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A Convenient Synthesis of *meso*-Substituted Porphyrins[1]

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Acid-catalyzed condensations of 1,19-diunsubstituted 1,19-dideoxybiladiene-ac dihydrobromides with aldehydes, R · CHO, afford the corresponding *meso*-substituted porphyrins (R = C_6H_5, *p*-Me·C_6H_4, *p*-MeO·C_6H_4, *p*-O_2N·C_6H_4, *p*-HOC·C_6H_4, *p*-$(MeO)_2CH$·C_6H_4, Me, *n*-Pr, CO_2Et), mostly in good yield.

INTRODUCTION

During the course of our recent work (1–3) on the preparation and properties of various *meso*-substituted porphyrins, it became apparent that there were few good methods for the preparation of mono-*meso*-alkyl and -aryl porphyrins, the former of which include many degradation products of chlorophyll. Two main methods have been used in the past. First, a lin.-tetrapyrrolic derivative containing the *meso*-alkyl substituent was synthesized and then cyclized. Both 1,19-dideoxybiladienes-ac (*4*, *5*) and bilenes-b (*6*) have been used in this connection, the latter approach including Woodward's classical chlorophyll synthesis (*7*). Thermal rearrangement of 1-alkyl-19-methyltetradehydrocorrin perchlorates also yields *meso*-alkyl porphyrins (*8*). In the second approach the *meso*-grouping is introduced by substitution into the porphyrin, this is of little value for use with unsymmetrical porphyrins, because of the difficulty of ensuring that substitution occurs at a given *meso*-position. Direct *meso*-alkylation of porphyrins is unusual, but a few examples have been cited with particular metalloporphyrins using methyl fluorosulfonate (*9*) or ethyl diazoacetate (*10*). However, other substituents, which may be easier to introduce onto the porphyrin ring, can often be transformed to methyl groups by standard reactions, e.g., $-CHO \rightarrow -CH_2OH \rightarrow CH_2OAc \rightarrow CH_3$ (*11*), and $CHO \rightarrow -CHOH \cdot CH_3 \rightarrow -CH{=}CH_2 \rightarrow -C_2H_5$ (*2*). Our present method comprises the condensation of aldehydes or the corresponding acetals, with a 1,19-diunsubstituted-1,19-dideoxybiladiene-ac dihydrobromide (the corresponding 1,19-dicarboxylic acid may also be used), in the presence of a small quantity of hydrogen bromide (*12*). These 1,19-diunsubstituted biladiene-ac dihydrobromides were prepared originally (*13*) as intermediates for the synthesis of corroles, but it was also shown that condensation with formaldehyde gave the corresponding porphyrin. The method was used later for a synthesis of coproporphyrin-II tetramethyl ester as well as of [15-^{13}C]protoporphyrin-IX dimethyl ester required for biosynthetic studies (*14*). Shortly after we had described our porphyrin synthesis based on 1,19-dideoxybiladienes-ac, Kenner and his co-workers announced (*15*) a similar synthesis from 1,19-dideoxybilene-b-1,19-dicarboxylic acids

[1] Dedicated to the late Professor George Kenner, FRS, University of Liverpool.

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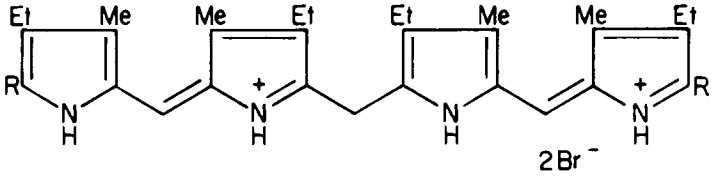
with orthoformic ester (reviews (*16*, *17*)), a method which later was extended in scope (*6*, *18*). The synthesis now described has been evaluated using 2,8,12,18-tetraethyl-3,7,13,17-tetramethyl-1,19-dideoxybiladiene-ac dihydrobromide (*19*) (**I**; R = H) as starting material, which by condensation with aldehydes has given 5-substituted etioporphyrins-II (**II**) as the main products. In the examples now quoted we describe [**II**, R = Ph (91%), *p*-MeC_6H_4 (46%), *p*-$MeOC_6H_4$ (81%), *p*$O_2NC_6H_4$ (40%), Me (28%) (from acetal), Pr^n (13%), and CO_2Et (68%)] from the appropriate aldehydes R·CHO, the yield figures referring to unpurified macrocycle formed in every case, other than *meso-p*-tolyl. All of these porphyrins were characterized as nickel(II) complexes which were formed in high yield from the metal-free porphyrin by the action of methanolic nickel acetate.

