Synthesis and Characterisation of the C_{30}-De-ethylaetioporphyrin Present in Petroleum[1]

Paul J. Clewlow and Anthony H. Jackson*
Department of Chemistry, University College, Cardiff CF1 1XL

The four de-ethyl analogues of the relatively ubiquitous and biogenetically significant petroporphyrin aetioporphyrin III (**3a—d**) have been synthesized utilising the *ac*-biladiene route. A reversed-phase HPLC method of separating a mixture of the four synthetic isomers was developed, and comparisons with the C_{30}-de-ethylaetioporphyrins occurring in Gilsonite and Serpiano shale revealed them to be identical with the synthetic *C*-ring isomer (**3c**). This significant result indicates that the C_{30}-aetioporphyrin present in petroleum results from degradative maturation processes on chlorophyll-*a* itself.

Porphyrins were first identified in samples of petroleum, oil shale, bitumen, mineral wax, asphalt, phosphorite, and coal[1,2] in the early 1930s. In petroleum they occur almost exclusively as their vanadyl[3] and nickel[4] chelates, but copper porphyrins[5] are known to occur in certain marine sediments, and iron[6,7] and gallium[7] porphyrins have been isolated from immature coals. Mass spectrometric studies[8–10] have revealed the presence of two major series of petroporphyrins based on the aetioporphyrin-III (aetio-) (**1**) and desoxophylloerythroaetioporphyrin (DPEP) (**2**) structural types. Both of these are presumably derived largely *via* degradation of chlorophyll over the course of geological time.[1] The fact that porphyrins from marine sources contain almost equal amounts of these series leads to the conclusion that the opening of the isocyclic five-membered ring of chlorophyll is a very important reaction indeed.[11] It is well known that this ring can be either hydrolytically or oxidatively cleaved[12,13] and these processes could lead geochemically to porphyrins lacking a substituent at C-6 in the *C*-ring; on the other hand thermally retorted oil shales have been found to contain a much larger proportion of aetioporphyrins than unretorted shales[14] and these presumably arise by a reductive ring-opening process.

Both aetioporphyrins and DPEPs occur as homologous series with carbon numbers ranging from C_{25} to C_{60}.[15] Thus, during the geochemical alteration of the chlorophyll molecule into stable geological pigments, a variety of reactions involving several branching pathways must occur to account for this distribution. Transalkylation has been proposed to account for the wide range of alkyl side-chains found in petroporphyrins.[10,16–18] However, this alone cannot account for the distribution of molecular weights observed. It seems more likely that the higher carbon-number components are produced as the direct result of reaction at specific carbon atoms on chlorophyll-*a* itself or on early-stage diagenetic products[19] by incorporation of the pigment moieties into kerogen (a disseminated organic material present in rocks capable of producing, or already having produced, oil[20]) and then subsequent thermal cracking due to the enhanced temperature and pressure at the zone of oil generation.[19] Conversely, petroporphyrins may themselves condense with the kerogenic material.[15] Support for both these mechanistic postulates is given by studies on certain oil shales of a uniform sedimentary distribution.[21] It is found that, with increased burial depth and associated temperature rise, an increase in the DPEP/aetio ratio is observed due to thermal cracking,[22] together with a decrease in the average molecular weight of the petroporphyrins due to the cleavage of alkyl side-chain substituents.[21,23,24] Superimposed on these processes, there is another homologous series of vanadyl porphyrins which are only generated at deep burial depths and are thought to arise *via* the thermal cracking of kerogen itself. The consequence of all these combined factors is a decrease in the ratio of nickel- to vanadyl-chelated porphyrins with increasing depth.[21]

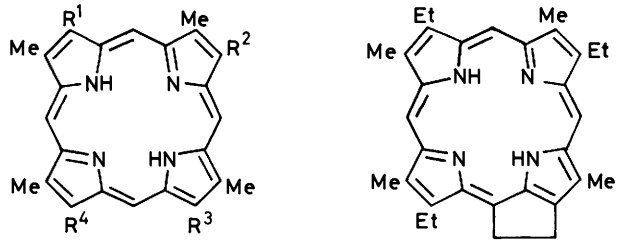
One of the more ubiquitous petroporphyrins, occurring together with aetioporphyrin (**1**), has been identified by chromatographic, mass spectrometric, and nuclear magnetic resonance studies as a C_{30}-analogue of aetioporphyrin lacking one of the peripheral ethyl groups.[25,26] It was, therefore, of considerable interest in relation to the origin of this C_{30}-porphyrin to discover which of the four positional isomers (**3a—d**) corresponded to this natural C_{30}-porphyrin of geochemically altered chlorophyll-*a*.[27] The present paper describes the synthesis of all four porphyrin isomers and comparisons with natural materials.

Results and Discussion

Of the methods which have been devised for the synthesis of unsymmetrical porphyrins, the MacDonald[28] and *ac*-biladiene[29] routes seemed to offer the most promising possibilities. It was decided that the de-ethylaetioporphyrins (**3a—d**) would be synthesized *via* devinylation[30] of the corresponding vinyl porphyrins because of past difficulties encountered during porphyrin-forming coupling reactions often giving mixtures of products with concomitant low yields.[31] In previous syntheses of porphyrins with unsubstituted peripheral (or β-) positions, it proved to be advantageous to prepare protected porphyrins containing for example a bromine substituent, which could readily be removed after porphyrin formation; in the present case we also wished to obtain the vinyl porphyrins for other purposes. Initially, the MacDonald route[28] was investigated for the synthesis of the *A*-ring isomer[32] (**3a**). However, because of very low yields obtained during the ring-closure stage and problems which might have been encountered during the synthesis of the 'unsymmetrical' *D*-ring isomer (**3d**), we decided to turn to the biladiene[29] and tripyrrene-biladiene[33] routes instead.

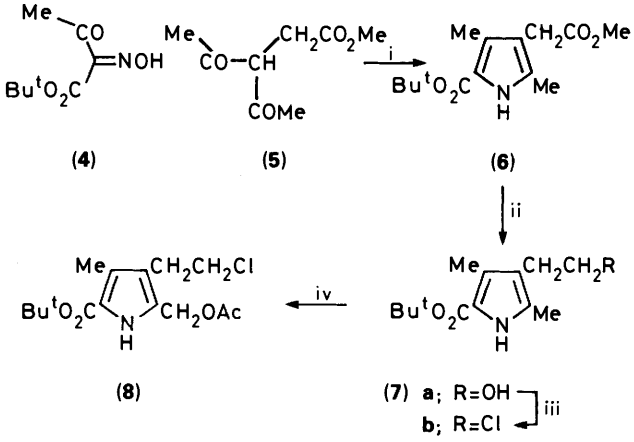
The strategy adopted for the synthesis of all four C_{30}-de-ethyl-aetioporphyrins (**3a—d**) was very similar; the 2′-chloroethyl analogues[34] being the initial targets due to their ease of conversion into the corresponding vinyl porphyrins.[35]

Synthesis of the A-*Ring Isomer:* 1,3,5,8-*Tetramethyl*-4,6,7-*triethylporphyrin* (**3a**).—The initial target of this synthetic route was the unsymmetrical 3-(2′-chloroethyl)pyrromethane (**14**),



(1) $R^1=R^2=R^3=R^4=Et$ (2)

(3) **a**; $R^1=H, R^2=R^3=R^4=Et$
b; $R^1=R^3=R^4=Et, R^2=H$
c; $R^1=R^2=R^4=Et, R^3=H$
d; $R^1=R^2=R^3=Et, R^4=H$

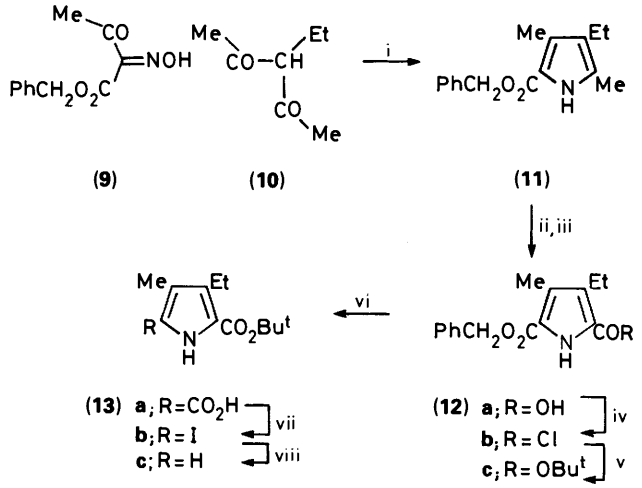


Scheme 1. *Reagents and conditions:* i, Zn–HOAc, 70—80 °C; ii, B_2H_6–diglyme; iii, SO_2Cl_2–CH_2Cl_2; iv, $Pb(OAc)_4$–AcOH

corresponding to the *A* and *B* rings of the porphyrin. This was formed by coupling the pyrrolic precursors (**8**) and (**13a**) in methanol containing toluene-*p*-sulphonic acid (PTSA) as catalyst. The pyrrole (**8**) was synthesized (Scheme 1) *via* the intermediate pyrrole[36] (**6**) which was first prepared from methyl 3-acetyl-4-oxopentanoate[37] (**5**) and t-butyl (hydroxyimino)acetoacetate (**4**) (*cf.* ref. 38) under Knorr-type conditions using zinc as reducing agent in acetic acid. This was then converted in high yield into the 4-(2′-hydroxyethyl)pyrrole[39] (**7a**) by diborane reduction and thence into the 2′-chloroethyl pyrrole (**7b**) by refluxing with thionyl chloride; the latter on stirring overnight with lead tetra-acetate yielded the required 5-acetoxymethylpyrrole (**8**).

The synthesis of the *B*-ring α-free pyrrole (**13c**) was accomplished utilising a multi-step synthetic route (Scheme 2) because direct formation was not feasible due to its inherent instability. Transesterification of ethyl acetoacetate with benzyl alcohol produced benzyl acetoacetate, and a Knorr reaction of the corresponding hydroxyimino derivative (**9**) with 3-ethylpentane-2,4-dione[40] (**10**) under standard conditions[41] afforded the pyrrole benzyl ester (**11**).

It is well documented that during the conversion of α-methyl pyrroles such as (**11**) into pyrrole-α-carboxylic acids (**12**), problems may arise.[42] These, however, can be largely overcome if the initial reaction of the pyrrole with freshly distilled sulphuryl chloride is monitored by NMR spectroscopy to follow the disappearance of the α-methyl proton resonances; hydrolysis of the α-trichloromethyl pyrrole is best carried out in high dilution in aqueous dioxane[43] or aqueous acetone–sodium



Scheme 2. *Reagents and conditions:* i, Zsn–HOAc, 70—80 °C; ii, $SOCl_2$–Et_2O, CH_2Cl_2; iii, NaOAc-aq. acetone; iv, $SOCl_2$–C_6H_6, reflux; v, Bu^tOH–Et_3N–C_6H_6; vi, H_2–Pd–C–THF; vii, I_2–KI–MeOH, 65 °C; viii, H_2–Pt–MeOH–NaOAc.

