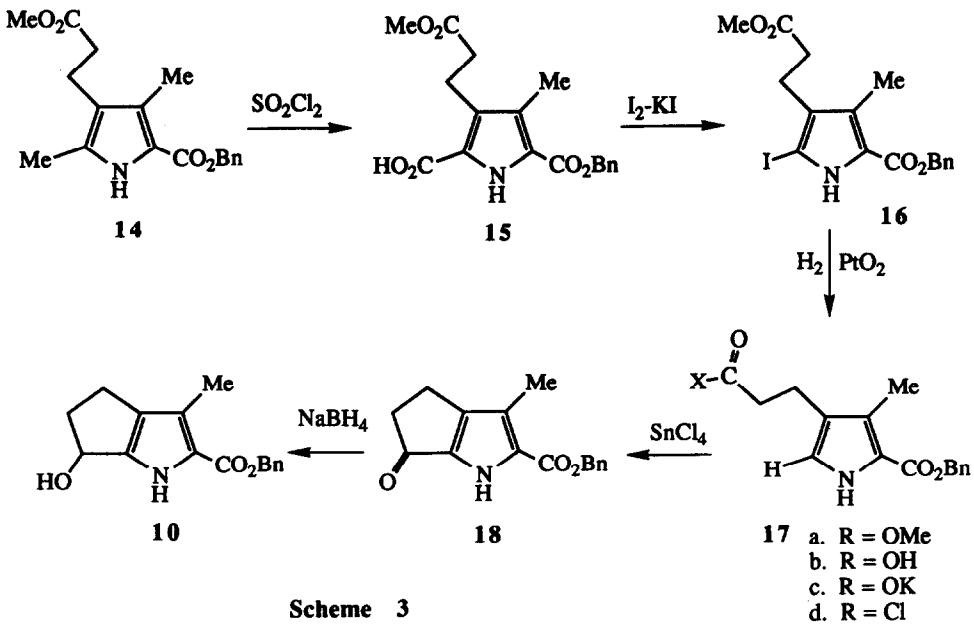
Prior to our studies, only one example of the third strategy had been reported. In this "classic" synthesis of DPEP,[29] a dipyrrylmethane **7** that incorporated a cyclopentanone ring was condensed with **8** in the presence of phosphorus oxychloride to give the b-bilene **9a** (Scheme 1). Hydrolysis of the imine salt afforded the formyl b-bilene **9b**, which underwent cyclization in the presence of 2.5% hydroiodic acid in acetic acid to give DPEP. Unfortunately, the yield in the final step was only 6%, and this was attributed to a deleterious steric interaction due to the presence of the carbocyclic ring. However, if a three-fold increase in the yield for this cyclization were possible, this would offer a route to DPEP and related petroporphyrins that was superior to any currently available synthetic methodology . With this in mind, we have reinvestigated the utility of cyclopenta[b]pyrroles in the synthesis of porphyrins.



12 **13** **11** **10**

Scheme 2

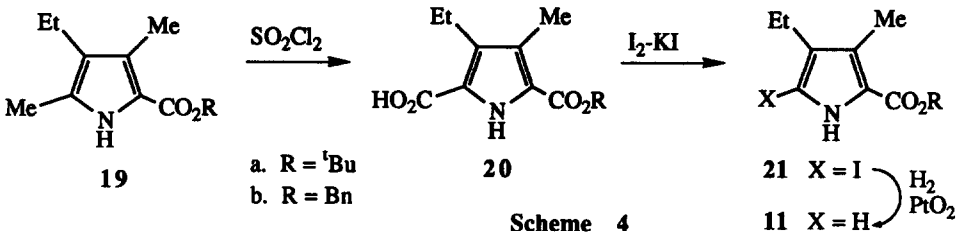
One of the most versatile methods for porphyrin synthesis is the tripyrrene-a,c-biladiene approach.[31] In Scheme 2, a retrosynthetic analysis for DPEP is given and the four pyrrolic units that were needed in this type of synthetic strategy are shown. Pyrroles **11-13** were prepared by known literature methods[32-34] and the cyclopenta[b]pyrrole was synthesized in six steps from pyrrole **14** (Scheme 3). Pyrrole **14**[35] was treated with 3.1 equivalents of sulfuryl chloride and subsequent hydrolysis with aqueous sodium acetate gave the carboxylic acid **15**. Treatment with iodine-potassium iodide induced an iodinative decarboxylation to give the iodopyrrole **16** and hydrogenolysis over Adam's catalyst afforded the α-free pyrrole **17a**. Selective hydrolysis of the methyl ester was effected by treating **17a** with dilute aqueous hydrochloric acid in refluxing acetone to give the corresponding carboxylic acid **17b** in excellent yield. Attempts to cyclize the propionic acid sidechain in polyphosphoric acid to give **18** were not successful. At lower temperatures (60°C) no reaction occurred but at slightly higher temperatures decomposition took place rather than cyclization, presumably due to the acid lability of the benzyl ester. Hence, milder conditions were sought for the cyclization reaction. The 3-pyrrolylpropanoic acid **17b** was converted to the corresponding potassium salt **17c** and further treatment with oxalyl chloride yielded the acyl chloride **17d**. Cyclization in the presence of tin(IV) chloride gave the required 6-oxocyclopenta[b]pyrrole **18**. Reduction with sodium borohydride then gave the related alcohol **10**. An α-unsubstituted pyrrole **11a** was required as the second subunit corresponding to the lower half of DPEP and this was prepared in three steps from *tert*-butyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate (**19a**).[36] Pyrrole **19a** (Scheme 4) was treated with sulfuryl chloride in the presence of potassium carbonate and anhydrous ether and subsequent hydrolysis gave the carboxylic acid **20a**. Iodinative decarboxylation yielded the iodopyrrole **21a** and subsequent treatment with hydrogen over platinum oxide gave the 5-unsubstituted pyrrole **11a**. Pyrrole **11a** condensed with hydroxycyclopenta[b]pyrrole **10** in the presence of p-toluenesulfonic acid in acetic acid to give the important intermediary dipyrrole **22a** in good yield (Scheme 5).



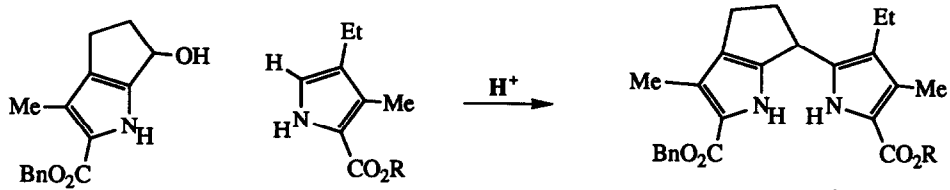
14 **15** **16**

10 **18** **17** a. R = OMe
b. R = OH
c. R = OK
d. R = Cl

Scheme 3



Scheme 4

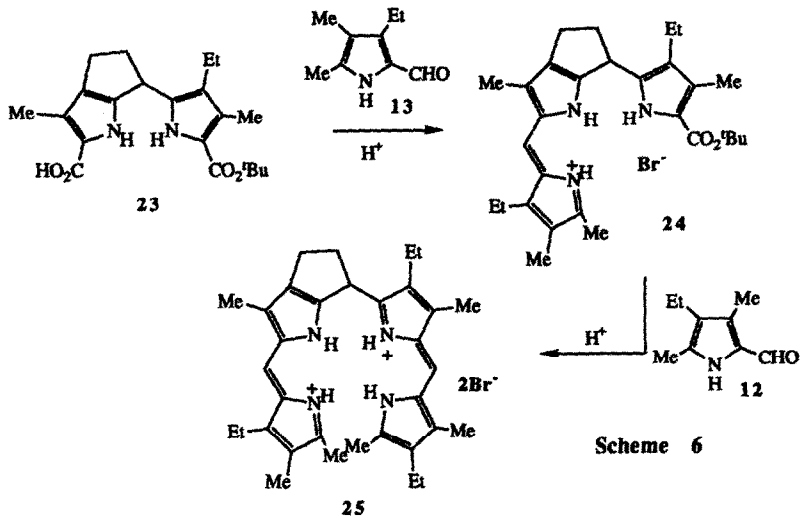


10 11a R = tBu
11b R = Bn

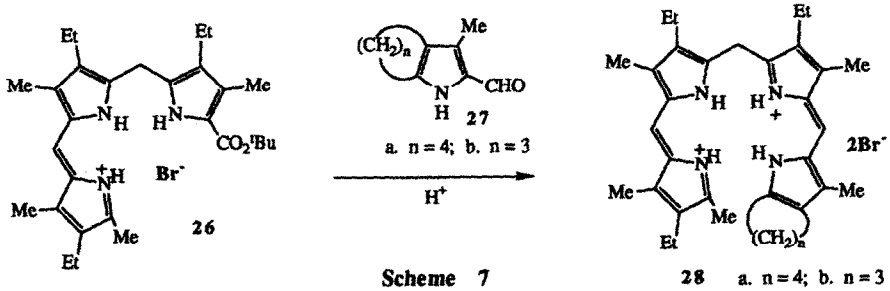
Scheme 5

Hydrogenolysis of the benzyl ester over 10% palladium-charcoal gave the corresponding pyrrolylcyclopenta[b]pyrrole carboxylic acid **23** and subsequent condensation with pyrrole aldehyde **13** in the presence of p-toluenesulfonic acid, followed by brief treatment with hydrogen bromide, gave the tripyrrene **24** (Scheme 6). Cleavage and decarboxylation of the *tert*-butyl ester with trifluoroacetic acid, followed by condensation with formylpyrrole **12** in the presence of hydrobromic acid then gave the a,c-biladiene **25**. All that remained was to cyclize the a,c-biladiene **25** to give DPEP. However, this proved to be impossible to implement. A variety of reagents were investigated including copper(II) chloride/dimethylformamide, copper(II) acetate/pyridine,[24,37] silver iodate/zinc acetate/dimethylformamide[38] and potassium chromate/zinc acetate/dimethylformamide[38] but only trace amounts of impure porphyrin was formed in each case. The a,c-biladiene appeared to be fairly unstable in solution, possibly due in part to ring strain induced by the presence of the cyclopentene ring. The steric interaction between the five-membered carbocyclic ring and the adjacent ethyl substituent probably inhibited cyclization and rapid decomposition presumably ensued.