Examples of *meso*-carboxylic acids, -esters, and -amides are rare in the porphyrin series, and a previous preparation of *meso*-ester (*8*) gave the product only in 2% yield. Clezy and his co-workers (*20*) reported a number of unsuccessful attempts to obtain the *meso*-carboxylic acid of etioporphyrin-I; although the nitrile is well known (*21*), hydrolysis of it proceeds only to the *meso*-amide.



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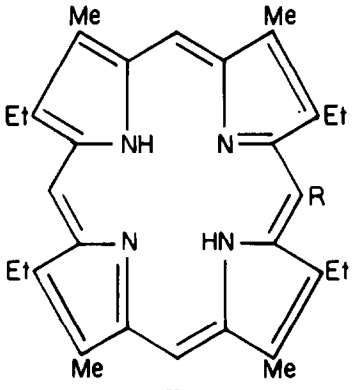


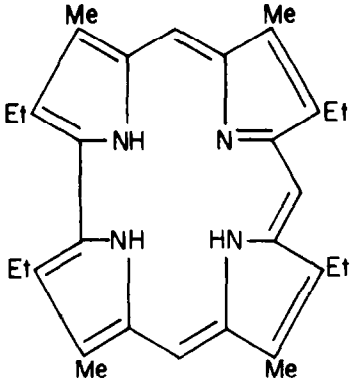
II

The physical properties of the various nickel *meso*-substituted etioporphyrins-II were unexceptional and similar. However, the bathochromic shift of the Soret band in the electronic spectrum caused by an aromatic substituent (the nature of the aromatic *p*-substituent, *p*-OMe or *p*-NO_2, had no effect in this context) was greater (12 nm) than that of ethoxycarbonyl (7 nm) or methyl (2 nm).

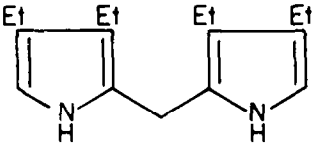
We have attempted to adapt the above porphyrin synthesis to give various types of bis-porphyrin. Thus the biladiene-ac dihydrobromide (**I**; R = H) was condensed with excess terephthalaldehyde in acidified methanol, but the main product proved to be a mixture (89%) of *p*-formylphenyletioporphyrin-II (**II**; R = C_6H_4·CHO) and the

corresponding dimethylacetal [**II**; R = $C_6H_4 \cdot CH(OMe)_2$]. This mixture was converted to the nickel complex when the derivative of the acetal was obtained as the major product (65%) along with that of the free aldehyde (5%). The same products were isolated when the ratio of biladiene-ac dihydrobromide to terephthalaldehyde was increased to 2:1. Identification of the condensation product from the nickel *meso-p*-formylphenylporphyrin and the biladiene-ac is in progress.

A condensation under the usual conditions of the biladiene-ac dihydrobromide with glyoxal failed to yield bis-5,5′-etioporphyrin-II, but instead etioporphyrin-II itself was the sole product. Side reactions would be expected in this case, especially if the bis-porphyrin were sterically strained, but the source of the added *meso*-carbon of the porphyrin was of interest. Indeed, a reexamination of most of the preparations of the *meso*-substituted porphyrins quoted above showed that the main products were accompanied by small quantities, not only of etioporphyrin-II, but also of the corresponding corrole (**III**) (*22*, *23*). The corrole was obtained by oxidative (air) cyclization of the biladiene salt.



