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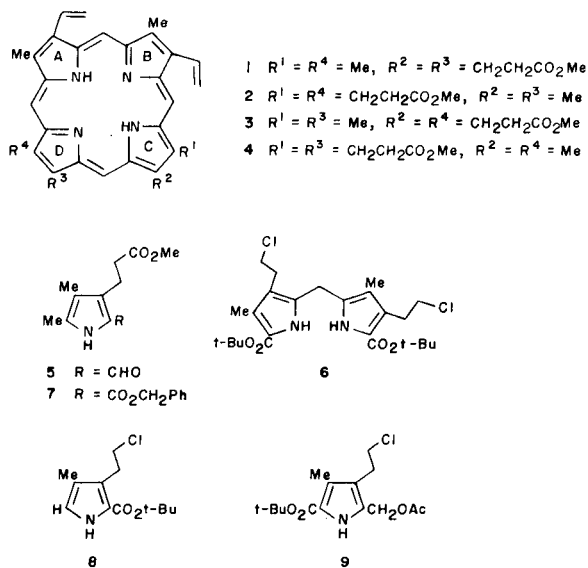
Received December 14, 1984

Total syntheses of hemins with permutations of the propionic side-chains in the C and D rings (compared with protoporphyrin-IX) are described. The products, **3**, **2** and **4**, are the dimethyl esters of protoporphyrins -I, -XI, and -XIV, respectively. They are of interest in connection with nmr studies designed to elucidate the structural features of the heme crevice in myoglobin and the effect of structural modifications of the C and D rings on the kinetics of heme-apoprotein reconstitutions, as well as studies of substrate specificity of the heme degradation enzyme, heme oxygenase.

*J. Heterocyclic Chem.*, **22**, 1041 (1985).

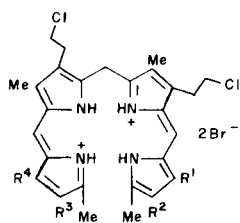
Recent nmr studies of heme proteins have revealed [1] that heterogeneity about the alpha/gamma meso axis can exist in the orientation of the heme in the apoprotein pocket. Moreover, nmr kinetic studies of the reconstitution of myoglobin [2] clearly show that the preferred (native) orientation is reached only after several hours at physiological pH. The rate of reorientation to give the natural conformation is heavily influenced by the nature of the substituents on the porphyrin but, up to the present time, structural variations mostly on rings A and B, deeply embedded within the protein pocket, have been studied. In an earlier paper [3] synthetic procedures for obtaining derivatives of protoporphyrin IX (**1**) bearing shortened (acetic) and lengthened (butyric) side chains in place of the natural propionates were outlined. In this paper we report syntheses of protoporphyrin-IX isomers **2-4** in which the positions of the propionic side chains on rings C and D are permuted. These compounds should be useful for further study of the structural requirements in the heme pocket of various heme proteins; they have already been used successfully for establishment of requirements for retention of substrate activity in the catabolic reaction catalyzed by heme oxygenase [4].

All three of the target protoporphyrin isomers were synthesized by way of copper(II) mediated cyclization [5] of unsymmetrically substituted 1',3'-a,c-biladiene salts [6], and 2-chloroethyl side chains were chosen as the protected vinyl substituents. Protoporphyrin-XI (**2**), which possesses symmetry in the lower (C,D) half of the molecule was synthesized by direct addition of two moles of the formylpyrrole **5** to the pyrromethane **68**. The formylpyrrole **5** was obtained from the corresponding benzyl pyrrole-5-carboxylate **7** by hydrogenation and Vilsmeier formylation (phosphoryl chloride/dimethylformamide). The pyrromethane **6** was obtained in 64% yield from the known 2-unsubstituted pyrrole **8** and the *t*-butyl 2-acetoxymethylpyrrole-5-carboxylate **9** by heating in acetic acid containing a catalytic amount of toluene *p*-sulfonic acid. Treatment of **6**



with two moles of formylpyrrole **5** in trifluoroacetic acid and hydrogen bromide in acetic acid gave an 80% yield of the a,c-biladiene dihydrobromide **10**, which, upon treatment with copper(II) chloride in boiling dimethylformamide, followed by removal of the chelated copper with sulfuric and trifluoroacetic acids, yielded 51% of the 2,4-di(2-chloroethyl)porphyrin **11**. Treatment with aqueous sodium hydroxide in pyridine then afforded a 70% yield of the required protoporphyrin-XI (**2**).