We briefly also considered the possibility of cyclizing a,c-biladienes with terminal carbocyclic rings to form cycloalkanoporphyrins. Professor K.M. Smith and coworkers have reported the cyclization of a,c-biladienes with terminal ethyl substituents to give *meso*-methylporphyrins[39,40] and a similar approach to *meso*,β-ethanoporphyrins seemed to be potentially viable. Treatment of tripyrrene **26** with trifluoroacetic acid, followed by reaction with **27a** or **27b** in the presence of HBr gave the a,c-biladienes **28a** and **28b**, respectively (Scheme 7). The ethanotetrapyrrole **28b** was somewhat impure by NMR spectroscopy and this appeared to be due to the diminished stability of this compound. In our hands, both of these a,c-biladiene systems failed to cyclize to give useful quantities of porphyrin and this approach to *meso*,β-ethanoporphyrins has also been abandoned. We should add, however, that the cyclization of an a,c-biladiene with two terminal six-membered carbocyclic rings has been noted[41] and it may yet be possible to prepare meso,β-ethanoporphyrins by this approach. On the other hand, it was recently reported[42] that cyclizations of b-bilenes with single terminating carbocyclic rings gave very poor yields of porphyrin products. The apparent decreased stability of a,c-biladienes that incorporate five-membered exocyclic rings further negates the potential application of this methodology.

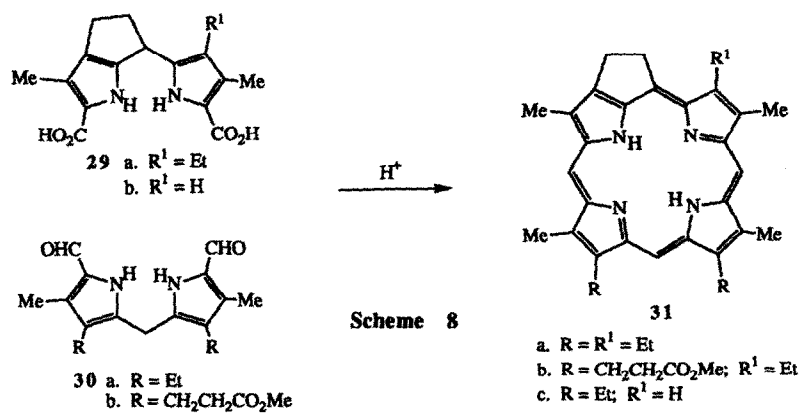


Scheme 6



Scheme 7

28 a. n = 4; b. n = 3



Scheme 8

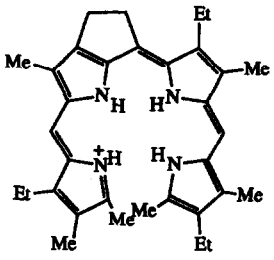
We also investigated the formation of meso,β-ethanoporphyrins **31** by the MacDonald condensation[43] (Scheme 8). Treatment of dipyrrole **23** with trifluoroacetic acid and further condensation with dipyrrylmethane dialdehyde **30a** in the presence of the acid catalyst p-toluenesulfonic acid, followed by addition of zinc acetate and air oxidation, gave low, somewhat variable yields of **31a**. The low yield appears to be due to the unexpected stability of the *tert*-butyl ester towards cleavage under acidic conditions. To overcome this difficulty, a related dipyrrole **22b** was prepared in good yield by the acid catalyzed condensation of hydroxycyclopenta[b]pyrrole **10** with α-free pyrrole **11b** (Scheme 5). Hydrogenolysis of the benzyl esters over 10% palladium-charcoal gave the corresponding dicarboxylic acid **29a**. Condensation of **29a** with the diformyldipyrrylmethane **30a** in the presence of p-toluenesulfonic acid, followed by air oxidation as before, gave cycloalkanoporphyrin **31a** in 19% yield. Porphyrin **31a** is formally a type II isomer of DPEP, since the peripheral methyl and ethyl substituents are arranged in the same sequence as in etioporphyrin-II (**1c**). Condensation of **29a** with the dialdehyde **30b** gave the related type II porphyrin **31b** in 18% yield. The β-unsubstituted dipyrrole **29b**[44] condensed with **30a** to give porphyrin **31c** in inferior, rather variable yields (5-12%). The absence of a β-substituent in **29b** reduces the reactivity of the pyrrole nucleus towards electrophilic substitution and this may be a factor in producing the relatively poor yields observed in this case. However, dipyrrole **29b** was also somewhat unstable (attempts to recrystallize the compound led to decomposition) and it seems likely that rapid decomposition took place before macrocyclic ring closure could occur.

The yields obtained in the synthesis of **31a** and **31b** are competitive with the best available syntheses of meso,β-ethanoporphyrins, although it should be noted that the MacDonald condensation is restricted by symmetry constraints, as one of the condensing dipyrrole units must be symmetrical or isomers result. Hence, DPEP itself cannot be prepared in this way. However, the results suggest that a stepwise variation on the MacDonald condensation (i.e., the b-bilene route[45]) should be effective in the synthesis of meso,β-ethanopetroporphyrins and this possibility is presently under investigation.

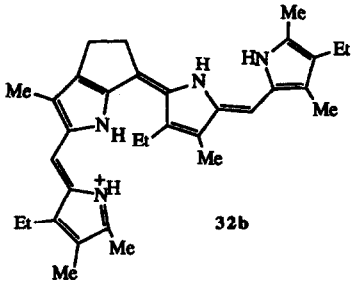
The efficacy of porphyrin formation in the MacDonald condensation (Scheme 8) contrasts with the low yields obtained in the b-bilene cyclization[29] shown in Scheme 1 and the attempted a,c-biladiene cyclizations (Scheme 6). In the cyclization of a,c-biladienes, a fully conjugated bilatriene **32a** is believed to be formed as as an early intermediate[46] and it is noteable that the bridging carbon incorporating the five-membered exocyclic ring is sp^2 hybridized. In intermediates **9** (Scheme 1) and **32a**, the cyclopentene ring is held in the same plane as the adjacent ethyl substituent and steric interference is likely to be severe. It is also possible that geometrical isomers such as **32b** will be formed under these circumstances, and structures of this type would be unlikely to give porphyrin products. By contrast, the probable intermediate in the MacDonald cyclization (Structure **33**) retains an sp^3 hybridized carbon bridge at the site of the carbocyclic ring and this undoubtably relieves much of the steric congestion that is associated with structures **9** and **32**. Hence, the deleterious influence of the carbocyclic ring is much reduced and this leads to the respectable yields observed in our studies. We are currently investigating the extension of this work to the synthesis of totally unsymmetrical meso,β-ethanoporphyrins and the results from these studies will be reported in due course.

EXPERIMENTAL

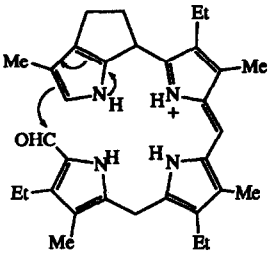
Sulfuryl chloride and oxalyl chloride were freshly distilled prior to use. Tin(IV) chloride, trifluoroacetic acid, benzoyl chloride, p-nitrobenzoyl chloride, N,N-dimethylformamide and 30% hydrogen bromide in acetic acid were purchased from Aldrich Chemical Co. and were used without further purification. Melting points were determined on a Thomas Hoover capillary melting point



32a



32b



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apparatus and are uncorrected. Hydrogenations were carried out on a Parr hydrogenator at 30-40 psi. 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. 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). Elemental analyses were obtained from Micro-Analysis, Inc., Wilmington, DE 19808.

5-Benzyloxycarbonyl-4-methyl-3-(2-methoxycarbonylethyl)pyrrole-2-carboxylic Acid (15).