III



IV

Acid condensation of a 1,19-dideoxybiladiene-ac-1,19-dicarboxylic acid (cf. **I**; R = CO_2H) dihydrobromide with ^{13}C-labeled formaldehyde had been shown (*14*) to give the *meso*-labeled porphyrin, although contaminated with unlabeled material, and on the results of pilot experiments, it was concluded that the source of the additional unlabeled carbon was one of the carboxy groups. However, in our experiments the carboxy groups were absent, and originally the methanol (solvent) seemed to be the likely source of the carbon. Indeed it was shown that etioporphyrin-II (48%) could be obtained from the biladiene-ac dihydrobromide (**I**; R = H) by heating under reflux with methanol containing a small quantity of acetic acid saturated with hydrogen bromide. However, etioporphyrin-II was also obtained when ethanol or benzene was substituted for methanol as solvent and also using acetic acid saturated with hydrogen bromide (yields

52, 38, and 8%, respectively). When 1-^{13}C-enriched ethanol was used as solvent there was no incorporation of the label into the porphyrin, thus indicating that the additional carbon was derived from decomposition of the biladiene salt.

Since our work was completed, Ogoshi *et al.* (*24*) have described a condensation of aromatic aldehydes with 3,3′,4,4′-tetraethyl-2,2′-dipyrromethane (**IV**) which gives a mixture of 5-aryl (15–25%)- and 5,15-diaryl-octaethylporphyrins (30–40%) (aryl = *o*-, *m*-, *p*-methoxyphenyl, *o*-, *m*-, *p*-tolyl, α-naphthyl).

EXPERIMENTAL

Nuclear magnetic resonance spectra were measured for solutions in [^{2}H]chloroform and uv-visible spectra for solutions in chloroform with instruments listed in an earlier paper (*1*). Mass spectra were determined with an A.E.I. MS30 instrument by direct insertion into the ion source.

5-Phenyl-etioporphyrinato-II nickel(II). A suspension of 1,19-dideoxy-2,8,12,18-tetraethyl-3,7,13,17-tetramethylbiladiene-ac dihydrobromide (*1*) (100 mg; 0.159 mmol) in methanol (25 ml) containing benzaldehyde (200 mg; 1.887 mmol) and acetic acid (four drops) saturated with hydrogen bromide were heated under reflux for 24 hr. The mixture was cooled and treated with an excess of solid sodium bicarbonate. The precipitate was separated, washed with water, and dried, giving the crude product (70 mg; 91%) which was dissolved in chloroform–acetic acid (25:1). A saturated methanolic solution (1 ml) of nickel acetate was then added, and the mixture was heated under reflux for 3 hr, cooled, and washed with water (2 × 50 ml) and then aqueous sodium bicarbonate (50 ml). The solvent was removed from the dried chloroform extract, and the residue dissolved in a little chloroform and chromatographed on alumina (activity III) using chloroform for elution. The main band was collected, the solvent removed, and after crystallization from methylene chloride–methanol gave the nickel derivative of the product as purple needles. λ, 403, 526, and 561 nm (ε, 164 470, 10 870, and 19 760, respectively). ν, 1599, 2870, 2930, and 2965 cm^{-1}. δ, 9.5 (*s*, 2 *meso* H), 9.43 (s, 1 *meso* H), 7.94 (m, 2 *o*-phenyl H), 7.55 (m, 3 phenyl H), 3.75 (q, 4H, 2 × CH_2·CH$_3$), 3.3, 3.24 (both s, 12H, 4 × CH$_3$), 2.55 (q, 4H, 2 × CH_2·CH$_3$), 1.68 (t, 6H, 2 × CH$_2$·CH_3), 0.9 (t, 6H, 2 × CH$_2$·CH_3).

Anal. Calcd for $C_{38}H_{40}N_4Ni$: C, 74.65; H, 6.55; N, 9.15%; M, 610. Found: C, 74.8; H, 6.65; N, 9.55, *m/e* 610.