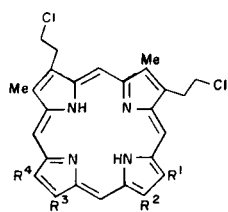
Owing to the unsymmetrical arrangement of the substituents in rings C and D for protoporphyrins -I and -XIV (**3** and **4**, respectively), it was necessary to approach these compounds through tripyrrenes. Thus, protoporphyrin-I was synthesized by the "clockwise" elongation of the pyrromethane **12** with the formylpyrrole **13** to give the tripyrene hydrobromide **14** [7]. After treatment of **14** with the formylpyrrole **5** in trifluoroacetic acid and hydrogen bromide in acetic acid for 6 hours, a 75% yield of the a,c-biladiene dihydrobromide **15** was obtained and this was cyclized, as previously, with copper(II) chloride in dimethyl



10  $R^1 = R^4 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$ ,  $R^2 = R^3 = \text{Me}$

15  $R^1 = R^3 = \text{Me}$ ,  $R^2 = R^4 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$

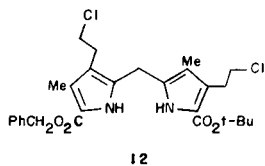
18  $R^1 = R^3 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$ ,  $R^2 = R^4 = \text{Me}$



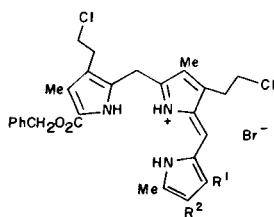
11  $R^1 = R^4 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$ ,  $R^2 = R^3 = \text{Me}$

16  $R^1 = R^3 = \text{Me}$ ,  $R^2 = R^4 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$

19  $R^1 = R^3 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$ ,  $R^2 = R^4 = \text{Me}$

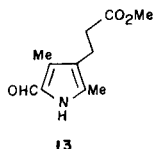


12



14  $R^1 = \text{Me}$ ,  $R^2 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$

17  $R^1 = \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$ ,  $R^2 = \text{Me}$



13

ylformamide to give a 58% yield of the porphyrin **16** after demetalation. Dehydrochlorination then gave a 72% yield of protoporphyrin-I dimethyl ester (**3**). Likewise, protoporphyrin-XIV dimethyl ester (**4**) was obtained from the porphyrin **12** by treatment first with formylpyrrole **5**, to give a 70% yield of the tripyrrene hydrobromide **17**, and then with the isomeric formylpyrrole **13** to give the a,c-biladiene dihydrobromide **18** in 72% yield. Cyclization in boiling dimethylformamide containing copper(II) chloride gave a 59% yield of the 2,4-di-(2-chloroethyl)porphyrin **19** after removal of copper. The vinyl groups were formed, as previously, using aqueous sodium hydroxide in pyridine, to give a 68% yield of protoporphyrin-XIV dimethyl ester (**4**).

In preparation for reconstitution into apomyoglobin, and for use as substrates for heme oxygenase [4], iron was inserted using the ferrous chloride method [8], and the esters were hydrolyzed using aqueous potassium hydroxide in methanol. Results of the heme oxygenase studies have already been reported [4], and nmr studies on the reconstituted myoglobins will be reported elsewhere.