Sulfuryl chloride (59.8 ml) was added dropwise to a stirred solution of benzyl 3,5-dimethyl-4-(2-methoxycarbonylethyl)pyrrole-2-carboxylate[35] (71.29 g) in ether (1120 ml), maintaining the temperature at 20°C throughout. The resulting solution was stirred for an additional two days at room temperature. The ether was removed under reduced pressure and the resulting orange oil dissolved in dioxane (560 ml). A mixture of sodium acetate trihydrate (224 g) in water (280 ml) was added to the solution, and the stirred mixture was heated at 70°C for 1.5 hours. The mixture was allowed to stand at room temperature overnight. The mixture was extracted with ether (3 x 250 ml) and the combined ether layers extracted with sodium bicarbonate solution (10%; 4 x 500 ml). The combined aqueous solutions were acidified with concentrated hydrochloric acid, while maintaining the temperature below 10°C. The resulting white precipitate was filtered, washed several times with hot water and dried *in vacuo*. Recrystallization from chloroform-petroleum ether (60-80°) gave the pyrrole carboxylic acid as a white powder (49.55 g; 63%), mp 149-151°C (lit.[47] mp 149-150°C). IR (Nujol mull): ν 3181 (NH str.), 3050 (st, br, OH str.), 1733 (st, C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.31 (3H, s, pyrrole-CH_3), 2.55 (2H, t, J = 7.7 Hz, pyrrole-CH_2), 3.07 (2H, t, J = 7.7 Hz, CH_2CO), 3.67 (3H, s, OCH_3), 5.34 (2H, s, CH_2Ph), 7.3-7.45 (5H, m, Ph), 9.63 (1H, br, NH), 11.3 (1H, vb, OH); ^{13}C NMR ($CDCl_3$): δ 10.02 (pyrrole-CH_3), 20.02 (4-CH_2), 34.41 (CH_2CO), 51.67 (OCH_3), 66.61 (CH_2Ph), 120.83, 122.70, 127.43, 128.40 (o-Ph), 128.47 (p-Ph), 128.67 (m-Ph), 131.49, 135.54 (Ph-C_{att}), 160.59 (CO_2Bn), 165.31 (CO_2H), 173.50 (aliphatic ester C=O).

5-Benzyloxycarbonyl-3-ethyl-4-methylpyrrole-2-carboxylic Acid (20b).

The title compound was prepared from benzyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate[35,48] (40.0 g) by the procedure detailed above. Recrystallization from ethanol-water gave **20b** as a white powder (30.5 g; 68%), mp 162-164°C (lit. mp[47] 165-166°C). IR (nujol mull): ν 3310 (NH str.), 1702, 1663 (2 x C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.30 (3H, s, pyrrole-CH_3), 2.77 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 5.34 (2H, s, OCH_2Ph), 7.3-7.45 (5H, m, Ph), 9.48 (1H, br, NH), 11.4 (1H, vb, OH); ^{13}C NMR ($CDCl_3$): δ 9.90 (pyrrole-CH_3), 14.92 (CH_2CH_3), 17.90 (pyrrole-CH_2), 66.49 (OCH_2), 120.22, 122.66, 127.04, 128.38 (o-Ph), 128.44 (p-Ph), 128.68 (m-Ph), 135.72 (Ph C_{att}), 160.67 (ester C=O), 165.96 (CO_2H).

5-*tert*-Butoxycarbonyl-3-ethyl-4-methylpyrrole-2-carboxylic Acid (20a).

Sulfuryl chloride (32.0 g; 19.0 mL) was added dropwise to a stirred mixture of *tert*-butyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate[36] (17.0 g) and potassium carbonate (34.0 g) in ether (1120 mL), maintaining the temperature at 20°C throughout. The resulting mixture was stirred for an additional 24 hr at room temperature. The ether was removed under reduced pressure and the resulting red oil dissolved in dioxane (255 ml). A 10% aqueous sodium bicarbonate solution (255 mL) was added and the vigorously stirred mixture heated at 70°C for 40 min. The mixture was extracted with ether (3 x 100 ml), and the combined ether layers extracted with sodium bicarbonate solution (5%; 3 x 100 mL). The combined aqueous solutions were acidified with concentrated hydrochloric acid, while maintaining the temperature below 10°C. The resulting precipitate was filtered, washed several times with water and dried *in vacuo*. Recrystallization from chloroform-petroleum ether (60-80°) gave the pyrrole carboxylic acid as a white powder (12.5 g; 65%), mp 207-208°C (lit.[49] mp 215-216°C); IR (nujol mull): ν 3295 (NH str.), 1669 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.10 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.57 (9H, s, ^{t}Bu), 2.26 (3H, s, pyrrole-CH_3), 2.76 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 9.36 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 9.88 (pyrrole-CH_3), 15.11 (CH_2CH_3), 17.78 (pyrrole-CH_2), 28.38 (^{t}Bu), 81.37 (-$C(CH_3)_3$), 120.81, 122.83, 125.67, 133.72, 160.43 (ester C=O), 163.01 (CO_2H).

Benzyl 5-Iodo-4-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate (16).

A solution of sodium bicarbonate (38.3 g) in water (374 ml) was added to a solution of 5-benzyloxycarbonyl-4-methyl-3-(2-methoxycarbonylethyl)pyrrole-2-carboxylic acid (49.55 g) in methanol and the resulting mixture was heated on a water bath to 60°C. A solution of iodine (37.88 g) and potassium iodide (57.40 g) in water (1500 mL) was added dropwise to a stirred mixture over a period of 1 hr, while maintaining the reaction temperature at 60-65°C, and stirring was continued for a further 1 hr. The

mixture was cooled and the precipitate filtered, washed well with 1% aqueous sodium thiosulfate solution to remove traces of iodine and then with deionized water. Recrystallization from ethanol-water afforded the iodopyrrole as white needles (58.5 g; 95%), mp 95-97°C (lit.[49] mp 95°C); IR (Nujol mull): ν 3270 (NH str.), 1726 (aliphatic ester C=O str.), 1654 (pyrrole C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.33 (3H, s, pyrrole-CH_3), 2.44 (2H, t, J = 7.9 Hz, pyrrole-CH_2), 2.71 (2H, t, J = 7.9 Hz, CH_2CO), 3.68 (3H, s, OCH_3), 5.31 (2H, s, CH_2Ph), 7.3-7.45 (5H, m, Ph), 9.1 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.91 (pyrrole-CH_3), 22.07 (pyrrole-CH_2), 34.31 (CH_2CO), 51.67 (OCH_3), 66.02 (CH_2Ph), 73.40 (C-5), 123.69, 127.18, 128.27 (o- and p- Ph), 128.61 (m-Ph), 136.04 (Ph C_{att}), 160.24 (pyrrole-C=O), 173.10 (aliphatic ester C=O).

Benzyl 4-Ethyl-5-iodo-3-methylpyrrole-2-carboxylate (21b).

Prepared from 5-benzyloxycarbonyl-3-ethyl-4-methylpyrrole-2-carboxylic acid (13.50 g) by the procedure detailed above. Recrystallization from ethanol gave the iodopyrrole as a white powder (15.95 g; 92%), mp 112-113°C (lit.[50] mp 112.5-113°C). IR (Nujol mull): ν 3214 (NH str.), 1665 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.04 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.32 (3H, s, pyrrole-CH_3), 2.38 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 5.32 (2H, s, OCH_2Ph), 7.3-7.45 (5H, m, Ph), 9.05 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.87 (pyrrole-CH_3), 14.74 (CH_2CH_3), 20.00 (pyrrole-CH_2), 65.93 (OCH_2), 72.89 (C-5), 123.50, 126.88, 128.23 (o- and p- Ph), 128.60 (m-Ph), 132.38, 136.20 (Ph C_{att}), 160.20 (C=O).

***tert*-Butyl 4-Ethyl-5-iodo-3-methylpyrrole-2-carboxylate (21a).**

Prepared from 5-*tert*-Butoxycarbonyl-3-ethyl-4-methylpyrrole-2-carboxylic acid (6.7 g) by the procedure described for **16**. Recrystallization from ethanol gave the iodopyrrole as white needles (7.1 g; 80%), mp 119-120°C (lit.[51] mp 123-124°C). IR (nujol mull): ν 3295 (NH str.), 1669 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.04 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.57 (9H, s, ^{t}Bu), 2.29 (3H, s, pyrrole-CH_3), 2.37 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 9.0 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.81 (pyrrole-CH_3), 14.79 (CH_2CH_3), 20.02 (pyrrole-CH_2), 28.51 (^{t}Bu), 71.42 (C-5), 80.92 (-$C(CH_3)_3$), 125.15, 125.48, 132.05, 160.20 (C=O).

Benzyl 4-(2-Methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate (17a).