5-(p-Tolyl)-etioporphyrinato-II nickel(II). A suspension of the biladiene-ac dihydrobromide (above; 100 mg) in methanol (15 ml) containing *p*-tolualdehyde (19.1 mg) and acetic acid (two drops) saturated with hydrogen bromide was heated under reflux for 18 hr and the product worked up as in the previous experiment. The crude product was chromatographed on silica plates and eluted with chloroform. Minor bands corresponding to etioporphyrin-II and etiocorrole-II were observed but the major band was separated, the solvent removed, and the residue crystallized from dichloromethane–methanol to yield *meso-p*-tolyletioporphyrin-II (41 mg; 46%) as red needles, mp > 300°C.

Anal. Calcd for $C_{39}H_{44}N_4$: N, 9.85%. Found: N, 9.9.

λ, 405, 505, 536, 572, and 624 nm (ε, 134 620, 12 260, 5530, 5050, and 1680,

respectively). δ, 10.15 (s 2 *meso*-H), 9.88 (s, 1 *meso*-H), 8.00 (d, 2 benzenoid H, $J = 8$ Hz), 7.44 (d, 2 benzenoid H, $J = 8$ Hz), 4.01 (q, 2 × $CH_2 \cdot CH_3$), 3.57 (s, 2 × CH_3), 3.49 (s, 2 × CH_3), 2.75 (q, 2 × $CH_2 \cdot CH_3$), 2.68 (s, 3H, benzenoid CH_3), 1.84, 1.16 (both t, both 2 × $CH_2 \cdot CH_3$), −3.18 (br s, 2 × NH). The porphyrin (15 mg) was dissolved in chloroform (3.5 ml) containing acetic acid (0.2 ml) and to this was added a saturated solution (0.2 ml) of nickel acetate in methanol and the mixture heated under reflux for 3 hr. It was cooled and washed with water, then aqueous sodium bicarbonate, and the chloroform layer was separated and dried. The solvent was removed under reduced pressure and the residue chromatographed on silica using light petroleum–chloroform (7:3) for elution. The product from the main band was crystallized from chloroform–methanol and formed red needles (12 mg; 73%), mp 254°C.

Anal. Calcd for $C_{39}H_{42}N_4Ni$: N, 8.95%. Found: N, 8.6.

λ_{max} 400, 524, and 559 nm (ε, 161 000, 9700 and 17 700, respectively). ν(KBr), 1505 and 1650 cm^{-1}. δ, 9.6 (s, 2 *meso*-H), 9.52 (s, 1 *meso*-H), 7.8 (d, 2 benzenoid H, $J = 8$ Hz), 7.38 (d, 2 benzenoid H, $J = 8$ Hz), 3.82 (q, 2 × $CH_2 \cdot CH_3$), 3.39 (s, 2 × CH_3), 3.29 (s, 2 × CH_3), 2.65 (s, CH_3), 2.58 (q, 2 × $CH_2 \cdot CH_3$), 1.71 (t, 2 × $CH_2 \cdot CH_3$), 0.93 (t, 2 × $CH_2 \cdot CH_3$).

5-(p-Methoxyphenyl)-etioporphyrinato-II nickel(II). A suspension of the biladiene-ac dihydrobromide (above; 131 mg; 0.208 mmol) in methanol (25 ml) containing *p*-methoxybenzaldehyde (330 mg; 2.43 mmol) and acetic acid (four drops) saturated with hydrogen bromide was heated under reflux for 48 hr and the product worked up as in the previous experiment. The crude product (95 mg; 81%) was converted into its nickel derivative (89 mg; 86%) as above and this was purified by crystallization from methylene chloride–methanol when it formed purple prisms.

Anal. Calcd for $C_{39}H_{42}N_4NiO$: C, 73.0; H, 6.55; N, 8.75%; M, 640. Found: C, 73.05; H, 6.6; N, 8.9. *m/e* 640.