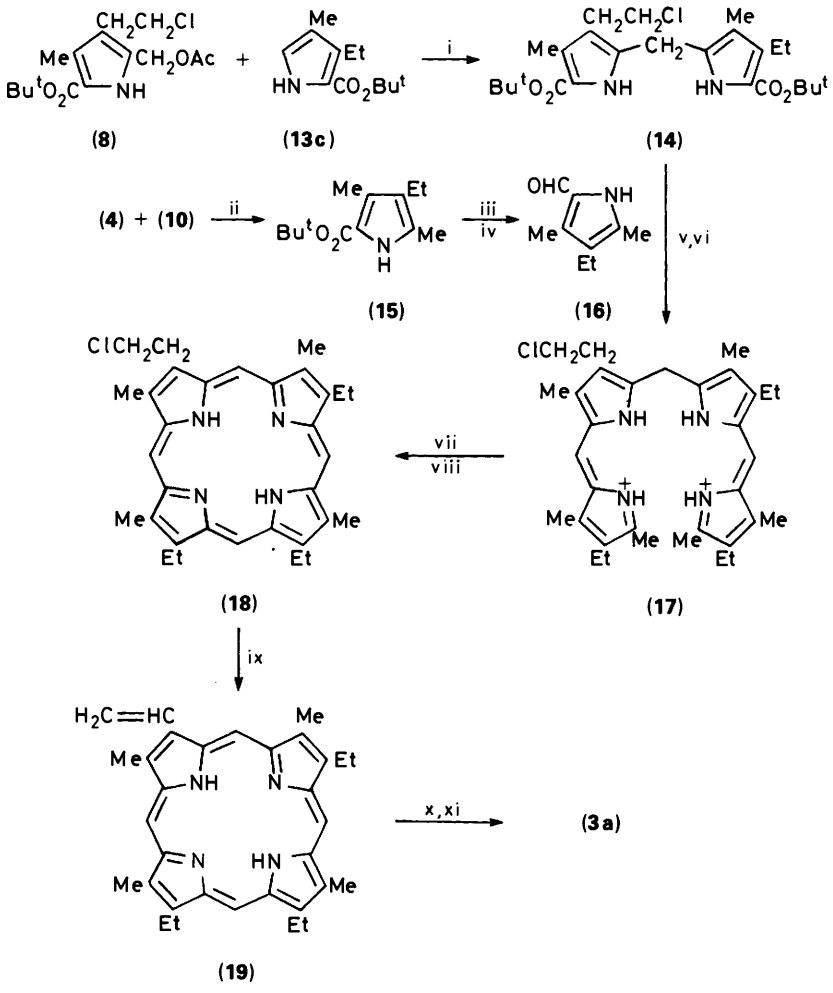
acetate.[44] In the present case, the latter method was used and gave a good yield of the pyrrole-2-carboxylic acid (**12a**), which was then converted into the dicarboxylic ester (**12c**) *via* the acid chloride (**12b**) using t-butyl alcohol–triethylamine.[45] Hydrogenolysis of the pyrrole (**12c**) gave a quantitative yield of the pyrrole-α-carboxylic acid (**13a**), which was then converted into the α-iodopyrrole (**13b**) using iodine–potassium iodide and subsequently hydrogenated to give the required α-free pyrrole (**13c**).

For the *ac*-biladiene-type synthesis,[33] it was necessary to condense the dipyrromethane unit (**14**) with two equivalents of the pyrrole aldehyde (**16**), in the presence of hydrogen bromide–glacial acetic acid (Scheme 3). Hence the 2-formylpyrrole (**16**) was prepared by treatment of the pyrrole t-butyl ester precursor (**15**) with trifluoroacetic acid (TFA) and trimethyl orthoformate; this pyrrole had originally been synthesized utilising the usual Johnson modification of the original Knorr-pyrrole synthesis,[46] *i.e.* condensation of t-butyl (hydroxyimino)acetoacetate (**4**) and the dione (**10**) in the presence of zinc and glacial acetic acid.

One of the most useful reactions in contemporary porphyrin chemistry is the copper(II)-catalysed cyclisation of 1′,8′-dimethyl-*ac*-biladiene salts to give copper-chelated porphyrins[47] in high yield; dimethylformamide (DMF) is the solvent of choice for such reactions.[48] Hence the pyrromethane di-t-butyl ester (**14**) was treated with TFA, followed by a solution of two equivalents of the α-formyl pyrrole (**16**) and 45% hydrogen bromide in glacial acetic acid, to afford the required 4-(2′-chloroethyl)-*ac*-biladiene salt (**17**) in excellent yield. Cyclisation of the latter was accomplished by heating in DMF at 140 °C for 4 min to give the copper(II) complex of the 2-(2′-chloroethyl) porphyrin (**18**). Conversion of this into the required 2-vinylporphyrin[35] (**19**) was accomplished by acid-catalysed demetallation followed by refluxing in pyridine–aqueous sodium hydroxide.

In order to prepare the mono-β-unsubstituted C_{30}-aetioporphyrin (**3a**), the zinc chelate of the 2-vinylporphyrin (**19**) was fused with resorcinol at 180 °C for 1 h.[30] Total conversion into the β-free porphyrin was not achieved and it was necessary to separate a 1:1 mixture of staring vinylporphyrin (**19**) and β-free porphyrin (**3a**) using preparative HPLC. The required *A*-ring isomer (**3a**) was then obtained as a single, isomerically pure product.

Synthesis of the B-*Ring Isomer:* 1,3,5,8-*Tetramethyl*-2,6,7-*triethylporphyrin* (**3b**).—As in the synthesis of the previously described C_{30}-porphyrin isomer (**3a**), the initial target of this



Scheme 3. *Reagents and conditions:* i, *p*-TsOH–CH_2Cl_2; ii, Zn–HOAc, 70—80 °C; iii, TFA; iv, $HC(OMe)_3$–TFA; v, (**14**) + TFA, 20 °C, 30 min; vi, (**16**), HBr–AcOH–MeOH; vii, $CuCl_2$–DMF, 145 °C 5 min; viii, 5% H_2SO_4/TFA; ix, aq.NaOH–pyridine, reflux; x, $Zn(OAc)_2$–MeOH–$CHCl_3$; xi, Resorcinol fusion

synthesis was a 2′-chloroethylporphyrin, *i.e.* (**28**). The 5-acetoxymethylpyrrole (**20**) which was to form the *A*-ring of this porphyrin was readily prepared by stirring the pyrrole-t-butyl ester (**15**) with lead tetra-acetate in glacial acetic acid overnight.

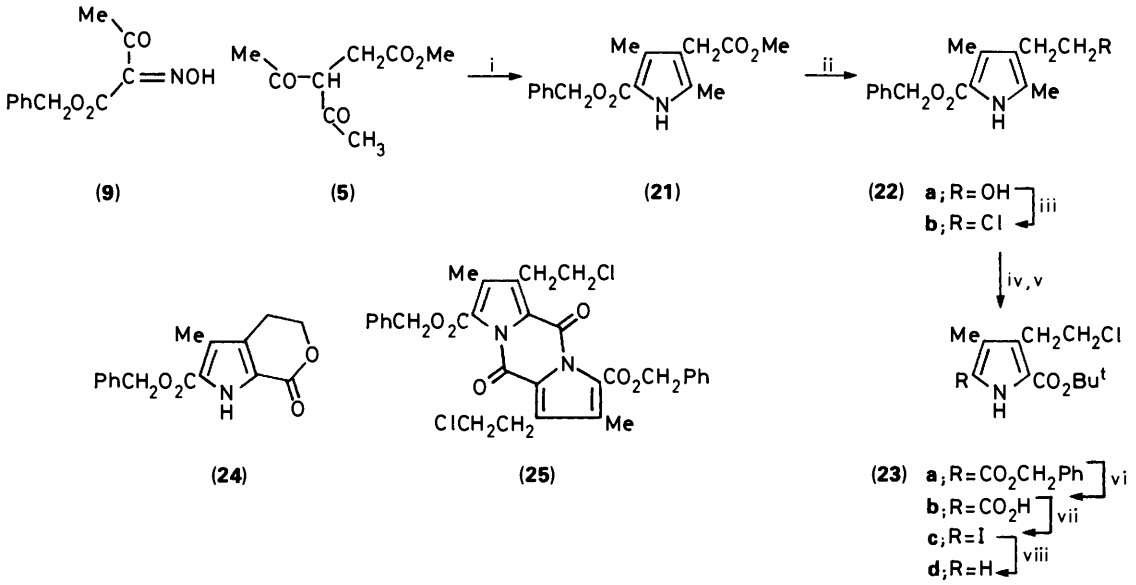
As with the analogous synthesis of pyrrole (**13c**) required for the porphyrin (**3a**), the pathway towards the formation of the *B*-ring α-free pyrrole (**23d**) required several stages (Scheme 4). The 4-(2′-methoxycarbonylmethyl)pyrrole (**21**) was prepared by reaction of benzyl (hydroxyimino)acetoacetate (**9**) with methyl 3-acetyl-4-oxopentanoate (**5**) under standard Knorr-type conditions.[46] This pyrrole was then converted into the 4-(2′-hydroxyethyl)pyrrole[49] (**22a**) by diborane reduction and, in turn, to the analogous 4-(2′-chloroethyl)pyrrole (**22b**) by refluxing with excess of thionyl chloride.[50,51]

As mentioned previously, problems are sometimes encountered during the hydrolysis of α-trichloromethyl pyrroles into their carboxylic acid analogues, but these can be largely overcome by carrying out the reaction in high dilution and using aqueous acetone–sodium acetate.[44] However, when this method was employed with the 3-(2′-chloroethyl)pyrrole (**22b**), no pyrrole-5-carboxylic acid was found, but instead the pyrrole lactone (**24**) and some pyrrocoll (**25**). To avoid these problems, we resorted to direct alcoholysis of the α-trichloromethyl pyrrole (*cf.* ref. 52). Thus, the 2-methylpyrrole (**22b**) was treated, as usual, with sulphuryl chloride to give the 2-trichloromethyl derivative, but this was then directly converted into the required t-butyl ester (**23a**) by being stirred withh a suspension of anhydrous sodium acetate in t-butyl alcohol for 24 h. Subsequent hydrogenolysis of the pyrrole mixed diester (**23a**) gave the pyrrolecarboxylic acid (**23b**), iodinative decarboxylation of which afforded the iodopyrrole (**23c**); the latter underwent hydrogenolysis over Adams catalyst to yield the required α-free pyrrole-t-butyl ester[51] (**23d**).

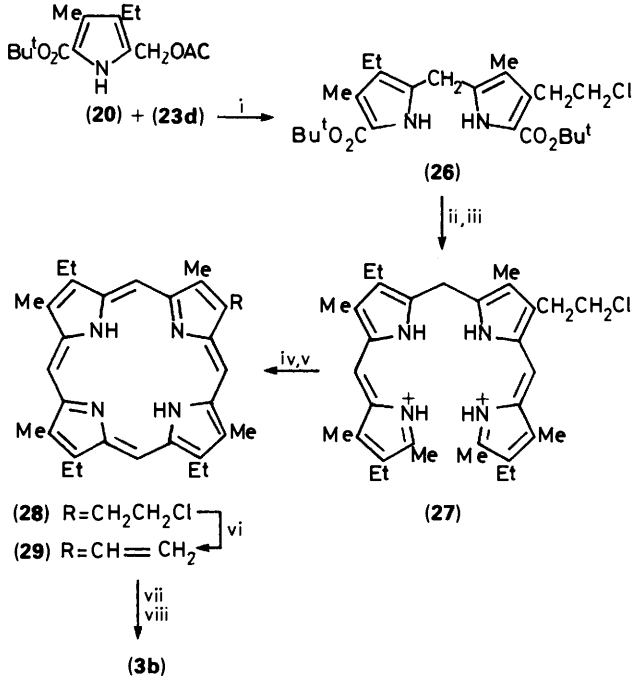
The 4-(2′-chloroethyl)pyrromethane[51,53] (**26**) [required for the synthesis of the 6-(2′-chloroethyl)-*ac*-biladiene (**27**)] was prepared in moderate yield by heating the 5-acetoxymethylpyrrole (**20**) with the α-free pyrrole (**23d**) and an acid catalyst in glacial acetic acid. The biladiene salt (**27**) was then prepared in good yield by treatment of the α,α′-unsubstituted pyrromethane [formed by TFA treatment of the pyrromethane di-t-butyl ester (**26**)] with 2.2 equivalents of the 2-formylpyrrole (**16**) and 45% hydrogen bromide in glacial acetic acid (Scheme 5).