Benzyl 5-iodo-4-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate (**16**; 58.5 g), anhydrous sodium acetate (19.5 g), platinum oxide (180 mg) and ethanol (210 mL) were placed in a hydrogenation vessel and the mixture was shaken under an atmosphere of hydrogen at room temperature and 30 psi for 24 hr. The mixture was filtered to remove the catalyst and evaporated under reduced pressure. The residue was taken up in chloroform, washed with water, dried over sodium sulfate and evaporated on a rotary evaporator to give the α-unsubstituted pyrrole (38.7 g; 92%) as a pale yellow oil (lit.[49] mp 41-42°C). IR (neat): ν 3329 (NH str.), 1734 (aliphatic ester C=O str.), 1685 (pyrrole C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.30 (3H, s, pyrrole-CH_3), 2.53 (2H, t, J = 7.6 Hz), 2.75 (2H, t, J = 7.6 Hz) (CH_2CH_2), 3.66 (3H, s, OCH_3), 5.30 (2H, s, CH_2Ph), 6.68 (1H, d, J = 2.7 Hz, pyrrole-H), 7.3-7.45 (5H, m, Ph), 8.85 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.31 (pyrrole-CH_3), 20.41 (pyrrole-CH_2), 34.73 (CH_2CO), 51.58 (OCH_3), 65.70 (CH_2Ph), 119.15, 120.00 (C-2 and C-5), 123.86 (C-4), 126.45 (C-3), 128.14 (o- and p- Ph), 128.57 (m-Ph), 136.37 (Ph C_{att}), 161.31 (pyrrole-C=O), 173.52 (aliphatic ester C=O).

Benzyl 4-Ethyl-3-methylpyrrole-2-carboxylate (11b).

Prepared by the foregoing procedure from benzyl 4-ethyl-5-iodo-3-methylpyrrole-2-carboxylate (**21b**; 30.7 g). Upon evaporation of the solvent, the 5-unsubstituted pyrrole (19.6 g; 97%) was isolated as a pale yellow oil (lit.[50] mp 31-32°C). IR (nujol mull): ν 3326 (NH str.), 1675 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.16 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.30 (3H, s, pyrrole-CH_3), 2.43 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 5.30 (2H, s, OCH_2Ph), 6.67 (1H, d, J = 2.8 Hz, 5-H), 7.3-7.45 (5H, m, Ph), 8.75 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.33 (pyrrole-CH_3), 14.57 (CH_2CH_3), 18.25 (pyrrole-CH_2), 65.63 (OCH_2), 119.03 (C-2), 119.40 (C-5), 126.43 (C-3), 127.71 (C-4), 128.11 (o- and p- Ph), 128.58 (m-Ph), 136.53 (Ph C_{att}), 161.47 (C=O).

***tert*-Butyl 4-Ethyl-3-methylpyrrole-2-carboxylate (11a).**

Hydrogenolysis of *tert*-butyl 4-ethyl-5-iodo-3-methylpyrrole-2-carboxylate (**21a**; 12.50 g) by the procedure detailed for **17a** gave the title compound as a pale yellow oil that solidified on standing (7.53 g; 95%). A sample was recrystallized from ethanol to give white needles, mp 92-93°C (lit.[51] mp 100-101°C). IR (nujol mull): ν 3319 (NH str.), 1668 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.16 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.56 (9H, s, ^{t}Bu), 2.26 (3H, s, pyrrole-CH_3), 2.42 (2H, q, J = 7.5 Hz, pyrrole-CH_2), 6.63 (1H, d, J = 2.6 Hz, 5-H), 8.9 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.26 (pyrrole-CH_3), 14.64 (CH_2CH_3), 18.28 (pyrrole-CH_2), 28.53 (^{t}Bu), 80.40 (-$C(CH_3)_3$), 118.46 (C-5), 120.60 (C-2), 124.90 (C-3), 127.38 (C-4), 161.52 (C=O).

Anal. calc. for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.91; H, 8.67; N, 6.67.

3-(5-Benzyloxycarbonyl-4-methyl-3-pyrrolyl)propanoic Acid (17b).

A mixture of concentrated hydrochloric acid (39 mL) and water (736 mL) was added to a solution of benzyl 4-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate (38.7 g) in acetone (774 mL), and the resulting mixture was stirred under reflux for 3 hr. The mixture was cooled to room temperature, poured into ice/water (4 L) and a milky pink precipitate formed. The mixture was transferred to a separatory funnel and extracted with ether (3 x 200 mL). The combined etherial solutions were extracted with 5% sodium bicarbonate solution (3 x 200 mL), and the aqueous solutions cooled to 5°C and neutralized with concentrated hydrochloric acid. The resulting precipitate was filtered, washed with liberal quantities of water and dried *in vacuo* to give the carboxylic acid as a white powder (33.67 g; 91%), mp 112-112.5°C. IR (nujol mull): ν 3316 (NH str.), 3066 (st, br, OH str.),

1728 (st, carboxylic acid C=O str.), 1678 (st, pyrrole C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.29 (3H, s, pyrrole-CH_3), 2.58 (2H, t, J = 7.3 Hz), 2.76 (2H, t, J = 7.3 Hz) (CH_2CH_2), 5.30 (2H, s, CH_2Ph), 6.71 (1H, d, J = 2.5 Hz, 5-H), 7.3-7.45 (5H, m, Ph), 9.2 (1H, br, NH), 11.0 (1H, vb, CO_2H); ^{13}C NMR ($CDCl_3$): δ 10.37 (pyrrole-CH_3), 20.16 (pyrrole-CH_2), 34.55 (CH_2CO), 65.88 (CH_2Ph), 119.11, 120.54 (C-2,5), 123.48 (C-4), 126.52 (C-3), 128.13 (o- and p- Ph), 128.56 (m-Ph), 136.23 (Ph C_{att}), 161.79 (ester C=O), 178.38 (CO_2H).

Anal. Calc. for $C_{16}H_{17}NO_4.{}^1/_4H_2O$: C, 65.84; H, 6.05; N, 4.80. Found: C, 65.74; H, 6.00; N, 5.07.

Benzyl 3-Methyl-6-oxocyclopenta[b]pyrrole-2-carboxylate (18).

The foregoing pyrrole carboxylic acid (0.25 g) was dissolved in methanol (5 mL) and the mixture neutralized with one equivalent of potassium hydroxide (0.098 g) in methanol (5 mL). The solvent was removed under reduced pressure and the residue dried overnight *in vacuo*. The resulting potassium salt was suspended in dry toluene (10 mL) and oxalyl chloride (0.11 g) in toluene (0.5 mL) was added to the stirred mixture. The resulting mixture was stirred for a further 3 hr at room temperature. After this time, 5 drops of tin(IV) chloride was added and the reaction mixture was stirred for a further 1 hr. The organic solution was washed successively with 5% hydrochloric acid, water, 5% sodium bicarbonate solution and water. The yellow organic solution was dried over magnesium sulfate and the solvent removed under reduced pressure. The residue was recrystallized from methanol to give the ketone as white crystals (0.101 g; 43%), mp 161-162°C. IR (nujol mull): ν 3178 (NH str.), 1668 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.32 (3H, s, pyrrole-CH_3), 2.80 (2H, m), 2.88 (2H, m) (CH_2CH_2), 5.35 (2H, s, CH_2Ph), 7.3-7.45 (5H, m, Ph), 9.4 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 10.60, 19.39, 41.28, 66.69, 123.22, 128.32, 128.48, 128.68, 129.31, 135.07, 135.48, 151.49, 161.38, 193.37.

Anal. Calc. for $C_{16}H_{15}NO_3.{}^1/_4H_2O$: C, 70.18; H, 5.72, N, 5.12. Found, C, 70.12; H, 5.67; N, 5.43.

Benzyl 6-Hydroxy-3-methylcyclopenta[b]pyrrole-2-carboxylate (10).

A mixture of pyrrole ketone 18 (0.85 g) and 95% ethanol (34 mL) were heated until the solid material had all dissolved and then cooled to room temperature to give a fine suspension. Sodium borohydride (0.70 g) was added and the mixture swirled for 10 min. At this stage the pyrrole dissolved and a noticeably exothermic reaction took place. Water (17 mL) was then added and the mixture was heated to its boiling point on a steam bath. An additional 34 mL of water was added and the mixture was allowed to cool to room temperature, and then chilled in ice. The resulting precipitate was filtered and dried *in vacuo*. Recrystallization from ethanol-water gave the pyrrole alcohol as white needles (0.70 g; 82%), mp 107-108°C. IR (nujol mull): 3297 (OH str.), 3185 (NH str.), 1677 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.7 (1H, OH), 2.28 (3H, s, pyrrole-CH_3), 2.15-2.3 (1H, m), 2.4-2.52 (1H, m), 2.65-2.9 (2H, m) (CH_2CH_2), 5.1 (1H, m, C*H*OH), 5.30 (2H, s, CH_2Ph), 7.3-7.45 (5H, m, Ph), 8.8 (1H, br, NH).

Anal. Calc. for $C_{16}H_{17}NO_3.{}^1/_8H_2O$: C, 70.25; H, 6.35; N, 5.12. Found: 70.16; H, 6.25; N, 5.28.