λ, 402, 525, and 561 nm (ε, 183 000, 15 000 and 21 800, respectively). ν, 1609, 2865, 2928, and 2960 cm^{-1}. δ, 9.5 (s, 2 *meso* H), 9.44 (s, 1 *meso* H), 7.78 (d, $J = 8$ Hz, 2 phenyl H), 7.03 (d, $J = 8$ Hz, 2 phenyl H), 3.93 (s, 3H, OCH_3), 3.76 (q, 4H, 2 × $CH_2 \cdot CH_3$), 3.31, 3.25 (both s, 12H, 4 × CH_3), 2.62 (q, 4H, 2 × $CH_2 \cdot CH_3$), 1.69 (t, 6H, 2 × $CH_2 \cdot CH_3$), 0.92 (t, 6H, 2 × $CH_2 \cdot CH_3$).

5-(p-Nitrophenyl)-etioporphyrinato-II nickel(II). The biladiene-ac dihydrobromide (above; 155 mg) was condensed with *p*-nitrobenzaldehyde (310 mg) by the foregoing method and gave the crude *meso-p*-nitrophenylporphyrin (41 mg; 40%) which was converted to the corresponding nickel derivative (58%). After crystallization from methylene chloride–methanol, the sample formed brownish-red needles.

Anal. Calcd for $C_{36}H_{39}N_5NiO_2$: C, 69.5; H, 5.95; N, 10.65%; M, 655. Found: C, 69.65; H, 5.95; N, 10.95. *m/e* 655.

λ, 402, 526, and 561 nm (ε, 219, 350, 11 155, and 19 280, respectively), ν, 1345, 1516, 1595, 2870, 2930, and 2965 cm^{-1}. δ, 9.5 (s, 2 *meso* H), 9.45 (s, 1 *meso* H), 8.37 (d, $J = 8$ Hz, 2 phenyl H), 8.08 (d, $J = 8$ Hz, 2 phenyl H), 3.75 (q, 2 × $CH_2 \cdot CH_3$), 3.3, 3.23 (both s, 4 × CH_3), 2.45 (q, 2 × $CH_2 \cdot CH_3$), 1.59 (t, 2 × $CH_2 \cdot CH_3$), 0.86 (t, 2 × $CH_2 \cdot CH_3$).

5-(p-Formylphenyl)-etioporphyrinato-II nickel(II). (i) The biladiene-ac dihydrobromide (200 mg; 0.317 mmol) was condensed with terephthalaldehyde (300 mg; 2.23 mmol) by the foregoing method and gave the crude porphyrin (169 mg; 89%). This was

converted to the nickel derivative which was separated into two components by quantitative tlc on silica. The major product (65%) was shown to be the dimethylacetal of the formyl compound, 5-(*p*-dimethoxymethylphenyl)-etioporphyrinato nickel(II) which was crystallized from methylene chloride–methanol when it formed small red needles.

Anal. Calcd for $C_{41}H_{46}N_4NiO_2$: C, 71.8; H, 6.7; N, 8.2%; M, 684. Found: C, 71.95; H, 6.8; N, 8.25. *m/e* 684.

λ, 404, 526, and 562 nm (ε, 201 875, 12 195, and 22 000, respectively). δ, 9.51 (s, 2 *meso* H), 9.44 (s, 1 *meso* H), 7.95 (d, $J = 8$ Hz, 2 phenyl H), 7.62 (d, $J = 8$ Hz, 2 phenyl H), 5.72 [s, $CH(OMe)_2$], 3.76 (q, 2 × $CH_2 \cdot CH_3$), 3.45 (s, 2 × OCH_3), 3.31, 3.25 (both s, 4 × CH_3), 2.55 (q, 2 × $CH_2 \cdot CH_3$), 1.69 (t, 2 × $CH_2 \cdot CH_3$), 0.9 (t, 2 × $CH_2 \cdot CH_3$).