By analogy with the reactions used to prepare the *A*-ring C_{30}-porphyrin isomer (**3a**), the 6-(2′-chloroethyl)biladiene salt (**27**) was cyclised[23] to the 4-(2′-chloroethyl)aetioporphyrin III (**28**) in good yield. The latter was then converted into the 4-vinylporphyrin (**29**), which was in turn fused with resorcinol to afford the 4-unsubstituted C_{30}-de-ethylaetioporphyrin (**3b**) after purification by HPLC.

Synthesis of the C- *and* D-*Ring Isomers:* 1,3,5,8-*Tetramethyl*-2,4,7-*triethylporphyrin* (**3c**) *and* 1,3,5,8-*Tetramethyl*-2,4,6-*tri*-



Scheme 4. *Reagents and conditions:* i, Zn–AcOH, 70—80 °C; ii, B_2H_6–diglyme; iii, $SOCl_2$–CH_2Cl_2, reflux; iv, SO_2Cl_2–CCl_4; v, Bu^{t}OH–NaOAc; vi, H_2–Pd–C–THF; vii, I_2–KI–MeOH, 65 °C; viii, H_2–Pt– MeOH–NaOAc



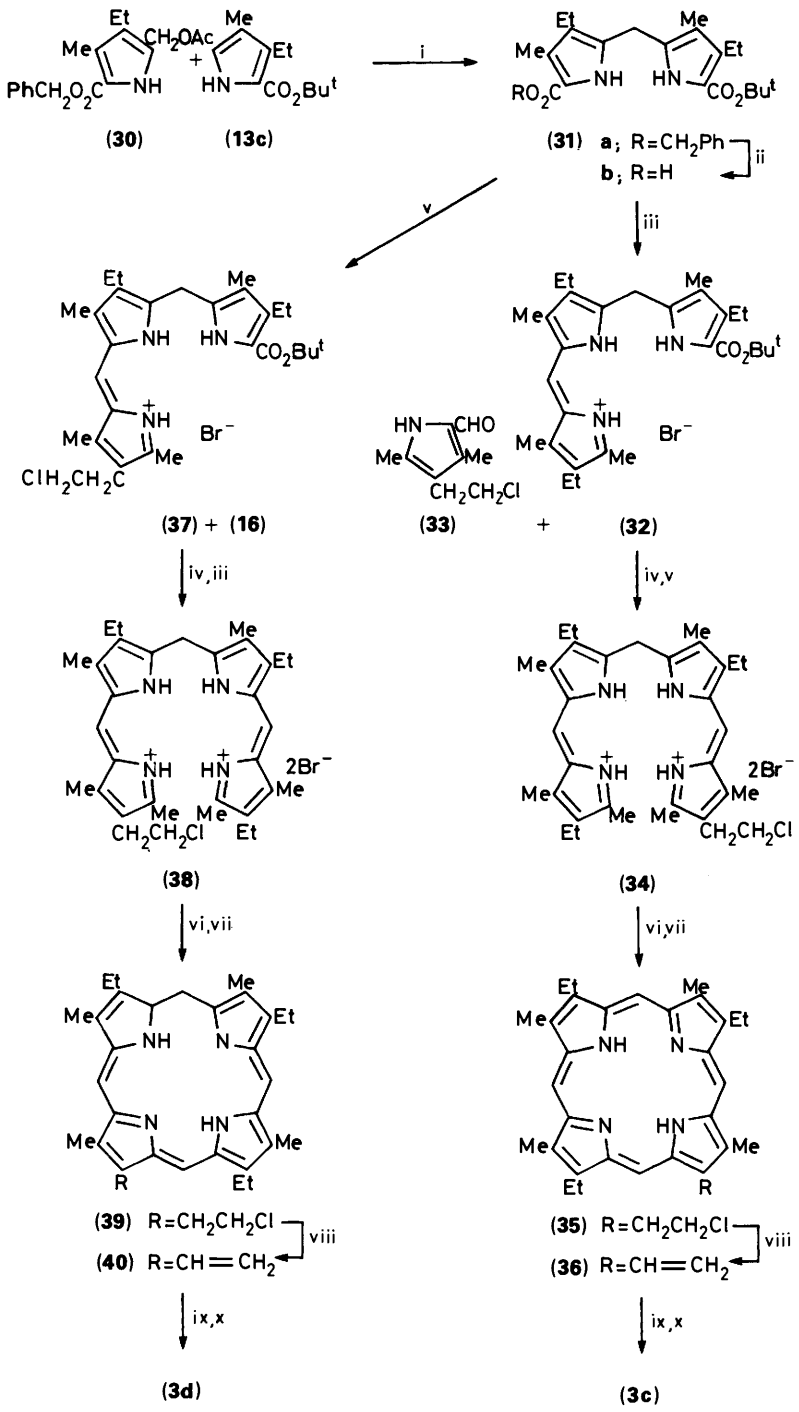
Scheme 5. *Reagents and conditions:* i, *p*-TsOH–AcOH; ii, TFA, 20 °C, 30 min; iii, (**16**), HBr–AcOH–MeOH; iv, $CuCl_2$–DMF, 145 °C; v, 5% H_2SO_4–TFA; vi, aq. NaOH–pyridine, reflux; vii, $Zn(OAc)_2$–MeOH–$CHCl_3$; viii, Resorcinol fusion

ethylporphyrin (**3d**).—Both of these porphyrins were synthesized by the tripyrrene-*ac*-biladiene route,[33] from the same dipyrromethane-α′-t-butyl ester (**31b**) (see Scheme 6). The pyrromethane[54] (**31a**) was first prepared by the condensation of the 5-acetoxymethylpyrrole[36] (**30**) with the α-free pyrrole t-butyl ester[55,56] (**13c**) in the presence of a mild acid catalyst; hydrogenolysis of the benzyl group afforded the pyrromethane-t-butyl ester α-carboxylic acid[34] (**31b**). Meanwhile, the 2-formyl-4-(2′-chloroethyl)pyrrole (**33**) was prepared by treating the related pyrrole t-butyl ester analogue (**7b**) with TFA–trimethyl orthoformate.

In the presence of PTSA, the pyrromethane-α-carboxylic acid (**31b**) was condensed with one equivalent of the 2-formylpyrrole (**16**) and formation of the tripyrrolic species monitored at 484 nm until the absorbance reached a maximum; after this time, dry hydrogen bromide was bubbled into the solution and the required tripyrrene hydrobromide salt (**32**) was formed. Treatment of the latter with TFA, followed by addition of one equivalent of the 2-formyl-4-(2′-chloroethyl)pyrrole (**33**) and 45% hydrogen bromide in glacial acetic acid, gave the required 8-(2′-chloroethyl)-*ac*-biladiene dibromide (**34**). Using the usual previously described methodology, this was cyclised to the 6-(2′-chloroethyl)porphyrin (**35**) with copper(II) chloride–DMF and then dehydrochlorination afforded the 6-vinyl analogue (**36**); the latter was subjected to resorcinol fusion and gave the required *C*-ring porphyrin isomer (**3c**) of the C_{30}-de-ethylaetioporphyrin III.

The pyrromethane-α-carboxylic acid[33] (**31b**) was also condensed with one equivalent of the 2-formyl-4-(2′-chloroethyl)pyrrole (**33**). After treatment with dry hydrogen bromide gas, the 1-(2′-chloroethyl)tripyrrene hydrobromide (**37**) formed was stirred in TFA and one equivalent of the 2-formyl pyrrole (**16**) with 45% hydrogen bromide–glacial acetic acid added. The 1-(2′-chloroethyl)-*ac*-biladiene (**38**) produced was then oxidatively cyclised to the 7-(2′-chloroethyl) porphyrin (**39**), converted into the 7-vinyl analogue (**40**) by the usual means and fused in resorcinol at 180 °C for 1 h to yield the required 7-β-free porphyrin (**3d**).

Comparisons of the Four Synthetic C_{30}*-De-ethylaetioporphyrin III Isomers* (**3a—d**) *with the Naturally Occurring* C_{30}*-Porphyrins.*—For comparisons with the naturally occurring C_{30}-de-ethylaetioporphyrin, it was necessary to devise an HPLC method for the separation of the four synthetic isomers. Whilst many studies have been carried out on the separation of isomeric mixtures of biologically derived porphyrins,[57,59] *e.g.* copro- and uro-porphyrin esters,[59] the separation of our synthetic isomers was much more difficult because of the lack of functionality of the associated alkyl side-chains. This made the differences in behaviour of the different isomers on the HPLC column less marked. However, after the investigation of several reversed-phase systems (*e.g.* Hypersil ODS, Spherisorb ODS, and Partisil ODS), and a wide variety of eluting solvents, a good separation was eventually achieved with two 30 cm Perkin-Elmer ODS-HC-Sil-X1 columns in series using acetonitrile as the mobile phase, as shown in the diagram published in our



Scheme 6. *Reagents and conditions:* i, *p*-TsOH–AcOH; ii, H_2–Pd–C–THF; iii, HBr–HOAc–(**16**)–MeOH; iv, TFA, 35 °C, 10 min; v, HBr–HOAc–(**33**)–MeOH; vi, $CuCl_2$–DMF, 145 °C, 5 min; vii, 5% H_2SO_4–TFA; viii, aq.NaOH–pyridine, reflux; ix, $Zn(OAc)_2$–MeOH–$CHCl_3$; x, Resorcinol fusion

preliminary communication.[1] The retention times of the four de-ethyl analogues of aetioporphyrin were (**3c**), 33 min; (**3d**), 36 min; (**3b**), 37 min; and (**3a**), 40 min (see Experimental Section for full details).

We were fortunate enough to have three samples containing the naturally occurring C_{30}-aetioporphyrin at our disposal. One of the samples was isolated from Gilsonite, an Eocene asphalt from the Uinta Basin, Utah and the second was from Serpiano oil shale, a Swiss Triassic oil shale; the third, a porphyrin mixture, was isolated from coal.

HPLC comparisons, including co-injection experiments, were then carried out, and the results[1] clearly showed that the major porphyrin present in both of the oil samples was the *C*-ring isomer of de-ethylaetioporphyrin III, *i.e.* compound (**3c**).[15] Interestingly, HPLC analysis of the C_{28}-, C_{30}-, and C_{32}-mixture obtained from coal again suggests the presence of the *C*-ring de-ethylaetioporphyrin isomer, although this result was not as clear cut because of the presence of another porphyrin (probably the C_{32}-aetioporphyrin) which eluted close to the *A*-ring isomer.

The predominance of the *C*-ring porphyrin isomer (**3c**) is presumably due to the ease with which the isocyclic ring of chlorophyll-*a* can be degraded[12] (hydrolytically or oxidatively) prior to the other maturation processes which take place over the course of geological time.

The Bristol group have also studied the structure of the C_{30}-de-ethylaetioporphyrin from Serpiano shale by NMR spectroscopy of the related acetyl derivative using NOE methods; they reached the same conclusions concerning its structure, and its likely origin from chlorophyll.[60]

Experimental

M.p.s were recorded using a Kofler hot-stage and are uncorrected. Elementary microanalyses were performed on a Technicon instrument.

IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer and were calibrated using a polystyrene film. UV-VIS spectra were recorded on a Pye-Unicam S.P. 800 spectrophotometer using a holmium filter as standard. NMR spectra were determined with Perkin-Elmer R32 (90 MHz) and Bruker WM 360 (360 MHz) instruments, for $CDCl_3$ solutions using tetramethylsilane as internal reference.

Mass spectra were determined on a Varian CH5D instrument with field desorption and electron-impact sources; spectra were normalised to the base peak and presented in line diagram form using a Varian 620 l computer.