Benzyl 6-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylate (22a).

Benzyl 6-hydroxy-3-methylcyclopenta[b]pyrrole-2-carboxylate (10; 4.00 g) and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate (11a; 3.08 g) were dissolved in glacial acetic acid (110 mL). p-Toluenesulfonic acid (180 mg) was added and the resulting mixture stirred at room temperature for 90 min. The dark 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 dark residue was chromatographed on silica, eluting with dichloromethane. Recrystallization from ethanol gave a white solid (4.96 g; 73%): mp 135-136°C. EI MS: m/e (Relative intensity) 462 (M^+, 51%), 406 (31%), 377 (83%), 315 (20%), 271 (37%), 178 (48), 91 (100%); HR MS calcd. for $C_{28}H_{34}N_2O_4$: 462.25202. Found: 462.25012. IR (nujol mull): ν 3238 (NH str.), 1658 (C=O str.), 1649 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.05 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.49 (9H, s, ^{t}Bu), 2.21 (3H, s), 2.30 (3H, s) (2 x pyrrole-CH_3), 2.38 (2H, q, J = 7.5 Hz, CH_2CH_3), 2.25 (1H, m), 2.5-2.9 (3H, m) (ring-CH_2CH_2), 4.33 (1H, t, J = 7.4 Hz, bridge-CH), 5.16-5.26 (2H, AB quartet, OCH_2), 7.3-7.4 (5H, m, Ph), 8.5 (1H, br), 9.1 (1H, br) (2 x NH). ^{13}C NMR ($CDCl_3$): δ 10.45, 11.71, 16.11, 17.14, 23.20, 28.48, 35.88, 39.14, 65.47, 80.29, 117.94, 122.47, 123.58, 123.80, 125.52, 127.96, 128.05, 128.47, 130.90, 133.28, 136.49, 140.19, 161.35, 161.55.

Anal. Calc. for $C_{28}H_{34}N_2O_4$: C, 72.69; H, 7.42; N, 6.06. Found: C, 72.64; H, 7.49; N, 6.04.

Benzyl 6-(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylate (22b).

The title compound was prepared from benzyl 6-hydroxy-3-methylcyclopenta[b]pyrrole-2-carboxylate (10; 1.00 g) and benzyl 4-ethyl-3-methylpyrrole-2-carboxylate (11b; 0.90 g) by the procedure described above. Recrystallization from ethanol gave the dipyrrole as white crystals (1.32 g; 72%), mp 149-150°C. EI MS: m/e (Relative intensity): 496 (M^+, 49%), 467 (34%), 405 (29%), 359 (23%), 297 (14%), 268 (10%), 91 (100%); HR MS calcd. for $C_{31}H_{32}N_2O_4$: 496.23636. Found: 496.23474. ^1H NMR ($CDCl_3$): δ 1.06 (3H, t, J = 7.4 Hz, CH_2CH_3), 2.27 (3H, s), 2.30 (3H, s) (2 x pyrrole-CH_3), 2.41 (2H, q, J = 7.4 Hz, CH_2CH_3), 2.2-2.3 (1H, m), 2.5-2.75 (2H, m), 2.75-2.9 (1H, m) (ring-CH_2CH_2), 4.34 (1H, t, bridge-CH), 5.25 (4H, s, 2 x OCH_2), 7.3-7.4 (10H, m, 2 x Ph), 8.49 (1H, br), 8.76 (1H, br) (2 x NH). ^{13}C NMR ($CDCl_3$): δ 10.55, 11.64, 16.10, 17.09, 23.23, 35.83, 39.09, 65.52, 65.57, 117.45, 122.51, 123.85, 124.07, 127.03, 128.00, 128.50, 131.07, 134.21, 136.43, 136.54, 139.92, 161.33, 161.45.

Anal. Calc. for $C_{31}H_{32}N_2O_4$: C, 74.96; H, 6.51; N, 5.64. Found: C, 74.63; H, 6.38; N, 5.65.

6-(*tert*-Butoxycarbonyl-5-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylic Acid (23).

Benzyl 6-(5-*tert*-butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylate (22a; 1.00 g) and triethylamine (33 drops) were dissolved in acetone (250 mL) and placed in a hydrogenation vessel. The air was flushed out with nitrogen and 10% palladium/charcoal (248 mg) was added. The mixture was shaken under an atmosphere of hydrogen at room temperature and 30 psi for 12 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% ammonia solution and the aqueous solutions were 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 carboxylic acid as a white powder (2.21 g; 94%), mp 120-122°C. IR (nujol mull): ν 3245 (NH str.), 2980 (vb, OH str.), 1661 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.07 (3H, t, J = 7.4 Hz, CH_2CH_3), 1.53 (9H, s, ^tBu), 2.24 (3H, s), 2.27 (3H, s) (2 x pyrrole-CH_3), 2.41 (2H, q, CH_2CH_3), 2.3 (1H, m), 2.5-2.9 (3H, m) (ring-CH_2CH_2), 4.35 (1H, t, bridge-CH), 8.6 (1H, br), 8.8 (1H, br) (2 x NH).

Anal. Calc. for $C_{21}H_{28}N_2O_4$: C, 67.71; H, 7.59; N, 7.52. Found: C, 67.99; H, 7.58; N, 7.24.

6-(5-Carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylic Acid (29a).

Prepared from benzyl 6-(5-benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylate (22b; 1.00 g) by the procedure detailed above. The dicarboxylic acid was isolated as an off-white powder (0.60 g; 94%), mp 119°C, dec. ^1H NMR (d_6-DMSO-$CDCl_3$): δ 1.07 (3H, t, CH_2CH_3), 2.29 (3H, s), 2.31 (3H, s) (2 x pyrrole-CH_3), 2.3-2.9 (6H, m, CH_2CH_2 and CH_2CH_3), 4.35 (1H, t, bridge-CH), 8.50 (1H, br), 9.01 (1H, br) (2 x NH).

Anal. Calc. for $C_{17}H_{20}N_2O_4$: C, 64.53; H, 6.38; N, 8.86. Found: 64.37; H, 6.41; N, 8.30.

3-Methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxaldehyde (27a).

Ethyl 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylate[18] was dissolved in methanol (50 mL), a solution of potassium hydroxide (25.0 g) in water (100 mL) was added and the resulting mixture stirred under reflux for 3 hr. On cooling, flaky lustrous crystals of the potassium salt were formed. The contents of the flask were poured into a 500 mL Erlenmeyer flask and cooled to 0°C. The solution was neutralized with 3M hydrochloric acid, keeping the temperature below 5°C. The resulting precipitate was filtered, washed with liberal quantities of water to remove all traces of acid and dried *in vacuo* overnight to give 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxylic acid as a pale pink solid (8.6 g; quantitative).

The foregoing carboxylic acid (8.6 g) was dissolved in trifluoroacetic acid (50 mL) and stirred at 40°C for 10 min. The mixture was poured into ice/water and a white precipitate formed. The mixture was extracted with chloroform, washed with 5% sodium bicarbonate solution and water, and dried over magnesium sulfate. On evaporation, 3-methyl-4,5,6,7-tetrahydro-1*H*-indole was obtained as a pale yellow solid in quantitative yield. ^1H NMR ($CDCl_3$): δ 1.76 (4H, m, $CH_2(CH_2)_2CH_2$), 1.98 (3H, s, pyrrole-CH_3), 2.3-2.7 (4H, m, 4,7-CH_2), 6.36 (1H, 2-H), 7.4 (1H, br, NH).

The residue was dissolved in N,N-dimethylformamide (74 mL) and cooled to 0°C. A solution of p-nitrobenzoyl chloride (11.3 g) in N,N-dimethylformamide (12 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 (200mL) 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 (105 mL) and stirred with potassium carbonate (11.0 g) in water (105 mL) at 70°C for 15 min. The resulting yellow solution was poured into a mixture of crushed ice and water (700 mL) and a pale yellow precipitate formed immediately. The precipitate was filtered and recrystallized from 95% ethanol to give the title aldehyde as yellow needles (5.66 g; 72%), mp 170-171°C (lit.[52] mp 170°C). IR (nujol mull): ν 3226 (NH str.), 1626 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.77 (4H, m, $CH_2(CH_2)_2CH_2$), 2.22 (3H, s, pyrrole-CH_3), 2.49 (2H, m, 4-CH_2), 2.64 (2H, m, 7-CH_2), 9.46 (1H, s, CHO), 10.3 (1H, br, NH); ^{13}C NMR ($CDCl_3$): δ 8.60, 20.81, 22.64, 23.05, 120.48, 128.20, 131.44, 138.76, 175.69.

3-Methylcyclopenta[b]pyrrole-2-carboxaldehyde (27b).