The minor product (5%) was purified similarly and was the 5-(*p*-formylphenyl) derivative although it was very easily transformed to the dimethylacetal. It formed purple prisms.

Anal. Calcd for $C_{39}H_{40}N_4NiO$: M, 638. Found: *m/e* 638.

λ, 404, 526, and 562 nm (ε, 148 570, 9860, and 17 710, respectively). δ, 10.39 (s, CHO), 9.64 (s, 2 *meso* H), 9.56 (s, 1 *meso* H), 8.19 (dd, $J = 8$ Hz, 4 phenyl H), 3.85 (q, 2 × $CH_2 \cdot CH_3$), 3.39, 3.29 (both s, 4 × CH_3), 2.52 (q, 2 × $CH_2 \cdot CH_3$), 1.69 (t, 2 × $CH_2 \cdot CH_3$), 0.88 (t, 2 × $CH_2 \cdot CH_3$).

(ii) A similar condensation of the biladiene-ac dihydrobromide (200 mg) and terephthalaldehyde (21.3 mg) gave etioporphyrin-II (3 mg; 2%) *meso*-(*p*-formylphenyl)-etioporphyrin-II (31.5 mg; 17%), and etiocorrole-II (21.5 mg; 14.5%) which formed purple needles after crystallization from dichloromethane–methanol and was identical with a sample prepared previously (*22*).

Anal. Calcd for $C_{31}H_{38}N_4$: M, 466. Found: *m/e* 466.

δ, 9.20 (s, 2 *meso*-H), 9.04 (s, 1 *meso*-H), 3.80 (q, 4 × $CH_2 \cdot CH_3$), 3.38, 3.30 (both s, and both 2 × CH_3), 1.68 (t, 12H, 4 × $CH_2 \cdot CH_3$), −3.4 (br s, 3 × NH).

5-Methyletioporphyrinato-II nickel(II). The compound was prepared from the biladiene-ac dihydrobromide (100 mg) and diethylacetal (1 ml) by the method described above. The crude porphyrin (20 mg; 28%) was converted to its nickel derivative (18 mg; 82%) which was crystallized from methylene chloride–methanol when it formed small reddish-purple prisms.

Anal. Calcd for $C_{33}H_{38}N_4Ni$: C, 72.1; H, 6.9; N, 10.2%; M, 548. Found: C, 71.5; H, 6.7; N, 10.6. *m/e* 548.

λ, 393, 520, and 554 nm (ε, 156 670, 10 290, and 25 290, respectively). δ, 9.56 (s, 2 *meso* H), 9.35 (s, 1 *meso* H), 3.75 (s, *meso* CH_3), 3.74 (q, 4 × $CH_2 \cdot CH_3$), 3.3 (4 × peripheral CH_3), 1.7 (t, 4 × $CH_2 \cdot CH_3$).

5-n-Propyletioporphyrinato-II nickel(II). The compound was prepared from the biladiene-ac dihydrobromide (120 mg) and *n*-butyraldehyde (1 ml) by the usual method, the reaction mixture being heated under reflux for 32 hr. The crude porphyrin (12 mg; 13%) was converted to its nickel derivative and purified as described above. The product was obtained as small reddish-purple prisms.

Anal. Calcd for $C_{33}H_{42}N_4Ni$: C, 72.8; H, 7.3; N, 9.7%; M, 576. Found: C, 72.2; H, 7.3; N, 8.95. *m/e* 576.

λ_{max}, 392, 520, and 553 nm (ε, 156 800, 11 100, and 26 070, respectively). δ, 9.71 (s,

2 *meso* H), 9.3 (s, 1 *meso* H), 4.35 (t, $CH_2 \cdot CH_2 \cdot CH_3$), 3.75 (m, 4 × $CH_2 \cdot CH_3$ and $CH_2 \cdot CH_2 \cdot CH_3$), 3.4 (s, 2 × CH_3), 3.25 (s, 2 × CH_3), 1.75 (m, 4 × $CH_2 \cdot CH_3$ and $CH_2 \cdot CH_2 \cdot CH_3$).