Solvents were purified before use by distillation and were dried, when required, using standard methods.

Methyl 3-Acetyl-4-oxopentanoate (**5**).—Methyl chloroacetate (690 g, 6.4 mol, 1.4 mol equiv.) was carefully added to a well stirred mixture of acetylacetone (450 g, 4.5 mol), anhydrous potassium carbonate (570 g), and dry acetone (1 l). During the addition, refluxing began spontaneously and the methyl chloroacetate was added at such a rate as to maintain boiling. After the addition was complete, the reaction mixture was stirred until refluxing ceased. The mixture was then heated under reflux for 1 h while being stirred continuously. After the reaction mixture had cooled (overnight), the potassium carbonate was filtered off and washed well with acetone. The combined filtrates were evaporated under reduced pressure to leave an orange oil, which was twice distilled under high vacuum. The required product (504 g, 52%) distilled as an oil, b.p. 96—102 °C/2 mmHg (lit.,[37] 96 °C/9 mmHg)(Found: C, 55.7; H, 6.9. Calc. for $C_8H_{12}O_4$: C, 55.8; H, 7.0%); δ_H 16.71 (1 H, s, OH of enol), 4.13 (1 H, t, CH of keto), 3.70 (3 H, s, CO_2Me of enol), 3.66 (3 H, s, CO_2Me of keto), 3.25 (2 H, s, CH_2 of enol), 2.86 (2 H, d, CH_2 of keto, 2.23 (6 H, s, 2 × Me of keto), and 2.13 (6 H, s, 2 × Me of enol).

Pyrroles

t-Butyl 4-(Methyloxycarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate (**6**).—t-Butyl acetoacetate (114.5 g, 0.72 mol) in glacial acetic acid (150 ml) was cooled to 0 °C and a solution of sodium nitrite (55 g, 1.1 mol equiv. 0.80 mol) in water (250 ml) was added dropwise whilst maintaining the temperature between 0—5 °C. The pale yellow solution was stored overnight at 0 °C, and then added dropwise to a well stirred solution of methyl 3-acetyl-4-oxopentanoate (124.6 g, 0.72 mol, 1 mol equiv.) in glacial acetic acid (165 ml), an intimate mixture of Zn dust (144 g) and anhydrous sodium acetate (144 g) was simultaneously added portionwise. The temperature rose quickly and cooling was necessary to maintain the temperature between 70—80 °C. After addition was complete, the mixture was stirred and heated under reflux for 1 h. After the mixture had cooled to 40 °C, it was poured into water (5 l) and left overnight. The pale brown precipitate formed was filtered off, dried in air, and recrystallised from light petroleum (b.p. 40—60 °C) to give the *pyrrole* (**6**) (60.7 g, 32%) as an off-white powder, m.p. 117—118 °C (Found: C, 62.85; H, 7.5. $C_{14}H_{21}NO_4$ requires C, 62.9; H, 7.9%); δ_H 8.78 (1 H, br s, NH), 3.65 (3 H, s, CO_2Me), 3.36 (2 H, s, CH_2CO_2Me), 2.23 and 2,21 (6 H, s, 2 × Me), and 1.15 (9 H, s, Bu^t).

t-Butyl 4-(2′-Hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate (**7a**).—t-Butyl 4-(methoxycarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate (**6**) (37.g, 0.14 mol) was dissolved in dry tetrahydrofuran (THF) (250 ml) and diborane was bubbled through the solution for 2 h. Cooling was required due to the exothermic nature of the reaction. The diborane was generated externally by dropwise addition of boron trifluoride–diethyl (250 ml) to a slurry of sodium borohydride (27.9 g) in dry diglyme (130 ml). After the reaction had gone to completion (TLC), dry methanol was carefully added dropwise to the pyrrolic solution until the effervescence ceased. After 10 min, the solvent was removed to give an off-white foam, which was crystallised from benzene–light petroleum (b.p. 60—80 °C) to give the *hydroxyethylpyrrole* (**7**) (27.9 g, 84%) as needles, m.p. 190—192 °C (Found: C, 65.2; H, 8.6; N, 6.0. $C_{13}H_{21}NO_3$ requires C, 65.55; H, 8.4; N, 5.9%); δ_H 8.96 (1 H, br s, NH), 3.65 (1 H, s, OH), 3.59 (2 H, t, CH_2OH), 2.58 (2 H, t, CH_2CH_2OH) 2.20 and 2.16 (2 × 3 H, s, 2 × Me), and 1.52 (9 H, s, Bu^t).

t-Butyl 4-(2′-Chloroethyl)-3,5-dimethylpyrrole-2-carboxylate (**7b**).—t-Butyl 4-(2′-hydroxyethyl)-3,5-pyrrole-2-carboxylate (**7a**) (4.11 g, 0.017 mol) was dissolved in dry dichloromethane (60 ml). To this solution were added freshly distilled thionyl chloride (2.05 g, 1.1 mol equiv.) and anhydrous pyridine (1.47 g, 1.1 mol equiv.). The solution was refluxed for 90 min under a $CaCl_2$ drying tube. After cooling, the organic layer was washed successively with saturated aqueous sodium hydrogen carbonate (3 × 50 ml) and water (3 × 50 ml), and dried ($MgSO_4$). After removal of solvent, the dark oily residue was chromatographed on alumina (Grade II) and eluted with dichloromethane. The appropriate fractions were collected and evaporated to dryness to afford *compound* (**7b**) as a yellow solid (3.96 g, 94%), m.p. 114—116 °C (from dichloromethane) (Found: C, 63.9; H, 8.1; N, 5.8. $C_{13}H_{20}ClNO_2$ requires C, 64.2; H, 8.2; N, 5.8%); δ_H 8.84 (1 H, br s, NH), 3.45 (2 H, t, CH_2Cl), 2.78 (2 H, t, CH_2CH_2Cl), 2.20 and 2.17 (each 3 H, s, 2 × Me), and 1.52 (9 H, s, Bu^t).

t-Butyl 5-Acetoxymethyl-4-(2′-chloroethyl)-3-methylpyrrole-2-carboxylate (**8**).—The foregoing pyrrole (**7b**) (3.96 g, 0.015 mol) was dissolved in acetic acid (50 ml) and treated with lead tetra-acetate (7.53 g, 1 mol equiv.). The mixture was stirred overnight at 35 °C and was then poured into ice–water (200 ml). After 2 h the *title product* (3.33 g, 69%) was filtered off, washed with water, and dried *in vacuo*, to give fine needles, m.p. 111—113 °C (Found: C, 57.6; H, 6.5; N, 4.4. $C_{15}H_{22}ClNO_4$ requires C, 57.1; H, 7.0; N, 4.4%); δ_H 9.00 (1 H, br s, NH), 5.01 (2 H, s, CH_2OAc), 3.50 (2 H, t, CH_2Cl), 2.87 (2 H, t, CH_2CH_2Cl), 2.21 (3 H, s, Me), 2.02 (3 H, s, OCOMe), and 1.51 (9 H, s, Bu^t).

5-Benzyl Hydrogen 3-Ethyl-4-methylpyrrole-2,5-dicarboxylate (**12a**).—Benzyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate (**11**) (20 g, 78 mmol) was dissolved in a mixture of dry dichloromethane (100 ml) and dry ether (310 ml). A solution of freshly distilled sulphuryl chloride (42.85 g, 328 mmol) in dry dichloromethane (50 ml) was added as rapidly as the very vigorous reaction would allow. The mixture was stirred at 20 °C under nitrogen and monitored at hourly intervals using NMR spectroscopy. As the methyl signal at δ_H 2.15 disappeared, resonances due to the formation of CH_2Cl (δ 4.6) and $CHCl_2$

(δ 6.6) appeared and then disappeared, and the reaction was found to be complete after 3 h. The organic solvents were removed under reduced pressure and the residual pale brown oil was dissolved in a mixture of acetone (400 ml) and water (100 ml). The solution was then heated under reflux for 1 h and, before addition of a solution of sodium acetate (40 g) in water (100 ml), the mixture was boiled for a further 2 h whilst the acetone was slowly allowed to evaporate off. The yellowish oil obtained solidified on cooling and was filtered off, washed well with water, and dissolved in boiling methanol (150 ml). To this solution was cautiously added an aqueous solution of sodium hydrogen carbonate (10.1 g in 75 ml) and, after a few minutes, the reaction mixture was diluted with water (500 ml) and cooled. The solution was extracted with ether (3 × 100 ml) and, after separation, the aqueous layer was acidified by the dropwise addition of conc. hydrochloric acid. A white precipitate of the desired pyrrole acid was formed, and was left to cool for a few hours before being filtered off and washing well with water. After drying *in vacuo* the *acid ester* had m.p. 148—149 °C (102 g, 73%) (Found: C, 66.6; H, 5.6; N, 5.2. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 5.9; N, 4.9%); δ_H 9.51 (1 H, br s, NH), 7.99 (1 H, br s, CO_2H), 7.39 (5 H, s, CH_2*Ph*), 5.34 (2 H, s, C*H*$_2$Ph), 2.78 (2 H, q, C*H*$_2$Me), 2.28 (3 H, s, CH_2), and 1.11 (3 H, t, CH_2*Me*).

2-*t-Butyl* 5-*Benzyl*-3-*Ethyl*-4-*methylpyrrole*-2,5-*dicarboxylate* (**12c**).—The acid ester (**12a**) (16.23 g) was dissolved in dry benzene (200 ml), together with thionyl chloride (67.35 g; 10 mol equiv.; freshly distilled), and the mixture was boiled under reflux for 3 h. The solvent was removed under reduced pressure to give a pale brown oily solid (17.2 g), which was characterised by NMR spectroscopy as the pyrrole acid chloride (**12b**), and was used immediately in the next reaction.

The acid chloride (**12b**) (17.23 g, 56 mmol) was dissolved in dry benzene (100 ml). To this were added t-butyl alcohol (4.6 ml, 62 mmol, 1.1 mol equiv.) and triethylamine (6.3 ml, 62 mmol, 1.1 mol equiv.) and the mixture was stirred and heated under reflux for 2 h. The reaction mixture was evaporated down under reduced pressure and the residual pale brown solid was taken up in chloroform (300 ml), washed with water (3 × 200 ml), and dried ($MgSO_4$). After removal of solvent the residual solid was recrystallised from dichloromethane–light petroleum (b.p. 40—60 °C) to afford the desired *pyrrole t-butyl ester* (**12c**) (14.5 g, 75%) as a crystalline solid, m.p. 74—76 °C (Found: C, 69.7; H, 8.1; N, 4.4. $C_{20}H_{25}NO_4$ requires C, 69.77; H, 7.56; N, 4.70%); δ_H 9.30 (1 H, br s, NH), 7.36 (5 H, s, CH_2*Ph*), 5.31 (2 H, s, C*H*$_2$Ph), 2.74 (2 H, q, C*H*$_2$Me), 2.71 (3 H, s, Me), 1.55 (9 H, s, Bu^t), and 1.09 (3 H, t, CH_2*Me*).