Ethyl 3-methylcyclopenta[b]pyrrole-2-carboxylate[44,52] (1.00 g) was refluxed for 45 min. with 1.00 g of sodium hydroxide in ethylene glycol (10 mL). The cloudy yellow mixture was dispersed between hexane and water, the aqueous layer was extracted with hexane and the combined organic solutions were washed with water and dried over sodium sulfate. The solvent was evaporated under reduced pressure to give a yellow oil: ^1H NMR ($CDCl_3$): δ 2.01 (3H, s, pyrrole-CH_3), 2.3-2.7 (6H, m, $(CH_2)_3$), 6.34 (1H, 2-H), 7.35 (1H, br, NH). The residual oil was taken up in N,N-dimethylformamide (3 mL) and cooled to 0°C in an ice-salt bath. Benzoyl chloride (1 mL) was added dropwise, maintaining the temperature below 5°C. When the temperature had dropped to -5°C, the salt ice bath was removed and the mixture was stirred for a further 15 min. Toluene (10 mL) was added and the mixture was cooled in a salt-ice bath for 1 hr. The dark mixture was filtered to give a buff colored solid, which was washed with an additional 10 mL of cold toluene. The solid was taken up in ethanol (8 mL), a solution of sodium carbonate (1.0 g) in water (8 mL) was added, and the resulting mixture was stirred on a boiling water bath for 15 min. Water (20 mL) was added and the mixture was stirred at room temperature overnight. The mixture was cooled in an ice bath and filtered to give a yellow-brown solid. Recrystallization from ethanol-water gave the pyrrole aldehyde as pale yellow needles (0.41 g; 53%), mp 134-134.5°C. IR (nujol mull): ν 3200 (NH str.), 1625 (C=O str.) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.26 (3H, s, pyrrole-CH_3), 2.44 (2H, m, $CH_2CH_2CH_2$), 2.56 (2H, t, J = 6.7 Hz, 4-CH_2), 2.71 (2H, t, J = 7.1 Hz, 6-CH_2), 9.0 (1H, br, NH), 9.42 (1H, s, CHO); ^{13}C NMR ($CDCl_3$): δ 9.72, 23.37, 25.20, 28.91, 128.16, 130.96, 133.27, 147.34, 175.75.

Anal. calc. for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39. Found: 72.03; H, 7.21; N, 9.51.

1-*tert*-Butoxycarbonyl-5,7-ethano-3,12-diethyl-2,8,13,14-tetramethyl-5,16-dihydrotripyrrin Hydrobromide (24).

6-(*tert*-Butoxycarbonyl-5-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylic acid (23; 1.00 g) and 3-ethyl-4,5-dimethylpyrrole-2-carboxaldehyde (13; 0.405 g) were dissolved in dichloromethane (130 mL) and placed in a 250 mL Erlenmeyer flask. A solution of p-toluenesulfonic acid (1.30 g) in methanol (15 mL) was added in one portion and the resulting mixture was stirred at room temperature for 40 min. The orange solution was washed successively with water, saturated sodium bicarbonate solution and water. The residue was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was taken up in dichloromethane (100 mL), hydrogen bromide gas was bubbled through the solution for 5 sec and the solvent immediately removed under reduced pressure. The residue was taken up in toluene (80 mL) and immediately reevaporated to azeotropically remove traces of water and hydrobromic acid. A second portion of toluene (80 mL) was added and the solution reevaporated. The residue was taken up in a minimal amount of ether and the mixture was cooled in an ice bath to initiate crystallization. The resulting precipitate was filtered and washed with ether to give the tripyrrene hydrobromide as a orange solid with a green sheen (1.078 g; 74%), mp 180-182°C. UV/Vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 495 (4.76) nm. ^1H NMR ($CDCl_3$): δ 1.10 (3H, t), 1.18 (3H, t) (2 x CH_2CH_3), 1.53 (9H, s, ^{t}Bu), 1.98 (3H, s), 2.21 (3H, s), 2.31 (3H, s), 2.61 (3H, s) (4 x pyrrole-CH_3), 2.2-2.5 (8H, m, CH_2CH_2 and 2 x CH_2CH_3), 4.71 (1H, m, bridge-CH), 7.01 (1H, s, =CH-), 8.4 (1H, br, NH), 13.0 (2H, br, NH).

Anal. calc. for $C_{29}H_{40}BrN_3O_2$: C, 64.18; H, 7.44; N, 7.74. Found: C, 63.88; H, 7.25; N, 7.68.

1-*tert*-Butoxycarbonyl-3,7,13-triethyl-2,8,12,14-tetramethyl-5,16-dihydrotripyrrin Hydrobromide (26).

Prepared from 5'-*tert*-butoxycarbonyl-3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5-carboxylic acid[53] (2.00 g) and 4-ethyl-3,5-dimethylpyrrole-2-carboxaldehyde (12; 0.81 g) by the procedure described above. The tripyrrene crystallized from anhydrous ether as bright orange crystals (2.20 g; 76%), mp 193-194°C; UV/Vis ($CHCl_3$): λ_{max} 497 (4.90) nm. ^1H NMR ($CDCl_3$): δ 1.01 (3H, t), 1.04 (3H, t), 1.09 (3H, t) (3 x CH_2CH_3), 1.57 (9H, s, ^{t}Bu), 2.25 (6H, s), 2.28 (3H, s) (2,8,12-CH_3), 2.4-2.5 (6H, m, 3 x CH_2CH_3), 2.68 (3H, s, 14-CH_3), 4.30 (2H, s, bridge-CH_2), 7.06 (1H, s, -CH=), 10.15 (1H, br, NH), 13.05 (2H, br, 2 x NH).

Anal. calc. for $C_{29}H_{42}BrN_3O_2$: C, 63.96; H, 7.77; N, 7.72. Found: C, 64.26; H, 7.66; N, 7.60.

8,10-Ethano-3,12,18-triethyl-1,2,7,13,17,19-hexamethyl-10,23-dihydrobilin Dihydrobromide (25).

Tripyrrene **24** (670 mg) was dissolved in trifluoroacetic acid (4 mL) and stirred at room temperature for 15 min. 4-Ethyl-3,5-dimethylpyrrole-2-carboxaldehyde (12; 188 mg) in methanol (17 mL) was added to the stirred solution, immediately followed by the addition of hydrogen bromide in acetic acid (31%; 3.4 mL), and the resulting mixture was stirred at room temperature for 30 min. Ether (134 mL) was added slowly over several minutes and the mixture was stirred for an additional 2 hr. The mixture was cooled in an ice bath and the resulting precipitate was filtered and washed with ether to give the a,c-biladiene as an orange-brown solid with a green sheen (651 mg; 86%), mp >300°C. UV/Vis ($CHCl_3$): λ_{max} 464, 519 nm. ^1H NMR ($CDCl_3$): δ 1.04 (3H, t), 1.08 (3H, t), 1.16 (3H, t) (3 x CH_2CH_3), 1.95 (3H, s, 2-CH_3), 2.24 (3H, s), 2.30 (3H, s) (7,13-CH_3), 2.32 (3H, s), 2.1-3.1 (10H, m, CH_2CH_2 and 3 x CH_2CH_3), 2.55 (3H, s), 2.63 (3H, s) (1,19-CH_3), 5.20 (1H, t, bridge-CH), 7.01 (1H, s), 7.12 (1H, s) (2 x =CH), 12.4 (1H, br), 12.9 (1H, br), 13.1 (2H, br) (4 x NH).

1,2-Butano-8,12,18-triethyl-3,7,13,17-tetramethyl-10,23-dihydrobilin Dihydrobromide (28a).

Prepared by the procedure detailed above from 3-methyl-4,5,6,7-tetrahydro-1*H*-indole-2-carboxaldehyde (**27a**; 0.15 g) and 1-*tert*-butoxycarbonyl-3,7,13-triethyl-2,8,12,14-tetramethyl-5,16-dihydrotripyrrin hydrobromide (**26**; 0.50 g). The title a,c-biladiene was isolated as a red-brown solid (0.51 g; 82%), mp >300°C;[54] UV/Vis ($CHCl_3$): λ_{max} 460, 530 nm. ^1H NMR ($CDCl_3$): δ 0.63 (6H, 2 overlapping triplets, 8,12-CH_2CH_3), 1.09 (3H, t, 18-CH_2CH_3), 1.82 (4H, m, $CH_2(CH_2)_2CH_2$), 2.23 (6H, s), 2.26 (3H, s), 2.30 (3H, s) (3,7,13,17-CH_3), 2.4-2.6 (8H, m, 4 x β-CH_2), 2.71 (3H, s, 19-CH_3), 3.15 (2H, m, 1-CH_2), 5.18 (2H, s, bridge-CH_2), 7.10 (1H, s), 7.11 (1H, s) (2 x =CH-), 13.16 (3H, br), 13.19 (1H, br) (4 x NH).

Anal. calc. for $C_{34}H_{46}Br_2N_4.^2/_3H_2O$: C, 59.83; H, 6.99; N, 8.20. Found: C, 59.78; H, 6.80; N, 7.97.

3,5-Ethano-7,13,17-triethyl-2,8,12,18-tetramethylporphyrin (31a).