5-(Methoxycarbonyl)-etioporphyrinato-II nickel(II). The compound was prepared by the usual method from the biladiene-ac dihydrobromide (200 mg) and ethyl glyoxylate (319 mg), the reaction mixture being heated under reflux for 24 hr. After the usual work-up procedure, the crude porphyrin (108 mg; 68%) was obtained which was converted to its nickel derivative (116 mg; 97%). This was crystallized from methylene chloride–methanol when it formed purple-red plates. Ester interchange occurred during crystallization.

Anal. Calcd for $C_{34}H_{38}N_4NiO_2$: C, 68.8; H, 6.4; N, 9.45%. Found: C, 68.4; H, 6.5; N, 9.1.

λ, 398, 523, and 560 nm (ε, 172 000, 17 330, and 38 780, respectively). ν, 1724, 1734, 2872, 2935, and 2965 cm^{-1}. δ, 9.5 (s, 2 *meso* H), 9.43 (s, 1 *meso* H), 4.28 (s, CO_2CH_3), 3.72, 3.52 (2 overlapping q; 4 × $CH_2 \cdot CH_3$), 3.31 (s; 2 × CH_3), 3.26 (s; 2 × CH_3), 1.65, 1.48 (2 overlapping t; 4 × $CH_2 \cdot CH_3$).

Etioporphyrin II. (i) A suspension of 1,19-dideoxy-2,8,12,18-tetraethyl-3,7,13,17-tetramethylbiladiene-ac dihydrobromide (100 mg) in methanol (25 ml) containing acetic acid (four drops) saturated with hydrogen bromide was heated under reflux for 48 hr. After cooling, the separated crystals (34 mg; 48%) were removed and washed with methanol. The product was shown to be etioporphyrin II by comparison with an authentic specimen.

(ii) The biladiene-ac dihydrobromide (222 mg) was treated similarly in ethanol (25 ml) solution. The precipitate was removed by filtration but a further quantity was obtained by treatment of the filtrate with solid sodium bicarbonate. Excess sodium bicarbonate was removed from the product by washing with water and the residue was then crystallized from methylene chloride-methanol to yield etioporphyrin-II (87 mg; 52%) as before. A repetition of this experiment using ethanol (5% enriched with [1-^{13}C]-ethanol) gave the porphyrin which showed no ^{13}C incorporation (mass spectrum and ^{13}C nmr).

(iii) A suspension of the biladiene-ac dihydrobromide (127 mg) in benzene (20 ml) containing acetic acid (four drops) saturated with hydrogen bromide was heated under reflux for 48 hr. The solvent was removed *in vacuo* and the residue purified by chromatography on silica using chloroform as eluant. The main band yielded etioporphyrin-II (36 mg; 38%), confirmed by comparison with an authentic specimen as before.

(iv) A suspension of the biladiene-ac dihydrobromide (134 mg) in acetic acid (15 ml) saturated with hydrogen bromide was heated under reflux for 48 hr. The reaction mixture was poured into water (100 ml), neutralized with sodium bicarbonate, and then extracted with chloroform. The extract was dried (Na_2SO_4) and the solvent removed *in vacuo*. The residue was purified by chromatography on silica using chloroform for elution. The product was again etioporphyrin-II (9 mg; 8%).

(v) A suspension of the biladiene-ac dihydrobromide (100 mg) and glyoxal (150 mg) in methanol (25 ml) containing acetic acid (four drops) saturated with hydrogen bromide was heated under reflux for 11 hr. The mixture was cooled and neutralized

with sodium bicarbonate. The precipitate, was separated, washed with water, and then crystallized from methylene chloride–methanol to yield etioporphyrin-II (25 mg; 35%) as the sole product.