2-*t-Butyl Hydrogen* 3-*Ethyl*-4-*methylpyrrole*-2,5-*dicarboxylate* (**13a**).—The foregoing pyrrole diester (**12c**) (14.5 g, 42 mmol) and 10% palladium on charcoal (150 mg) were mixed with dry THF (200 ml) and the mixture was shaken overnight in hydrogen. The catalyst was filtered off through Celite and the solvent was removed to give the pyrrole acid ester (10.6 g, 99%) as a white solid, m.p. 166—167 °C (decomp.) (Found: C, 61.8; H, 7.2; N, 5.5. $C_{13}H_{19}NO_4$ requires C, 61.66; H, 7.51; N, 5.53%); δ_H 10.62 (1 H, br s, CO_2H), 9.42 (1 H, br s, NH, 2.73 (2 H, q, C*H*$_2$Me), 2.39 (3 H, s, Me), 1.58 (9 H, s, Bu^t), and 1.11 (3 H, t, CH_2*Me*).

t-Butyl 3-*Ethyl*-5-*iodomethylpyrrole*-2-*carboxylate* (**13b**).—The foregoing pyrrole acid ester (**13a**) (10.58 g, 42 mmol) was dissolved in methanol (80 ml) and the solution was heated to 65 °C before careful addition of aqueous sodium hydrogen carbonate (5.3 g, 63 mmol in 30 ml). During 1 h, a solution of iodine (5.84 g, 46 mmol, 1.1 mol equiv.) and potassium iodide (7.64 g, 46 mmol, 1.1 mol equiv.) in a mixture of methanol (75 ml) and water (75 ml) was added dropwise. The temperature was kept between 65 and 70 °C for a further 1 h after this addition. The reaction mixture was then left at 0 °C and the pale yellow precipitate formed was filtered off, washed well with hot water, and dried *in vacuo* to afford the *iodopyrrole* (**13b**) (9.0 g, 65%), m.p. 105—107 °C (Found: C, 43.9; H, 5.0; N, 4.2. $C_{12}H_{18}INO_2$ requires C, 43.00; H, 5.07; N, 4.18%); δ_H 8.79 (1 H, br s, NH), 2.72 (2 H, q, C*H*$_2$Me), 1.95 (3 H, s, Me), 1.55 (9 H, s, Bu^t), and 1.09 (3 H, t, CH_2*Me*).

t-Butyl 3-*Ethyl*-4-*methylpyrrole*-2-*carboxylate* (**13c**).—The foregoing iodopyrrole (**13b**) (2.44 g, 7.3 mmol) and anhydrous sodium acetate (1.22 g, 15 mmol; 2 mol equiv.) were dissolved in methanol (100 ml) and shaken over Adams platinum oxide catalyst (10 mg) under hydrogen overnight. The catalyst was then filtered off through Celite, the solvent was removed, and the residue was partitioned between ethyl acetate (100 ml) and water (100 ml). The yellow organic layer was separated off, washed with more water (2 × 100 ml), and dried ($MgSO_4$). After removal of drying agent and then of solvent (under reduced pressure), the α-free pyrrole (1.42 g, 94%) was obtained as a pale brown oil, which was used immediately for dipyrromethane preparation; δ_H 8.78 (1 H, br s, NH), 6.60 (1 H, d, 5-H), 2.72 (2 H, q, C*H*$_2$Me), 2.00 (3 H, s, Me), 1.55 (9 H, s, Bu^t), and 1.10 (3 H, t, CH_2*Me*).

2-*t-Butyl* 5-*Benzyl* 3-(2′-*Chloroethyl*)-4-*methylpyrrole*-2,5-*dicarboxylate* (**23a**).—Benzyl 4-(2′-chloroethyl) 3,5-dimethylpyrrole-2-carboxylate (**22b**) (5.35 g, 18.4 mmol) was dissolved in dry tetrachloromethane (300 ml) at 40 °C under nitrogen. To this was added sulphuryl chloride (7.39 g, 3 mol equiv.). Almost immediately, a precipitate of the monochloromethylpyrrole appeared. This disappeared after the mixture had been stirred for a while and the reaction was monitored by NMR spectroscopy. After 3 h the reaction had gone to completion (*i.e.* the α-CH_3 resonance at α 2.15, the CH_2Cl resonance at δ 4.6, and the $CHCl_2$ resonance at δ 6.6 had all disappeared). The organic solvent was then removed under reduced pressure and benzene (100 ml) was added and distilled off to ensure that all the sulphuryl chloride had been removed. The yellow oily trichloromethylpyrrole remaining was then dissolved in t-butyl alcohol (100 ml) containing a suspension of anhydrous sodium acetate (8 g). After being stirred under nitrogen for 24 h at 60 °C, the solution was cooled, diluted with dichloromethane (200 ml), and washed with water (3 × 100 ml). After drying ($MgSO_4$), the organic phase was evaporated under reduced pressure and the crude product was chromatographed on alumina (Grade II) with 20% ethyl acetate–cyclohexane as eluant. The appropriate fractions were collected and evaporated to dryness, giving a yellow oil, which was crystallised from ether to give the pyrrole t-butyl ester (**23a**) (4.29 g, 62%) as crystals, m.p. 58—60 °C (lit.,[51] 59.5—60.5 °C) (Found: C, 63.9; H, 6.4; N, 4.0. Calc. for $C_{20}H_{24}ClNO_4$: C, 63.7; H, 6.4; N, 3.7%); δ_H 9.42 (1 H, s, NH), 7.33 (5 H, s, CH_2*Ph*), 5.28 (2 H, s, C*H*$_2$Ph), 3.56 (2 H, s, CH_2Cl), 3.11 (2 H, s, C*H*$_2$$CH_2Cl$), 2.27 (3 H, s, Me), and 1.55 (9 H, s, Bu^t).

2-*t-Butyl Hydrogen* 4-(2′-*Chloroethyl*)-3-*methylpyrrole*-2,5-*dicarboxylate* (**23b**).—Compound (**23a**) (2.86 g, 7.6 mmol) was dissolved in dry THF (50 ml) and hydrogenated overnight over palladium–carbon caralyst (300 mg). The catalyst was filtered off through Clite and the solvent was removed to give the title compound as a white foam (2.08 g, 96%), m.p. 192—194 °C (lit., [51]192—194 °C) (Found: C, 54.7; H, 6.3; N, 4.2. Calc. for $C_{13}H_{18}ClNO_4$: 54.5; H, 6.3; N, 4.9%); δ_H 9.54 (1 H, br s, NH), 7.60 (1 H, br s, CO_2H), 3.59 (2 H, t, CH_2Cl), 3.13 (2 H, t, C*H*$_2$$CH_2Cl$), 2.31 (3 H, s, Me), and 1.56 (9 H, s, Bu^t).

t-Butyl 3-(2′-*chloroethyl*)-5-*iodo*-4-*methylpyrrole*-2-*carboxylate* (**23c**).—Compound (**23b**) (2.08 g, 7.2 mmol) was dissolved in

methanol (50 ml) and the solution was heated to 65 °C and then aqueous sodium hydrogen carbonate (0.91 g, 1.5 mol equiv. in 20 ml) was added. A solution of iodine (1.01 g, 1.1 mol equiv.) and potassium iodide (1.32 g, 1.1 mol equiv.) in aqueous methanol (50 ml) was added to the stirred pyrrolic solution during 30 min. The mixture was then kept at 65 °C for 1 h more before being cooled to 0 °C overnight. The yellow precipitate which formed was filtered off, washed with hot water, and dried to afford the *iodopyrrole* (**23c**) (2.27 g, 85%), m.p. 136—137 °C (Found: C, 39.2; H, 4.5; N, 3.6. $C_{12}H_{17}ClINO_2$ requires C, 39.2; H, 4.6; N, 3.8%); δ_H 8.90 (1 H, br s, NH), 3.56 (2 H, t, CH_2Cl), 3.12 (2 H, t, CH_2CH_2Cl), 1.96 (3 H, s, Me), and 1.55 (9 H, s, Bu^t).

t-Butyl 3-(2′-Chloroethyl)-4-methylpyrrole-2-carboxylate (**23d**).—Compound (**23c**) (2.27 g, 6.2 mmol) and anhydrous sodium acetate (2 g) were dissolved in dry methanol (50 ml) and hydrogenated over platinum oxide catalyst (50 mg) overnight. After filtration of the solution through Celite to remove the catalyst, the solvent was removed to give a pale yellow solid, which was partitioned between ethyl acetate (100 ml) and water (100 ml). The aqueous portion was extracted with more ethyl acetate (2 × 50 ml) and the combined organic extracts were washed with water (3 × 50 ml) and dried ($MgSO_4$). After filtration and evaporation of the solvent, the α-free pyrrole (**23d**) (1.4 g, 94%), m.p. 96—97 °C (lit.,[51] 97—98 °C), was obtained and was used immediately in dipyrromethane synthesis (Found: C, 59.2; H, 7.4; N, 5.7. Calc. for $C_{12}H_{18}ClNO_2$: C, 59.24; H, 7.4; N, 5.8%); δ_H 9.00 (1 H, br s, NH), 6.61 (1 H, d, 5-H), 3.59 (2 H, t, CH_2Cl), 3.10 (2 H, t, CH_2CH_2Cl), 2.02 (3 H, s, Me), and 1.55 (9 H, s, Bu^t).

4-(2′-Chloroethyl)-2-formyl-3,5-dimethylpyrrole (**33**).—t-Butyl 4-(2′-chloroethyl)-3,5-dimethylpyrrole-2-carboxylate (**7b**) (5 g, 19 mmol) was dissolved in TFA and the solution was stirred at 35 °C under nitrogen for 10 min. The reaction mixture was then cooled to 0 °C and trimethyl orthoformate (2.27 g, 21.5 mmol, 1.1 mol equiv.) added dropwise. The mixture was then allowed to warm up to 20 °C and was stirred for 2 h before being poured into ice–water (100 ml). This was then extracted with chloroform (3 × 50 ml), and the extracts were washed successively with 10% aqueous ammonia (2 × 50 ml) and water (3 × 50 ml) and dried ($MgSO_4$). After filtration, and evaporation under reduced pressure, a dark brown solid was obtained. This was recrystallised from diethyl ether to give the *formylpyrrole* (**33**) (2.41 g, 72%) as a pale brown powder, m.p. 110—112 °C (Found: C, 58.2; H, 6.7; N, 7.1. $C_9H_{12}ClNO$ requires C, 58.4; H, 6.5; N, 7.6%); δ_H 9.85 (1 H, br s, NH), 9.45 (1 H, s, CHO), 3.50 (2 H, t, CH_2Cl), 2.81 (2 H, t, CH_2CH_2), and 2.25 (6 H, s, 2 × Me).

Pyrromethanes

Di-t-butyl 3-(2-Chloroethyl)-4′-ethyl-3′,4-dimethylpyrromethane-5,5′-dicarboxylate (**14**).—t-Butyl 3-ethyl-4-methylpyrrole-2-carboxylate (**13c**) (1.42 g, 6.8 mmol) and PTSA (50 mg) were dissolved in glacial acetic acid (20 ml) and the solution was stirred under nitrogen and treated dropwise with a solution of t-butyl 5-acetoxymethyl-4-(2′-chloroethyl)-3-ethylpyrrole-2-carboxylate (**8**) (2.14 g, 6.8 mmol, 1 mol equiv.) in glacial acetic acid (20 ml). After the addition was complete (*ca.* 30 min) the reaction mixture was stirred for 4 h at 35 °C under nitrogen. Chloroform (100 ml) was then added, and the solution was poured into water (200 ml). The aqueous layer was extracted with more chloroform and the organic extracts were combined, washed successively with saturated aqueous sodium hydrogen carbonate (3 × 50 ml) and water (3 × 50 ml), and dried ($MgSO_4$). After filtration of the drying agent and removal of the solvent, the red oil obtained was chromatographed on alumina (Grade III) with dichloromethane as eluant. The fractions containing the dipyrromethane were identified by TLC and combined. After removal of the solvent, the *dipyrromethane* (**14**) (1.94 g, 62%) was obtained as a pink solid foam, m.p. 134—136 °C (Found: C, 64.9; H, 8.05; N, 3.65. $C_{25}H_{37}ClN_2O_4$ requires C, 64.7; H, 8.0; N, 3.0%); δ_H 8.60 (2 H, br s, 2 × NH), 3.85 (2 H, s, CH_2), 3.42 (2 H, t, CH_2CH_2Cl), 2.79 (2 H, t, CH_2CH_2), 2.67 (2 H, br, CH_2Me), 2.21 (3 H, s, 4-Me), 1.92 (3 H, s, 3′-Me), 1.50 (18 H, s, 2 × Bu^t), and 1.09 (3 H, t, CH_2Me).