## EXPERIMENTAL

Melting points were measured on a hot-stage apparatus, and are uncorrected. Silica gel 60 (Merck, 70-230 mesh) or alumina (Merck) were used for column chromatography, and preparative tlc was carried out on 20 × 20 cm glass plates coated with Merck GF 254 silica gel (1 mm thick). Analytical tlc was performed using Merck silica gel 60 F 254 precoated sheets (0.2 mm). Proton nmr spectra were measured in deuteriochloroform solution at 360 MHz using a Nicolet NT-360 spectrometer or at 90

MHz with a Varian EM-390 spectrometer with tetramethylsilane as internal standard. Electronic absorption spectra were measured, in dichloromethane solution, using a Hewlett-Packard 8450A spectrophotometer. Organic solutions were dried over anhydrous sodium sulfate. Elemental analyses were performed at the Berkeley Microchemical Analysis Laboratory, UC Berkeley.

### *t*-Butyl 4-Methoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate.

A well-stirred solution of *t*-butyl acetoacetate (Aldrich) (36 g) in acetic acid (48 ml) was treated with a solution of sodium nitrite (16.8 g) in water (30 ml) at a rate which kept the mixture temperature below 10° (ice-bath). After 3 hours further stirring at room temperature the solution was stored overnight in a refrigerator. This mixture was then added during 2 hours to a solution of methyl 3-acetyl-4-ketopentanoate [9] (35 g) in acetic acid (100 ml) kept at 60-65°, and simultaneously, an intimate mixture of zinc dust (35 g) and anhydrous sodium acetate (35 g) was added at a rate such that zinc was always in excess of *t*-butyl oximinoacetoacetate. The mixture was then kept at 60-65° for a further 2 hours with stirring, before being cooled and poured into iced water (2 l). After standing for a few hours, the product was filtered off, recrystallized from methanol/water and then dried to give 26.4 g (44%) of white crystals, mp 122-123°; nmr:  $\delta$ , ppm, 1.50 (s, 9H, *t*-Bu), 2.18 and 2.20 (each s, 3H, Me), 3.30 (s, 2H, CH<sub>2</sub>), 3.60 (s, 3H, OMe), 8.75 (s, 1H, NH).

Anal. Calcd. for C<sub>14</sub>H<sub>21</sub>NO<sub>4</sub>: C, 62.90; H, 7.92; N, 5.24. Found: C, 63.07; H, 7.89; N, 5.25.

### *t*-Butyl 4-(2-Hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate.

Borane-tetrahydrofuran complex (Aldrich, 1N in tetrahydrofuran) (100 ml) was added during 30 minutes to the foregoing pyrrole (15 g) in dry tetrahydrofuran (100 ml) at < 10° under nitrogen. The mixture was then stirred overnight at room temperature, when tlc analysis showed the reaction to be complete. Methanol (10 ml) was added and the solution was evaporated to give an oil which was passed through a short column of silica gel (elution with 30% ethyl acetate in cyclohexane). The elates were evaporated and the desired product was crystallized from dichloromethane/hexane, giving 10.7 g (80%) of white crystals, mp 128-129°; nmr:  $\delta$ , ppm, 1.50 (s, 9H, *t*-Bu), 2.20 and 2.25 (each s, 3H, Me), 2.62 and 3.62 (each t, 2H, CH<sub>2</sub>), 8.85 (br s, 1H, NH).

Anal. Calcd. for C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>: C, 65.25; H, 8.85; N, 5.85. Found: C, 64.99; H, 8.83; N, 5.68.

### *t*-Butyl 4-(2-Chloroethyl)-3,5-dimethylpyrrole-2-carboxylate.

The foregoing pyrrole (13.5 g) in dichloromethane (200 ml) and dry pyridine (5 ml) was treated with freshly distilled thionyl chloride (4.7 ml) dropwise, over 15 minutes. The mixture was then stirred at 40-45° for 2 hours with monitoring by analytical tlc. After cooling, the mixture was diluted with dichloromethane (100 ml), washed with 2N hydrochloric acid, then aqueous sodium bicarbonate, water, and finally dried. After evaporation, the residual oil was chromatographed on silica gel (elution with dichloromethane) and evaporation of the eluates gave a residue which was recrystallized from dichloromethane/hexane to give 10 g (69%) of white crystals, mp 106-107°; nmr:  $\delta$ , ppm, 1.58 (s, 9H, *t*-Bu), 2.20 and 2.22 (each s, 3H, Me), 2.60 and 3.50 (each t, 2H, CH<sub>2</sub>), 8.90 (br s, 1H, NH).