A solution of p-toluenesulfonic acid monohydrate (450 mg) in methanol (7.5 mL) was added to a stirred mixture of 6-(5-carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylic acid (**29a**; 250 mg) and 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (**30a**; 215 mg) in dichloromethane (75 mL) and methanol (7.5 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} 410, 456, 495 nm. A saturated solution of zinc acetate in methanol (8 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} 403 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 dichloromethane. The colored fractions were evaporated and further purified by chromatography on a grade 3 alumina column, eluting with dichloromethane, and the major red band was collected and recrystallized from dichloromethane-methanol to give **31a** as purple crystals (69 mg; 19%), mp >300°C. EI MS: m/e (Relative abundance) 476 (M^+, 100%), 461 (14%); HR MS calcd. for $C_{32}H_{36}N_4$: 476.29428. Found: 476.29296. UV/Vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.34), 500 (4.18), 535 (3.59), 564 (3.77), 616 (3.75) nm. ^1H NMR ($CDCl_3$): δ -3.7 (1H, br), -3.0 (1H, br) (2 x NH), 1.79 (3H, t), 1.85 (3H, t), 1.89 (3H, t) (3 x

CH_2CH_3), 3.57 (3H, s), 3.59 (3H, s), 3.68 (3H, s), 3.70 (3H, s) (4 x porphyrin-CH_3), 4.0-4.1 (8H, m, 4 x β-CH_2), 5.46 (2H, m, meso-CH_2), 10.00 (1H, s), 10.02 (1H, s), 10.07 (1H, s) (3 x meso-H).

3,5-Ethano-7-ethyl-13,17-bis-(2-methoxycarbonylethyl)-2,8,12,18-tetramethylporphyrin (31b).

Prepared from 6-(5-carboxy-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylic acid (**29a**; 250 mg) and 3,3'-bis(2-methoxycarbonylethyl)-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (**30b**; 302 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 dichloromethane-methanol gave the title porphyrin as purple crystals (79 mg; 18%), mp 237-238.5°C. FAB MS: m/e 593 ($[M+H]^+$); HR MS calcd. for $C_{36}H_{40}N_4O_4$ + H: 593.31303. Found: 593.31043. UV/Vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 402 (5.35), 501 (4.20), 535 (3.58), 565 (3.80), 618 (3.76) nm. ^1H NMR ($CDCl_3$): δ -3.7 (1H, br), -2.9 (1H, br) (2 x NH), 1.78 (3H, t, J = 7.6 Hz, CH_2CH_3), 3.25-3.34 (4H, m, 2 x CH_2CO), 3.60 (6H, s), 3.66 (3H, s), 3.69 (6H, s), 3.71 (3H, s) (4 x porphyrin-CH_3 and 2 x OCH_3), 4.08-4.14 (4H, m, 3,7-CH_2), 4.36 (2H, t), 4.50 (2H, t) (2 x $CH_2CH_2CO_2Me$), 5.45 (2H, m, meso-CH_2), 10.02 (1H, s), 10.03 (1H, s), 10.08 (1H, s) (3 x meso-H).

3,5-Ethano-13,17-diethyl-2,8,12,18-tetramethylporphyrin (31c).

Benzyl 6-(5-benzyloxycarbonyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[b]pyrrole-2-carboxylate[44] (0.30 g) and triethylamine (10 drops) were dissolved in ethanol (150 mL) and placed in a hydrogenation vessel. The air was flushed out with nitrogen and 10% palladium/charcoal (50 mg) was added. The mixture was shaken under an atmosphere of hydrogen at room temperature and 30 psi for 12 hr. The catalyst was filtered off and the solvent removed on a rotary evaporator, maintaining the temperature of the water bath below 35°C. The oily residue was reacted with 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrylmethane-5,5'-dicarboxaldehyde (**30a**; 165 mg) under the conditions detailed for the preparation of **31a**. Recrystallization from chloroform-methanol gave **31c** as purple crystals (30 mg; 12%), mp >300°C. EI MS: m/e (Relative abundance) 448 (M^+, 100%), 433 (15%); HR MS calcd. for $C_{30}H_{32}N_4$: 448.26296. Found: 448.26153. UV/Vis ($CHCl_3$): λ_{max} ($\log_{10}\varepsilon$) 401 (5.31), 499 (4.15), 534 (3.55), 564 (3.74), 617 (3.73) nm. ^1H NMR ($CDCl_3$): δ -3.4 (1H, br), -2.7 (1H, br) (2 x NH), 1.85 (3H, t), 1.88 (3H, t) (2 x CH_2CH_3), 3.56 (6H, s), 3.66 (3H, s), 3.80 (3H, s) (4 x porphyrin-CH_3), 4.02 (2H, q), 4.15 (2H, q) (2 x CH_2CH_3), 4.11 (2H, m, 3-CH_2), 5.36 (2H, m, meso-CH_2), 9.11 (1H, s, β-H), 9.93 (1H, s), 10.02 (1H, s), 10.07 (1H, s) (3 x meso-H).

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REFERENCES

1. Part 2: May, D.M., Jr.; Lash, T.D. *J. Org. Chem.* **1992**, *57*, 4820.
2. Results presented, in part, at the 21st Great Lakes Regional ACS Meeting, Loyola University, Chicago, Illinois, June 1987: Catarello, J.J.; Lash, T.D. *Program and Abstracts*, 248.
3. Treibs, A. *Justus Liebigs Ann. Chem.* **1934**, *510*, 42.
4. (a) Baker, E.W.; Palmer, S.E. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 1, pp. 486-552, (b) Callot, H.J. In *The Chlorophylls*, Scheer, H., Ed.; CRC Press, Boca Raton, 1991, pp 339-364.
5. Treibs, A. *Angew. Chem.* **1936**, *49*, 682.
6. Baker, E.W. *J. Am. Chem. Soc.* **1966**, *88*, 2311; Baker, E.W.; Yen, T.F.; Dickie, J.P.; Rhodes, R.E.; Clark, L.F. *ibid.*, **1967**, *89*, 3631.
7. Quirke, J.M.E.; Maxwell, J.R.; Eglinton, G.; Sanders, J.K.M. *Tetrahedron Lett.* **1980**, *21*, 2987. Fookes, C.J.R. *J. Chem. Soc., Chem. Commun.* **1983**, 1472. Ekstrom, A.; Fookes, C.J.R.; Hambley, T.; Loeh, H.J.; Miller, S.A.; Taylor, J.C. *Nature* **1983**, *306*, 173. Shulga, A.M.; Serebrennikova, O.V.; Mozzhelina, T.K. *Neftekhimiya* **1986**, *26*, 309.
8. Quirke, J.M.E.; Maxwell, J.R. *Tetrahedron* **1980**, *36*, 3453. Fookes, C.J.R. *J. Chem. Soc., Chem. Commun.* **1985**, 706. Chicarelli, M.I.; Wolff, G.A.; Maxwell, J.R. *ibid.*, 723.
9. (a) Filby; R.H.; Van Berkel; G.J. In In *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing.* Filby, R.H.; Branthaver, J.F., Ed., American Chemical Society: Washington DC, 1987, pp 2-39. (b) Chicarelli; M.I., Kaur; S. and Maxwell: J.R. *Ibid.*, pp. 40-67. (c) Ocampo, R.; Callot, H.J.; Albrecht, P. *Ibid.*, pp. 68-73.
10. (a) Callot, H.J.; Ocampo, R.; Albrecht, P. *Energy Fuels* **1990**, *4*, 635. (b) Verne-Mismer, J.; Ocampo, R.; Bauder, C.; Callot, H.J.; Albrecht, P. *Energy Fuels* **1990**, *4*, 639. (c) Keely, B.J.; Prowse, W.G.; Maxwell, J.R. *Energy Fuels* **1990**, *4*, 628. (d) Eckardt, C.B.; Keely, B.J.; Waring, J.R.; Chicarelli, M.I.; Maxwell, J.R. *Phil. Trans. R. Soc. Lond. B* **1991**, *333*, 339. (e) Ocampo, R.; Bauder, C.; Callot, H.J.; Albrecht, P. *Geochim. Cosmochim. Acta* **1992**, *56*, 745.
11. Wolff, G.A.; Murray, M.; Maxwell, J.R.; Hunter, B.K.; Sanders, J.K.M. *J. Chem. Soc., Chem. Commun.* **1983**, 922. Fookes, C.J.R. *Ibid.*, 1474. Storm, C.B.; Krane, J.; Skjetne, T.; Telnaes, N.; Branthaver, J.F.; Baker, E.W. *Science* **1984**, *223*, 1075. Chicarelli, M.I.; Maxwell, J.R. *Tetrahedron Lett.* **1984**, *25*, 4701. Ocampo, R.; Callot, H.J.; Albrecht, P.; Kintzinger, J.P. *ibid.*, 2589. Chicarelli, M.I.; Wolff, G.A.; Murray, M.; Maxwell, J.R. *Tetrahedron* **1984**, *40*, 4033. Ocampo, R.; Callot, H.J.; Albrecht, P. *J. Chem. Soc., Chem. Commun.* **1985**, 200. Kaur, S.; Chicarelli, M.I.; Maxwell, J.R. *J. Am. Chem. Soc.* **1986**, *108*, 1347. Chicarelli, M.I.; Maxwell, J.R. *Tetrahedron Lett.* **1986**, *27*, 4653. Verne-Mismer, J.; Ocampo, R.; Callot, H.J.; Albrecht P. *J. Chem. Soc., Chem. Commun.* **1987**, 1581. Prowse, W.G.; Chicarelli, M.I.; Keely, B.J.; Kaur, S.; Maxwell J.R. *Geochim. Cosmochim. Acta* **1987**, *51*, 2875. Prowse, W.G.; Maxwell, J.R. *Geochim. Cosmochim. Acta* **1989**, *53*, 3081.