Di-t-butyl 4′-(2′-Chloroethyl)-3′,4-dimethyl-3-ethylpyrromethane-5,5′-dicarboxylate (**26**).—A solution of t-butyl 3-(2′-chloroethyl)-4-methylpyrrole-2-carboxylate (**23d**) (262 mg, 1.08 mmol) and PTSA (20 mg) in glacial acetic acid (20 ml) was stirred under nitrogen and treated dropwise with a solution of t-butyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate (**20**) (290 mg; 1.08 mmol; 1 mol equiv.) in glacial acetic acid (20 ml). The reaction mixture was then stirred for 4 h at 35 °C. Chloroform (100 ml) was added, and the solution was poured into water (200 ml). The aqueous layer was extracted with more chloroform until it was colourless. The pinkish organic washings were combined, washed successively with saturated aqueous sodium hydrogen carbonate (3 × 50 ml) and water (3 × 100 ml), and dried ($MgSO_4$). After filtration and evaporation, a red oil was obtained and this was chromatographed on alumina (Grade III) with dichloromethane as eluant. The appropriate fractions were combined and the solvent was removed to afford the *dipyrromethane* (**26**) (290 mg, 58%) as an orange foam (Found: C, 64.7; H, 8.0; N, 2.4. $C_{25}H_{37}ClN_2O_4$ requires C, 64.7; H, 8.0; N, 3.0%); δ_H 8.60 (2 H, br s, 2 × NH), 3.85 (2 H, s, bridging CH_2), 3.42 (2 H, t, CH_2CH_2Cl), 2.79 (2 H, t, CH_2CH_2Cl), 2.67 (2 H, t, CH_2Me), 2.21 (3 H, s, 4-Me), 1.92 (3 H, s, 3′-Me), 1.50 (18 H, s, 2 × Bu^t), and 1.09 (3 H, t, CH_2Me).

5-Benzyl 5′-t-Butyl 3,4′-Diethyl-3′,4-dimethylpyrromethane-5,5,′-dicarboxylate (**31a**).—t-Butyl 3-ethyl-4-methylpyrrole-2-carboxylate (6.23 g; 3.0 mmol) (**13c**) and PTSA (200 mg) were dissolved in glacial acid (50 ml) and the solution was treated dropwise under nitrogen, at 35 °C, with a solution of benzyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate (**30**) (9.39 g, 30 mmol; 1 mol equiv.) in glacial acetic acid (50 ml) during 30 min. The reaction mixture was then stirred for 4 h before dilution with $CHCl_3$ (200 ml). The organic layer was washed successively with saturated aqueous sodium hydrogen carbonate (3 × 100 ml) and water (3 × 100 ml) before being dried ($MgSO_4$). After removal of the drying agent and solvent, a reddish-brown oil was obtained and this was chromatographed on alumina (Grade III) with dichloromethane as eluant. The relevant fractions were combined and evaporated to give a pale brown oily solid, which was crystallised from dichloromethane–light petroleum (b.p. 60—80 °C) to give the dipyrromethane (**31a**) (9.9 g, 72%) as a white powder, m.p. 132—134 °C (lit.,[54] 133—135 °C) (Found: C, 71.9; H, 8.3; N, 5.5. Calc. for $C_{28}H_{36}N_2O_4$: C, 72.4; H, 7.8; N, 6.0%); δ_H 9.12 (1 H, br s, 1-NH), 8.76 (1 H, br s, 1′-NH), 7.30 (5 H, s, CH_2Ph), 5.25 (2 H, s, CH_2Ph), 3.81 (2 H, s, CH_2 bridge), 2.68 (2 H, q, 4′-CH_2Me), 2.39 (2 H, q, 3-CH_2Me), 2.25 (3 H, s, 4-Me), 1.93 (3 H, s, 3′-Me), 1.50 (9 H, s, Bu^t), and 1.04 (6 H, q, 3- and 4′-CH_2Me).

5′-t-Butyl Hydrogen 3,4′-Diethyl-3′,4-dimethylpyrromethane-5,5′-dicarboxylate (**31b**).—5-Benzyl 5′-t-butyl 3,4′-diethyl-3′,4-dimethylpyrromethane-5,5′-dicarboxylate (**31a**) (300 mg, 64.7 μmol) (**31a**) was dissolved in dry THF (50 ml) and the solution was shaken with 10% palladium on carbon (50 mg) under hydrogen overnight. The catalyst was filtered off through Celite,

washed well with more THF, and the eluants were combined and evaporated to give *compound* (**31b**) as an oil (231 mg; 96%), which was used immediately in the next stage without crystallisation (Found: C, 65.6; H, 8.8; N, 7.0. $C_{20}H_{30}N_2O_4$ requires C, 66.1; H, 8.3; N, 7.7%); δ_H 10.88 (1 H, br s, CO_2H), 9.15 and 8.80 (each 1 H, br s, 2 × NH), 3.81 (2 H, s, bridging CH_2), 2.68 (2 H, q, 4′-CH_2Me), 2.39 (2 H, q, 3-CH_2Me), 2.25 (3 H, s, 4-Me), 1.93 (3 H, s, 3′-Me), 1.50 (9 H, s, Bu^t), and 1.04 (6 H, overlapping qs, 3- and 4′-CH_2*Me*).

Tripyrrenes

t-Butyl 1,4,6-*Triethyl*-1′,2,3,5-*tetramethyltripyrren*-a-6′-*carboxylate Hydrobromide* (**32**).—Compound (**31b**) (398 mg, 1.06 mmol) was dissolved in dry dichloromethane (100 ml) and a solution of PTSA (500 mg; 2.5 mol equiv.) in dry methanol (10 ml) was added. A solution of 4-ethyl-2-formyl-3,5-dimethylpyrrole (**16**) (161 mg, 1.06 mmol; 1 mol equiv.) in dry methanol (5 ml) was added to the stirred mixture, under nitrogen, at 20 °C. The reaction was followed by visible spectroscopy, samples of the neat reaction mixture being taken and monitored at 484 nm. The reaction was allowed to continue until this peak ceased to increase (~1 h) and the solution had become a pale brown in colour. The reaction mixture was washed successively with 10% aqueous sodium hydrogen carbonate (3 × 50 ml) and water (3 × 50 ml), and dried ($MgSO_4$). After filtration and evaporation, the brown oil obtained was dissolved in dry dichloromethane (50 ml) and hydrogen bromide gas (dried by passage over calcium chloride) was bubbled into the solution for 4 s. The deep red solution formed was evaporated to dryness, and benzene (2 × 50 ml) was added and evaporated off to azeotrope any water present. The *tripyrrene* (**32**) (5.455 g, 92%) obtained was a deep reddish crystalline solid, m.p. 165 °C (decomp.) (Found: C, 75.0; H, 8.5; N, 9.1. $C_{25}H_{42}N_3O_2$ requires C, 75.2; H, 8.8; N, 9.1%); δ_H 12.82, 12.89, and 11.08 (1 H, br s, NH), 7.39 (1 H, s, methine bridge CH), 4.25 (2 H, s, *meso*-CH_2), 2.57 and 2.25 (4 H, and 2 H, each q, CH_2CH$_3$), 2.55, 2.38, 2.32, and 1.89 (3 H, each s, Me), 1.50 (9 H, s, Bu^t), and 1.10 and 1.02 (6 H and 3 H, each t, CH_2*Me*); $\lambda_{max.}$(CH_2Cl_2) 484 nm; FD, *m*/*z* (%) 463 (100, M^+) and 462 (98.5, M^+).

t-Butyl 1-(2′-*Chloroethyl*)-4,6-*diethyl*-1′,2,3,5-*tetramethyltripyrren*-a-6′-*carboxylate Hydrobromide* (**37**).—Compound (**31b**) (231 mg, 0.64 mmol) was dissolved in dry dichloromethane (100 ml), together with PTSA (290 mg, 2.5 mol equiv.) and dry methanol (5 ml). A solution of 4-(2′-chloroethyl)-2-formyl-3,5-dimethylpyrrole (**33**) (118 mg; 0.64 mmol, 1 mol equiv.) in dry methanol (5 ml) was added to the well stirred mixture, under nitrogen, at 20 °C. The reaction was followed by visible spectroscopy until the peak at 484 nm ceased to increase in size (~1 h). The solution was then washed successively with 10% aqueous sodium hydrogen carbonate (3 × 50 ml) and water (3 × 50 ml), and dried ($MgSO_4$). After filtration and removal of the solvent, the brownish oil obtained was dissolved in dry dichloromethane (50 ml), and dry hydrogen bromide was bubbled into the solution for 4 s. The solvent was then removed and benzene (2 × 50 ml) was added and distilled off to azeotrope away any water. The *tripyrren* (**37**) (279 mg, 91%) obtained was a deep reddish crystalline solid, m.p. 165 °C (decomp.); δ_H 13.28, 13.16, and 10.20 (3 × 1 H, 3 br s, 3 × NH), 7.12 (1 H, s, –CH=), 4.33 (2 H, s, *meso*-CH_2), 3.56 and 2.90 (2 × 2 H, each t, CH_2CH_2Cl), 2.68 and 2.44 (2 × 2 H, 2 q, CH_2Me), 2.70, 2.32, 2.27, and 2.06 (4 × 3 H, 4 s, 4 × Me), 1.52 (9 H, s, Bu^t), and 1.10 and 1.00 (2 × 3 H, 2 t, 2 × CH_2*Me*); $\lambda_{max.}$(CH_2Cl_2) 484 nm; FD, *m*/*z* (%) 497 (100, M^+).

ac-*Biladienes*

4-(2′-*Chloroethyl*)-1,6,8-*triethyl*-1,2,3,5,7,8′-*hexamethyl*-ac-*biladiene Dihydrobromide* (**17**).—A solution of di-t-butyl 3-(2′-chloroethyl)-4′-ethyl-3′,4-dimethylpyrromethane-5,5′-dicarboxylate (**14**) (500 mg, 1.08 mmol) was dissolved in TFA (5 ml) under nitrogen at 35 °C was stirred for 30 min. To the resulting dark red solution were added solutions of 4-ethyl-2-formyl-3,5-dimethylpyrrole (**16**) (358 mg, 2.37 mmol, 2.2 mol equiv.) in dry methanol (10 ml) and 45% hydrogen bromide in glacial acetic acid (2 ml). The reaction was monitored by visible spectroscopy until the peaks for the *ac*-biladiene ($\lambda_{max.}$ 451, 522 nm) had reached a maximum (*ca.* 4 h). Dry diethyl ether (50 ml) was then added dropwise to the stirred solution, which was further stirred for 2h. The *ac*-biladiene precipitate (**17**) (428 mg, 75%) was filtered off through a glass sinter and washed well with cold diethyl ether to give dark greenish-red microcrystals, m.p. 150 °C (decomp.) δ_H 13.31, 13.23, and 13.11 (1 H, 2 H, and 1 H, 3 br s, 4 NH), 7.17 and 7.12 (each 1 H, 2 s, methine H), 5.22 (2 H, s, bridge CH_2), 3.52 (2 H, t, CH_2Cl), 2.83 (2 H, t, CH_2CH_2Cl), 2.69, 2.68, 2.62, 2.30, and 1.95 (3 H, 3 H, 3 H, 6 H, and 3 H, each s, 6 × Me), 2.43 (3 × 2 H, 2 q, 3 × CH_2Me), and 1.12 (9 H, m, 3 × CH_2*Me*); $\lambda_{max.}$(CH_2Cl_2) 451 and 522 nm; FD, *m*/*z* (%) 532 (100, M^+) and 531 (98, $M^+ - 1$).