Anal. Calcd. for C<sub>13</sub>H<sub>20</sub>ClNO<sub>2</sub>: C, 60.58; H, 7.76; N, 5.43. Found: C, 60.59; H, 7.59; N, 5.26.

### 2-Formyl-3-(2-methoxycarbonyl)ethyl-4,5-dimethylpyrrole (5).

Benzyl 3-(2-methoxycarbonyl)ethyl-4,5-dimethylpyrrole-2-carboxylate (**7**) [10] (2 g) in tetrahydrofuran (50 ml) containing triethylamine (0.1 ml) and 10% palladized charcoal (200 mg) was hydrogenated at room temperature and atmospheric pressure until uptake of hydrogen ceased (5 hours). The solution was then filtered through Celite and the solvent was evaporated to give a residue which was treated with trifluoroacetic acid (5 ml) for 10 minutes at room temperature. Trimethyl orthoformate (3 ml) was then added and the mixture was stirred at 40° for 10 minutes. After cooling, the mixture was diluted with water (50 ml), and then extracted with dichloromethane (50 ml) which was subsequently washed with dilute aqueous ammonia, then water, and dried. Evaporation of the

solvent gave a residue which was chromatographed on a silica gel column (elution with 50% ethyl acetate/cyclohexane) and evaporation of the eluates gave the product which was recrystallized from aqueous methanol to give 790 mg (60%) of the formyl pyrrole, mp 93-94°; nmr:  $\delta$ , ppm, 1.90 and 2.20 (each s, 3H, Me), 2.50 and 3.80 (each t, 2H, CH<sub>2</sub>), 3.65 (s, 3H, OMe), 9.48 (br s, 1H, NH), 9.50 (s, 1H, CHO).

*Anal.* Calcd. for C<sub>11</sub>H<sub>13</sub>NO<sub>3</sub>: C, 63.14; H, 7.23; N, 6.69. Found: C, 62.89; H, 7.26; N, 6.59.

Di-*t*-butyl 4,4'-Di-(2-chloroethyl)-3,3'-dimethylpyromethane-2,2'-dicarboxylate (**6**).

*t*-Butyl 3-(2-chloroethyl)-4-methylpyrrole-2-carboxylate (**8**) [11] (590 mg) in glacial acetic acid (30 ml) was treated with *t*-butyl 5-acetoxymethyl-4-(2-chloroethyl)-3-methylpyrrole-2-carboxylate (**9**) (765 mg) [obtained [12] from the corresponding 5-methylpyrrole (see above) by treatment with lead tetra-acetate], and then toluene *p*-sulfonic acid hydrate (26 mg) was added. The mixture was stirred under nitrogen at 45° for 4 hours before being poured into water (50 ml), extracted with dichloromethane (50 ml) and then washed with aqueous sodium bicarbonate and water. After drying, the solvent was evaporated and the residual oil was chromatographed on a silica gel column (elution with dichloromethane). The eluates were evaporated and the product was recrystallized from dichloromethane/hexane to give light pink crystals, (780 mg, 64%) with mp 73-75°; nmr:  $\delta$ , ppm, 1.52 (s, 18H, *t*-Bu), 1.98 and 2.20 (each s, 3H, Me), 2.70-3.70 (m, 8H, CH<sub>2</sub>), 3.85 (s, 2H, bridging CH<sub>2</sub>), 8.55 (br s, 2H, NH).

*Anal.* Calcd. for C<sub>25</sub>H<sub>36</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>: C, 60.12; H, 7.21; N, 5.61. Found: C, 59.93; H, 6.99; N, 5.62.