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REFERENCES

1. D. P. ARNOLD, A. W. JOHNSON, AND M. WINTER, *J. Chem. Soc. Perkin Trans. 1*, 1643 (1977).
2. D. P. ARNOLD, A. W. JOHNSON, AND M. MAHENDRAN, *J. Chem. Soc. Perkin Trans. 1*, 366 (1978).
3. D. P. ARNOLD, R. GAETE-HOLMES, A. W. JOHNSON, A. R. P. SMITH, AND G. A. WILLIAMS, *J. Chem. Soc. Perkin Trans. 1*, 1660 (1978).
4. R. L. N. HARRIS, A. W. JOHNSON, AND I. T. KAY, *J. Chem. Soc. C*, 22 (1966).
5. D. A. CLARKE, R. GRIGG, R. L. N. HARRIS, A. W. JOHNSON, I. T. KAY, AND K. W. SHELTON, *J. Chem. Soc. C*, 1648 (1967).
6. M. T. COX, A. H. JACKSON, AND G. W. KENNER, *J. Chem. Soc. C*, 1974 (1971).
7. R. B. WOODWARD, W. A. AYER, J. M. BEATON, F. BICKELHAUPT, R. BONNETT, P. BUCHSCHACHER, G. L. CLOSS, H. DUTLER, W. LEIMGRUBER, J. HANNAH, F. B. HAUCK, S. ITÔ, A. LANGEMANN, E. LE. GOFF, W. LWOWSKI, J. SAUER, Z. VALENTA, AND H. VOLZ, *J. Amer. Chem. Soc.* **82**, 3800 (1960).
8. R. GRIGG, A. W. JOHNSON, K. RICHARDSON, AND K. W. SHELTON, *J. Chem. Soc. C*, 655 (1969).
9. R. GRIGG, G. SHELTON, A. SWEENEY, AND A. W. JOHNSON, *J. Chem. Soc. Perkin Trans. 1*, 1789 (1972).
10. H. J. CALLOT, A. W. JOHNSON, AND A. SWEENEY, *J. Chem. Soc. Perkin Trans. 1*, 1424 (1972).
11. M. J. BUSHELL, B. EVANS, G. W. KENNER, AND K. M. SMITH, *Heterocycles* **7**, 67 (1977).
12. D. HARRIS AND A. W. JOHNSON, *Chem. Commun.*, 771 (1977).
13. A. W. JOHNSON AND I. T. KAY, *J. Chem. Soc.*, 1620 (1965).
14. A. R. BATTERSBY, G. L. HODGSON, M. IHARA, E. MCDONALD, AND J. SAUNDERS, *J. Chem. Soc. Perkin Trans. 1*, 2923 (1973).
15. A. H. JACKSON, G. W. KENNER, AND G. S. SACH, *J. Chem. Soc.*, 2045 (1967).
16. G. W. KENNER, *Ann. N.Y. Acad. Sci.* **206**, 138 (1973).
17. P. S. CLEZY AND A. H. JACKSON, "The Porphyrins," Vol. 1, p. 265 (D. Dolphin, Ed.). Academic Press, New York, 1978.
18. A. H. JACKSON, G. W. KENNER, AND K. M. SMITH, *J. Chem. Soc. C*, 502 (1971).
19. R. GRIGG, A. W. JOHNSON, AND G. SHELTON, *Leipzig's Annalen* **746**, 32 (1971).
20. P. S. CLEZY, C. L. LIM, AND J. S. SHANNON, *Aust. J. Chem.* **27**, 1103 (1974).
21. A. W. JOHNSON AND D. OLDFIELD, *J. Chem. Soc. C*, 794 (1966).
22. R. GRIGG, A. W. JOHNSON, AND G. SHELTON, *J. Chem. Soc. C*, 2287 (1971).
23. M. J. BROADHURST, R. GRIGG, G. SHELTON, AND A. W. JOHNSON, *J. Chem. Soc. Perkin Trans. 1*, 143 (1972).
24. H. OGOSHI, H. SUGIMOTO, T. NISHIGUCHI, T. WATANABE, Y. MATSUDA, AND Z. YOSHIDA, *Chem. Lett.*, 29 (1978).