6-(2′-*Chloroethyl*)-1,4,8-*triethyl*-1′,2,3,5,7,8′-*hexamethyl*-ac-*biladiene Dihydrobromide* (**27**).—A solution of di-t-butyl 4′-(2′-chloroethyl)-3-ethyl-3′,4-dimethylpyrromethane-5,5′-dicarboxylate (**26**) (290 mg, 0.625 mmol) TFA (5 ml) under nitrogen at 35 °C was stirred for 30 min. To the resulting dark red solution were added solutions of 4-ethyl-2-formyl-3,5-dimethylpyrrole (**16**) (210 mg, 1.38 mmol, 2.2 mol equiv.) in dry methanol (5 ml) and 45% hydrogen bromide in glacial acetic acid (1 ml). The reaction was monitored by visible spectroscopy until the *ac*-biladiene formation had reached a maximum (*ca.* 1 h). Dry diethyl ether (50 ml) was then added dropwise to the stirred solution which was then left for a further 2 h. The ac-*biladiene* (**27**) (246 mg, 74%) was filtered off and washed well with cold diethyl ether to afford dark lustrous plates, m.p. ~150 °C (decomp.) δ_H 13.39, 13.29, 13.26, and 13.11 (4 × 1 H, each br s, 4 × NH), 7.13 and 17.12 (2 × 1 H, s, 2 × methine H), 5.20 (2 H, s, bridge CH_2), 3.57 (2 H, t, CH_2Cl), 3.07 (2 H, t, CH_2CH_2Cl), 2.73, 2.71, 2.33, 2.31, 2.25, and 1.95 (6 × 3 H, each s, 6 × Me), 2.46 (3 × 2 H, 3 m, 3 × –CH_2Me), and 1.09 (3 × 3 H, 3 m, 3 × CH_2*Me*); $\lambda_{max.}$(CH_2Cl_2) 451 and 522 nm; FD, *m*/*z* (%) 532 (100, M^+) and 531 (98.5, $M^+ - 1$).

8-(2-*Chloroethyl*)-1,4,6-*triethyl*-1′,2,3,5,7,8′-*hexamethyl*-ac-*biladiene Dihydrobromide* (**34**).—A solution of t-butyl 1,4,6-triethyl-1′,2,3,5-tetramethyltripyrren-*a*-6′-carboxylate hydrobromide (**32**) (160 mg; 0.345 μmol) in TFA (3 ml) was stirred under nitrogen at 35 °C for 10 min. A solution of 4-(2′-chloroethyl)-2-formyl-3,5-dimethylpyrrole (**33**) (70 mg, 0.380 mmol, 1.1 mol equiv.) in dry methanol (5 ml) was then added, followed immediately by 45% hydrogen bromide in glacial acetic acid (1 ml). The mixture was stirred until the absorption peaks for the *ac*-biladiene had reached a maximum (*ca.* 4 h). Dry diethyl ether was then added dropwise (50 ml) and the mixture was stirred for 2 h. The *biladiene* (**34**) (150 mg, 82%) was filtered off, and washed with cold diethyl ether, to yield dark reddish microcrystals, m.p. 150 °C (decomp.); δ_H 13.49, 13.29, 13.26, and 13.17 (4 H, 4 s, 4 × NH), 7.15 and 7.16 (2 H, 2 s, 2 × –CH=), 5.23 (2 H, s, *meso*-CH_2), 3.68 and 2.95 (2 × 2 H, 2 t, CH_2CH_2Cl), 2.63 and 2.46 (2 H and 4 H, q and m, 3 × CH_2Me), 2.73, 2.71, 2.37, 2.32, 2.25, and 1.93 (6 × 3 H, 6 s, 6 × Me), 1.11 and 0.65 (6 H and 3 H, q and t, 3 × CH_2*Me*); $\lambda_{max.}$(CH_2Cl_2) 452 and 525 nm; FD, *m*/*z* (%) 530 (100, M^+).

1-(2′-*Chloroethyl*-4,6,8-*triethyl*-1′,2,3,5,7,8′-*hexamethyl*-*ac*-*biladiene Dihydrobromide* (**38**).—A solution of t-butyl 1-(2′-chloroethyl)-4,6-diethyl-1′,2,3,5-tetramethyltripyrren-*a*-6′-carboxylate hydrobromide (**37**) (257 mg, 0.52 mmol) in TFA (5 ml) was stirred under nitrogen at 35 °C for 10 min. A solution of 4-ethyl-2-formyl-3,5-dimethylpyrrole (**16**) (86 mg, 0.57 mmol, 1.1 mol equiv.) in dry methanol (5 ml) was then added, followed immediately by 45% hydrogen bromide in glacial acetic acid (2 ml). The mixture was stirred until the peaks for the *ac*-biladiene had reached a maximum (*ca.* 4 h). Dry diethyl ether (50 ml) was then added dropwise and the mixture was stirred for 2 h. The solution was then filtered and the residue was washed with ether to give the *biladiene dihydrobromide* (**38**) (212 mg, 77%) as reddish crystals, m.p. ~15 °C (decomp.); $\lambda_{max.}(CH_2Cl_2)$ 452 and 525 nm; FD, *m/z* (%) 532 (100 M^+); δ_H 13.35, 13.26, 13.19, ad 13.15 (4 × 1 H, 4 br s, 4 × NH), 7.16 and 7.09 (2 × 1 H, each s, 2 × –CH=), 5.20 (2 H, s, *meso*-CH_2), 3.56 and 2.94 (2 × 2 H, each t, CH_2CH_2Cl), 2.69, 2.68, 2.34, 2.29, 2.25, and 1.91 (6 × 3 H, 6 s, 6 × Me), 2.59 and 2.44 (2 H and 4 H, each q, 3 × CH_2Me), 1.10 (2 × 3 H, 2 t, 2 × CH_2Me), and 0.60 (3 H, t, CH_2Me).

Porphyrins

2-(2′-*Chloroethyl*)-4,6,7-*triethyl*-1,3,5,8-*tetramethylporphyrin* (**18**).—4-(2′-Chloroethyl)-1,6,8-triethyl-1′,2,3,5,7,8′-hexamethyl-*ac*-biladiene dihydrobromide (**17**) (428 mg, 0.8 mmol) was added to a solution of copper(II) chloride (2 g) in dry DMF (30 ml) at 145 °C and the mixture was stirred for 4 min under nitrogen. After cooling, the solution was poured into water (50 ml) and extracted with dichloromethane (2 × 30 ml). The extract was washed with water (2 × 30 ml) and dried ($MgSO_4$). After filtration and evaporation, the residue was stirred in 5% conc. H_2SO_4 in TFA for 20 min and the mixture was then poured into water (50 ml). Extraction with dichloromethane (2 × 30 ml), washing with aqueous hydrogen carbonate, and chromatography on alumina Grade (III) with dichloromethane as eluant gave the required *porphyrin* (**18**) (115 mg, 28%), m.p. >300 °C (decomp.) (Found: C, 74.9; H, 7.4; N, 11.1. $C_{32}H_{37}ClN_4$ requires C, 75.0; H, 7.2; N, 10.9%); $\lambda_{max.}(CH_2Cl_2)$ 400, 486, 528, 562, and 616 nm; FD, *m/z* (%) 512 (100, M^+) and 514 (36, M + 2); δ_H 10.08, 10.00, and 9.93 (2 H, 1 H, and 1 H, 3 s, 4 × *meso*-H), 4.42 and 4.28 (2 × 2 H, 2 t, CH_2CH_2Cl), 4.08 (6 H, 3 m, 3 × CH_2Me), 3.62, 3.61, 3.60, and 3.56 (4 × 3 H, 4 s, 4 × Me), 1.88 (9 H, m, 3 × CH_2Me), and 3.88 (2 H, br s, 2 × NH).

4,6,7-*Triethyl*-1,3,5,8-*tetramethyl*-2-*vinylporphyrin* (**19**).—2-(2′-Chloroethyl)-4,6,7-triethyl-1,3,5,8-tetramethylporphyrin (**18**) (125 mg, 0.24 mmol) was dissolved in pyridine (50 ml) and the solution was heated to reflux, under nitrogen, for 15 min; this was followed by the addition of water (10 ml) and the mixture was heated for a further 10 min. 10% Aqueous sodium hydroxide (10 ml) was then added, and the reaction mixture was heated under reflux for 3 h before being cooled and treated with 25% aqueous acetic acid (10 ml). The bulk of the pyridine was evaporated off, water (150 ml) was added, and the mixture was kept at 0 °C overnight. The precipitate formed was filtered off *via* a sinter and sucked to dryness. The filtrate was chromatographed on alumina (Grade III) with dichloromethane as eluant. Evaporation of the red eluate gave the required 2-*vinylporphyrin* (**19**) (88 mg, 76%) as a purple solid, m.p. >300 °C (Found: C, 81.0; H, 7.7; N, 12.0. $C_{32}H_{36}N_4$ requires C, 80.7; H, 7.6; N, 11.8%); $\lambda_{max.}(CH_2Cl_2)$ 402, 502, 536, 569, and 622 nm; FD, *m/z* (%) 476 (100, M^+); δ_H 10.23, 10.15, and 10.07 (1 H, 1 H, and 2 H, 3 s, 4 × *meso*-H), 8.35 (1 H, 1, vinyl CH), 6.40 and 6.19 (2 × H, d, vinyl CH_2), 4.10 (6 H, m, 3 × CH_2Me), 3.72, 3.66, 3.64, and 3.50 (4 × 3 H, 4 s, 4 × Me), 1.86 (9 H, m, 3 × CH_2Me), and –3.65 (2 H, br s, NH).

4,6,7-*Triethyl*-1,3,5,8-*tetramethylporphyrin* (**3a**).—2-Vinyl-4,6,7-triethyl-1,3,5,8-tetramethylporphyrin (**19**) (5 mg) was converted into its zinc complex (using a chloroform solution with saturated zinc acetate in methanol) and this was ground together with resorcinol (15 mg, recrystallised) with a pestle and mortar. The mixture was placed in a narrow glass tube and the air inside was purged with nitrogen. After sealing, the tube was placed in a melting point apparatus which had been preheated to 180 °C. After 1 h at this temperature, the tube was removed, allowed to cool, and the purple reaction mixture was extracted with chloroform. After chromatography on alumina (Grade III) in dichloromethane, the crude porphyrin product was analysed by HPLC and found to be a mixture of the required β-free porphyrin and the vinylporphyrin (in a 2:1 ratio). Semipreparative HPLC (5 Hypersil 25 cm × 0.4 cm column, with 2% ethyl acetate in n-hexane as eluant at 1.5 ml min^{-1}), the two porphyrins were separated and the desired 2-unsubstituted porphyrin was obtained (as the zinc chelate). The zinc was removed when the complex was stirred in a two-phase system of dichloromethane–2M-hydrochloric acid for 2 h under nitrogen. Reverse-phase HPLC (5 ODS Spherisorb with CH_3CN as eluant at 3 ml min^{-1}) confirmed that only one porphyrin was present. The *porphyrin* (**3a**) (2 mg, 42%) was obtained as violet crystals, m.p. >300 °C; $\lambda_{max.}(CH_2Cl_2)$ 396, 494, 527, 563, and 616 nm; FD, *m/z* (%) 450 (100) (Found: M^+, 450.281. $C_{30}H_{34}N_4$ requires M, 450.278); δ_H 10.15, 10.12, 10.11, and 10.04 (4 × 1 H, 4 s, *meso*-H), 9.09 (1 H, s, β-H), 4.10 (6 H, m, 3 × CH_2Me), 3.76, 3.67, 3.64, and 3.63 (4 × 3 H, each s, 4 × Me), 1.83 (9 H, m, 3 × –CH_2Me), and –3.77 (2 H, br, 2 × NH).