Benzyl 3,5-Di-(2-chloroethyl)-6-(2-methoxycarbonylethyl)-1,1',2,4-tetramethyltripyrrene-a-6'-carboxylate Hydrobromide (**17**).

Benzyl 5'-*t*-butoxycarbonyl-3,4'-di-(2-chloroethyl)-3',4-dimethylpyromethane-5-carboxylate (**12**) (549 mg) was treated with trifluoroacetic acid (5 ml) for 5 minutes, followed by addition of formylpyrrole (**5**) (216 mg) in dry methanol (20 ml) under a nitrogen atmosphere. After stirring for 90 minutes, 31% hydrogen bromide in acetic acid (1.5 ml) was added at ice bath temperature. Diethyl ether was then added dropwise to precipitate the tripyrrene hydrobromide, which was filtered off (510 mg, 70%) and washed with dry ether, mp > 150° dec; nmr:  $\delta$ , ppm, 1.56, 2.02, 2.10 and 2.26 (each s, 3H, 3H, 6H, 3H, Me), 2.53-3.67 (t and m, 12H, CH<sub>2</sub>), 3.62 (s, 3H, OMe), 4.35 (s, 2H, bridging CH<sub>2</sub>), 5.31 (s, 2H, CH<sub>2</sub>Ph), 7.26 (s, 5H, Ph), 7.35 (s, 1H, bridging CH), 10.68 (s, 1H, NH), 13.21 (s, 2H, NH); vis:  $\lambda$  max 496 nm ( $\epsilon$  66,200).

*Anal.* Calcd. for C<sub>34</sub>H<sub>46</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>4</sub>: C, 57.87; H, 5.67; N, 5.95. Found: C, 57.83; H, 5.61; N, 5.85.

4,6-Di-(2-chloroethyl)-1,7-di-(2-methoxycarbonylethyl)-1',2,3,5,8,8'-hexamethyl-a,c-biladiene Dihydrobromide (**18**).

Benzyl 3,5-di-(2-chloroethyl)-6-(2-methoxycarbonylethyl)-1,1',2,4-tetramethyltripyrrene-a-6'-carboxylate hydrobromide (**17**) (324 mg) in 31% hydrogen bromide/acetic acid (2.5 ml) and trifluoroacetic acid (10 ml) was allowed to stand at room temperature for 6 hours before addition of 2-formyl-4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole (**13**) [13] (100 mg) in dry methanol (20 ml). The mixture was stirred for 30 minutes and then diethyl ether was added dropwise to precipitate the a,c-biladiene, which was collected by filtration. The mother liquors were retreated with 31% hydrogen bromide/acetic acid (1 ml) and a second crop was precipitated by addition of ether. The total yield was 280 mg (72%), mp > 300°; nmr:  $\delta$ , ppm, 2.00, 2.03, 2.30, 2.33, 2.70, 2.74 (each s, 3H, Me), 2.48-3.62 (t, and m, 16H, CH<sub>2</sub>), 3.63 and 3.67 (each s, 3H, OMe), 5.24 (s, 2H, bridging CH<sub>2</sub>), 7.14 and 7.36 (each s, 1H, bridging CH), 13.22, 13.33, 13.45, 13.51 (each s, 1H, NH); vis:  $\lambda$  max 450 nm ( $\epsilon$  73,500), 524 (135,300).

*Anal.* Calcd. for C<sub>37</sub>H<sub>48</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>: C, 52.66; H, 5.69; N, 6.64. Found: C, 52.97; H, 5.61; N, 6.56.

4,6-Di-(2-chloroethyl)-2,8-di-(2-methoxycarbonylethyl)-1,1',3,5,7,8'-hexamethyl-a,c-biladiene Dihydrobromide (**15**).