12. Palmer, S.E.; Baker, E.W. *Science* **1978**, *201*, 49. Baker, E.W.; Louda, J.W. *Org. Geochem.* **1984**, *6*, 183.
13. E.g. Baker, E.W.; Palmer, S.E.; Huang, W.Y. *Initial Rep. Deep Sea Drill. Proj.* **1978**, *41*, 825.
14. 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
15. (a) Bonnett, R.; Czechowski, F.; Latos-Grazynski, L. *Energy Fuels* **1990**, *4*, 710 and references cited therein. (b) Bonnett, R.; Burke, P.J.; Czechowski, F. In *Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing.* Filby, R.H.; Branthaver, J.F., Ed., American Chemical Society: Washington DC, 1987, pp 173-185. (c) Bonnett, R.; Burke, P.J.; Reszka, A. *Fuel* **1987**, *66*, 515.
16. Bonnett, R.; Czechowski, F. *J. Chem. Soc., Perkin Trans. I* **1984**, 125.
17. Bonnett, R.; Czechowski, F. *Phil. Trans. R. Soc. London, A* **1981**, *300*, 51.
18. Lash, T.D.; Bladel, K.A.; Shiner, C.M.; Zajeski, D.L.; Balasubramaniam, R.P. *J. Org. Chem.* **1992**, *57*, 4809.
19. Lash, T.D.; Perun, T.J., Jr. *Tetrahedron Lett.* **1987**, *28*, 6265.
20. Lash, T.D. *Tetrahedron Lett.* **1988**, *29*, 6877.
21. (a) Lash, T.D. *Organic 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. (c) Lash, T.D.; Quizon-Colquitt; D.M.; Shiner, C.M.; Nguyen, T.H.; Hu, Z. *Energy Fuels*, in press.
22. Lash, T.D.; Johnson, M.C. *Tetrahedron Lett.* **1989**, *30*, 5697.
23. Lash, T.D.; Balasubramaniam, R.P. *Tetrahedron Lett.* **1990**, *31*, 7545.
24. Lash, T.D. In *Advances in Nitrogen Heterocycles*, Vol. 1; Moody, C.J., Ed.; JAI Press, in press.
25. (a) Fischer, H.; Hofmann, H.J. *Justus Liebigs Ann. Chem.* **1935**, *517*, 274. (b) Sugihara, J.M.; McGee, L.R. *J. Org. Chem.* **1957**, *22*, 795.
26. Baker, E.W.; Corwin, A.H.; Klesper, E.; Wei P.E. *J. Org. Chem.* **1968**, *33*, 3144. Verne-Mismer, J.; Ocampo, R.; Callot, H.J.; Albrecht P. *Tetrahedron Lett.* **1986**, *27*, 5257. *Ibid.*, **1988**, *29*, 371. Smith, N.W.; Smith, K.M. *Energy Fuels* **1990**, *4*, 675.
27. (a) Chaudry, I.A.; Clezy, P.S.; Mirza, A.H. *Aust. J. Chem.* **1980**, *33*, 1095. (b) Evstigneeva, R.P. *Pure Appl. Chem.* **1981**, *53*, 1129. (c) Pomonarev, G.V.; Shul'ga, A.M.; Subock, V.P. *Dokl. Akad. Nauk SSSR* **1981**, *259*, 1121. (d) Pomonarev, G.V. *Khim. Geterotsikl. Soedin.* **1981**, 1693. (e) Smith, K.M.; Langry, K.C.; Minnetian, O.M. *J. Org. Chem.* **1984**, *49*, 4602. (f) Clezy, P.S.; Mirza, A.H.; Prashar, J.K. *Aust. J. Chem.* **1990**, *43*, 857. (g) Clezy, P.S.; Van Phuc, L.; Prashar, J.K. *ibid.* **1991**, *44*, 1061. (h) Clezy, P.S.; Fookes, C.J.R.; Prashar, J.K.; Salek, A. *ibid.* **1992**, *45*, 703.
28. (a) Bauder, C.; Ocampo, R.; Callot, H.J. *Synlett* **1990**, 335. (b) *Ibid.*, *Tetrahedron Lett.* **1991**, *32*, 2537. (c) *Ibid.*, *Tetrahedron* **1992**, *48*, 5135.
29. Flaugh M.E.; Rapoport H. *J. Am. Chem. Soc.* **1968**, *90*, 6877.
30. Kampfen, U.; Eschenmoser, A. *Helv. Chim. Acta* **1989**, *72*, 185. These conditions have been used to prepare DPEP from chlorophyll-a in superior yields: Ocampo, R.; Jeandon, C.; Callot, H.J. 204th National Meeting of the American Chemical Society, Washington, DC, August 24, 1992.
31. Baptista de Almeida, J.A.P.; Kenner, G.W.; Rimmer, R.; Smith, K.M. *Tetrahedron* **1976**, *32*, 1793.
32. (a) Jackson, A.H.; Smith, K.M. In *The Total Synthesis of Natural Products* ; Ed. ApSimon, J.; 1973, Vol. 1, pp 143-278, Wiley, New York. (b) *Ibid.*, Vol 6. pp. 237-280, 1984.
33. Paine, J.B., III In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 1, pp 101-234.
34. Paine, J.B., III; Dolphin, D. *J. Org. Chem.* **1985**, *50*, 5598.
35. Johnson, A.W.; Markham, E.; Price, R.; Shaw, K.B. *J. Chem. Soc.* **1958**, 1430.
36. Johnson, A.W.; Kay, I.T.; Markham, E.; Price, R.; Shaw, K.B. *J. Chem. Soc.* **1959**, 3416.
37. Al-Hazimi, H.M.G.; Jackson, A.H.; Knight, D.W.; Lash, T.D. *J. Chem. Soc., Perkin Trans. I* **1987**, 265.
38. Smith, K.M.; Minnetian, O.M. *J. Chem. Soc., Perkin Trans. I* **1986**, 277.
39. Smith, K.M.; Pandey, R.K. *Synth. Commun.* **1986**, *16*, 929.
40. Smith, K.M.; Pandey, R.K. *J. Chem. Soc., Perkin Trans. I* **1987**, 1229.
41. Smith, K.M., 199th National Meeting of the American Chemical Society, Boston, MA, April 1990.
42. Clezy, P.S.; Prashar, J.K. *Aust. J. Chem.* **1990**, *43*, 825.
43. Arsenault, G.P.; Bullock, E.; MacDonald, S.F. *J. Am. Chem. Soc.* **1960**, *82*, 4384.
44. Lash, T.D.; Quizon-Colquitt, D.M. Unpublished work. Quizon, D.M.; Lash, T.D. Book of Abstracts for the 203rd National American Chemical Society Meeting, San Francisco, CA, April 1992, ORGN 28.
45. Jackson, A.H.; Kenner, G.W.; Smith, K.M. *J. Chem. Soc. (C)* **1971**, 502.
46. Dolphin, D.; Harris, R.L.N.; Huppatz, J.L.; Johnson, A.W.; Kay, I.T.; Leng, J. *J. Chem. Soc.* **1966**, 98. Grigg, R.; Johnson, A.W.; Kenyon, R.; Math, V.B.; Richardson, K. *J. Chem. Soc. (C)* **1969**, 176. See also reference 50.
47. Jackson, A.H.; Kenner, G.W.; Warburton, D. *J. Chem. Soc.* **1965**, 1328.
48. Hayes, A.; Kenner, G.W.; Williams, N.R. *J. Chem. Soc.* **1958**, 3779.
49. Crook, P.J.; Jackson, A.H.; Kenner, G.W. *J. Chem. Soc. (C)* **1971**, 474.
50. Smith, K.M.; Minnetian, O.M. *J. Org. Chem.* **1985**, *50*, 2073.
51. Barton, D.H.R.; Kervagoret, J.; Zard, S.Z. *Tetrahedron* **1990**, *46*, 7587.
52. Treibs, A.; Dinelli, D. *Justus Liebigs Ann. Chem.* **1935**, *517*, 152.
53. Jackson, A.H.; Kenner, G.W.; Smith, K.M.; Suckling, C.J. *J. Chem. Soc., Perkin Trans. I* **1982**, 1441.
54. The sample gradually turned dark during heating, indicating that decomposition was occurring. Rapid heating gave a mp of approximately 250°C.