4-(2′-*Chloroethyl*)-2,6,7-*triethyl*-1,3,5,8-*tetramethylporphyrin* (**28**).—6-(2′-Chloroethyl)-1,4,8-triethyl-1′,2,3,5,7,8′-hexamethyl-*ac*-biladiene dihydrobromide (**27**) (290 mg, 0.545 mmol) was treated with copper(II) chloride in hot DMF in the same manner as the analogue (**17**) and the product was worked up in the same way. The *chloroethylporphyrin* (**28**) (61 mg, 26%) formed violet crystals from chloroform–methanol, m.p. ~300 °C (Found: C, 74.9; H, 7.4; N, 11.1. $C_{32}H_{37}ClN_4$ requires C, 75.0; H, 7.2; N, 10.9%); $\lambda_{max.}(CH_2Cl_2)$ 400, 486, 562, and 616 nm; FD, *m/z* (%) 512 (100, M^+) and 514 (36, M + 2); δ_H 10.05, 10.01, and 9.91 (2 H, 1 H, and 1 H, 3 br s, 4 × *meso*-H), 4.48 (2 H, t, CH_2CH_2Cl), 4.32 (2 H, t, CH_2CH_2Cl), 4.06 (6 H, m, 3 × CH_2Me), 3.65, 3.61, 3.59, and 3.55 (4 × 3 H, 4 s, 4 × Me), 1.89 (9 H, m, 3 × CH_2Me), and –3.89 (2 H, br, NH).

2,6,7-*Triethyl*-4-*vinyl*-1,3,5,8-*tetramethylporphyrin* (**29**) was prepared from 4-(2′-chloroethyl)-2,6,7-triethyl-1,3,5,8-tetramethylporphyrin (**28**) in the same way as was the analogous vinylporphyrin (**19**) from the chloroethylporphyrin (**18**). The *vinylporphyrin* (**29**) (75 mg, 75%) was crystallised from chloroform–methanol as purple needles, m.p. >300 °C (Found: C, 80.7; H, 7.9; N, 12.0. $C_{32}H_{36}N_4$ requires C, 80.8; H, 7.6; N, 11.8%); $\lambda_{max.}(CH_2Cl_2)$ 402, 502, 536, 569, and 622 nm; δ_H 10.17, 10.05, 10.02, and 10.01 (4 × 1 H, 4 s, 4 × *meso*-H), 8.30 (1 H, q, –CH=), 6.32 and 6.12 (2 × 1 H, 2 d, =CH_2), 4.02 (6 H, m, 3 × CH_2Me), 3.68, 3.59, 3.58, and 3.55 (4 × 3 H, 4 s, 4 × Me), 1.85 (9 H, m, 3 × CH_2Me), and –3.82 (2 H, br s, NH).

2,6,7-*Triethyl*-1,3,5,8-*tetramethylporphyrin* (**3b**) was prepared from the zinc chelate (5 mg) of the foregoing porphyrin (**29**) by the same method as the analogue (**3a**), and was purified by semipreparative HPLC on 5 Hypersil with 2% ethyl acetate in hexane as eluant. The desired *porphyrin* (**36**) (1.5 mg, 32%) formed purple crystals, m.p. >300 °C; $\lambda_{max.}(CH_2Cl_2)$ 396, 494,

527, 563, and 616 nm; *m/z* (%) 450 (100) (Found: M^+, 450.282. $C_{30}H_{34}N_4$ requires *M*, 450.278); HPLC: single peak at t_R 7.10 min (CH_3CN elution at 3 ml min^{-1} from a 25 cm × 4 cm column packed with 5 Spherisorb ODS); δ_H 10.17, 10.10, 10.09, and 10.05 (each 1 H, each s, *meso*-H), 9.09 (1 H, s, β-H), 4.10 (6 H, m, 3 × CH_2Me), 3.76, 3.67, 3.64, and 3.63 (4 × 3 H, 4 s, 4 × Me), 1.86 (9 H, m, 3 × CH_2Me), and −3.67 (2 H, b, NH).

6-(2′-*Chloroethyl*)-2,4,7-*triethyl*-1,3,5,8-*tetramethylporphyrin* (**35**).—8-(2′-Chloroethyl)-1,4,6,-triethyl-1′,2,3,5,7,8′-hexamethyl-*ac*-biladiene dihydrobromide (**34**) (150 mg, 0.282 mmol) was converted into the *porphyrin* (**35**) (36 mg, 25%) on being heated with copper(II) chloride in DMF in the usual manner (Found: C, 75.3; H, 7.25; N, 10.95. $C_{32}H_{37}ClN_4$ requires C, 75.0; H, 7.2; N, 10.9%), $\lambda_{max.}(CH_2Cl_2)$, 404, 500, 532, 570, and 619 nm; FD, *m/z* (%) 512 (100) and 514 (36); δ_H 10.09, 10.08, 10.07, and 9.98 (4 × 1 H, each s, 4 × *meso*-H), 4.43 and 4.27 (2 × 2 H, 2 t, CH_2CH_2Cl), 4.06 (6 H, m, 3 × CH_2Me), 3.61, 3.59, 3.58, and 3.53 (4 × 3 H, 4 s, 4 × Me), 1.82 (9 H, m, 3 × CH_2Me), and −4.00 (2 H, br, NH).

2,4,7-*Triethyl*-1,3,5,8-*tetramethyl*-6-*vinylporphyrin* (**36**) (25 mg, 74%) was prepared from the foregoing chloroethylporphyrin (**35**) (35 mg) by treatment with sodium hydroxide in aqueous pyridine as in the analogous examples above, and had m.p. >300 °C (Found: C, 81.0; H, 7.8; N, 11.9. $C_{32}H_{36}N_4$ requires C, 80.7; H, 7.6; N, 11.8%); $\lambda_{max.}(CH_2Cl_2)$ 402, 520, 536, 569, and 622 nm; FD, *m/z* (%) 476 (100); δ_H 10.21, 10.09, and 10.05 (1 H, 1 H, and 2 H, 3 s, 4 × *meso*-H), 8.34 (1 H, q, –CH=), 6.38 and 6.16 (2 H, 2 d, $=CH_2$), 4.10 (6 H, m, 3 × CH_2Me), 3.65, 3.59, 3.54, and 3.53 (4 × 3 H, 4 s, 4 × Me), 1.85 (9 H, m, 3 × CH_2Me), and −3.80 (2 H, br s, NH).

2,4,7-*Triethyl*-1,3,5,8-*tetramethylporphyrin* (**3c**) (1.5 mg, 32%) was prepared from the zinc chelate (5 mg) of the preceding vinylporphyrin (**36**) in the same manner as for the analogous porphyrins (**3a**) and (**3b**); $\lambda_{max.}(CH_2Cl_2)$ 396, 494, 527, 563, and 616 nm; FD, *m/z* (%) 450 (M^+) (Found: M^+, 450.281. $C_{30}H_{34}N_4$ requires *M*, 450.278); HPLC t_R 7.00 min (CH_3CN elution at 3 ml min^{-1}; ODS, Spherisorb column); δ_H 10.14, 10.11, 10.10, and 10.04 (4 × 1 H, 4 s, 4 × *meso*-H), 9.09 (1 H, s, β-H), 4.11 (6 H, m, 3 × CH_2Me), 3.77, 3.68, 3.66, and 3.63 (4 × 3 H, 4 s, 4 × Me), 1.89 (9 H, m, 3 × CH_2Me), and −3.80 (2 H, br, NH).

7-(2′-*Chloroethyl*)-2,4,6-*triethyl*-1,3,5,8-*tetramethylporphyrin* (**39**) (73 mg, 36%) was prepared from 1-(2′-chloroethyl)-4,6,8-triethyl-1′,2,3,5,7,8′-hexamethyl-*ac*-biladiene dihydrobromide (**38**) (212 mg, 0.39 mmol) by heating with copper(II) chloride in DMF in the usual manner (Found: C, 75.3; H, 7.25; N, 10.95. $C_{32}H_{37}ClN_4$ requires C, 75.0; H, 7.2; N, 10.9%); $\lambda_{max.}(CH_2Cl_2)$ 404, 500, 532, and 619 nm; FD, *m/z* (%) 514 (36) and 512 (100); δ_H 10.03, 9.96, and 9.90 (2 H, 1 H, and 1 H, 3 s, 4 × *meso*-H), 4.43 and 4.27 (2 × 2 H, 2 t, CH_2CH_2Cl), 4.03 (6 H, m, 3 × CH_2Me), 3.63, 3.59, and 3.56 (3 H, 6 H, and 3 H, 3 s, 4 × Me), 1.84 (9 H, m, 3 × CH_2Me), and −3.89 (2 H, br s, NH).

2,4,6-*Triethyl*-1,3,5,8-*tetramethyl*-7-*vinylporphyrin* (**40**) was prepared from the foregoing chloroethylporphyrin (**39**) (73 mg) and formed purple needles, m.p. >300 °C (55 mg, 81%) (Found: C, 80.5; H, 7.4; N, 11.5. $C_{32}H_{36}N_4$ requires C, 80.67; H, 7.56; N, 11.76%); $\lambda_{max.}(CH_2Cl_2)$ 402, 502, 536, 569, and 622 nm; FD, *m/z* (%) 476 (100, M^+); δ_H 10.17, 10.01, 10.00, and 9.98 (4 × 1 H, 4 s, 4 × *meso*-H), 8.28 (1 H, q, –CH=), 6.37 and 6.14 (2 × 1 H, 2 d, $=CH_2$), 4.00 (6 H, q, 3 × CH_2Me), 3.65, 3.59, 3.54, and 3.53 (4 × 3 H, s, 4 × Me), 1.87 (9 H, m, 3 × CH_2Me), and −3.85 (2 H, br s, NH).

2,4,6-*Triethyl*-1,3,5,8-*tetramethylporphyrin* (**3d**) was prepared by resorcinol fusion of the foregoing porphyrin (**40**) as its zinc chelate (5 mg), and was purified by HPLC It formed purple needles (2 mg, 43%), m.p. >300 °C; $\lambda_{max.}(CH_2Cl_2)$ 396, 494, 527, 563, and 616 nm; FD, *m/z* (%) 450 (100, M^+) (Found: M^+, 450.281. $C_{30}H_{34}N_4$ requires *M*, 450.278); HPLC: t_R 6.73 min; δ_H 10.16, 10.12, 10.10, and 10.04 (4 × 1 H, s, 4 × *meso*-H), 9.09 (1 H, s, β-H), 4.10 (6 H, m, 3 × CH_2Me), 3.76, 3.67, 3.66, and 3.64 (4 × 3 H, 4 s, 4 × Me), 1.86 (9 H, m, 3 × CH_2Me), and −3.79 (2 H, br, NH).

HPLC Separation of the Isomers of De-ethylaetioporphyrin III.—The four porphyrins were separated by injection onto two reversed-phase Perkin-Elmer ODS-HC-SilXI columns, each 25 cm long × 0.3 cm i.d. and assembled in series. The mobile phase was acetonitrile and the detector was set at 400 nm. The retention times under these conditions at 20 °C were 33 min (**3c**); 36 min (**3d**); 37 min (**3b**); and 40 min (**3a**).

The de-ethylaetioporphyrin fractions obtained from Gilsonite and Serpiano shale each showed the presence of one main porphyrin corresponding to isomer (**3c**), although other smaller peaks (<15%) were also present at retention times corresponding to the other isomers. The actual chromatographic traces are reproduced in our preliminary publication.[1]

Similarly, HPLC analysis of the de-ethylaetioporphyrin fraction obtained from coal also showed that the major porphyrin present was the *C*-ring isomer (**3c**), although another porphyrin (probably aetioporphyrin itself) co-eluted with a retention time slightly longer than that of the *A*-ring isomer.

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