Benzyl 3,5-di-(2-chloroethyl)-1-(2-methoxycarbonylethyl)-1',2,4,6-tetra-

methyltripyrrene-a-6'-carboxylate (**14**) (453 mg) was treated as above with formylpyrrole (**5**) (140 mg) in dry methanol (20 ml) and gave the title compound (406 mg, 75%), mp > 300°; nmr:  $\delta$ , ppm, 2.01, 2.03, 2.70, 2.74 (each s, 3H, Me), 2.34 (s, 6H, Me), 2.47-3.60 (t and m, 16H, CH<sub>2</sub>), 3.64 and 3.68 (each s, 3H, OMe), 5.24 (s, 2H, bridging CH<sub>2</sub>), 7.14 and 7.31 (each s, 1H, bridging CH), 13.22, 13.37, 13.45, 13.54 (each s, 1H, NH); vis:  $\lambda$  max 450 nm ( $\epsilon$  71,500), 522 (138,800).

*Anal.* Calcd. for C<sub>37</sub>H<sub>48</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>: C, 52.66; H, 5.69; N, 6.64. Found: C, 52.47; H, 5.67; N, 6.46.

4,6-Di-(2-chloroethyl)-2,7-di-(2-methoxycarbonylethyl)-1,1',3,5,8,8'-hexamethyl-a,c-biladiene Dihydrobromide (**10**).

The di-*t*-butyl pyromethane-5,5'-dicarboxylate (**6**) (500 mg) was treated with trifluoroacetic acid (10 ml) at room temperature for 30 minutes before addition of the formylpyrrole (**5**) (425 mg) in dry methanol (20 ml) and 31% hydrogen bromide in acetic acid (7 ml). The mixture was stirred for 30 minutes, was cooled, and then diethyl ether was added dropwise until precipitation of the a,c-biladiene salt was complete. It was filtered off, washed with ether, and afforded 675 mg (80%) with mp > 300°; nmr:  $\delta$ , ppm, 1.55, 2.00, 2.33, 2.56 (each s, 3H, Me), 2.03 (s, 6H, Me), 2.51-3.20 (t, and m, 16H, CH<sub>2</sub>), 5.25 (s, 2H, bridging CH<sub>2</sub>), 7.36 and 7.38 (each s, 1H, bridging CH), 13.33, 13.35, 13.45, 13.53 (each s, 1H, NH); vis:  $\lambda$  max, 450 nm ( $\epsilon$  71,800), 522 (142,000).

*Anal.* Calcd. for C<sub>37</sub>H<sub>48</sub>Br<sub>2</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>: C, 52.66; H, 5.69; N, 6.64. Found: C, 52.94; H, 5.68; N, 6.43.

2,4-Di-(2-chloroethyl)-5,8-di-(2-methoxycarbonylethyl)-1,3,6,7-tetramethylporphyrin (**11**).

The foregoing a,c-biladiene salt **10** (190 mg) was treated with copper(II) chloride (720 mg) in dimethylformamide (10 ml) at 150° for 4 minutes. The mixture was poured into water (50 ml), extracted with dichloromethane (50 ml), and the organic phase was then washed with water (50 ml) and dried. Evaporation gave the copper(II) porphyrin which was immediately dissolved in 10% sulfuric acid in trifluoroacetic acid (20 ml) and stirred at room temperature for 30 minutes. This mixture was poured into water (100 ml), extracted with chloroform, which was washed with aqueous sodium bicarbonate, then water, and dried. Evaporation gave a red residue which was dissolved in 5% sulfuric acid in methanol (20 ml) and set aside overnight. The solution was then poured into aqueous sodium acetate, extracted with dichloromethane (100 ml), washed with aqueous sodium bicarbonate, then water, and dried. Evaporation gave a crude red product which was chromatographed on alumina (Brockmann Grade III, elution with dichloromethane), and the appropriate eluates were evaporated to give 88 mg (59%) after recrystallization from dichloromethane/hexane, mp 190-192°; nmr:  $\delta$ , ppm, -3.79 (s, 2H, NH), 3.27-3.33 and 4.32-4.48 (each m, 16H, CH<sub>2</sub>), 3.60, 3.62, 3.65, 3.66, 3.73 and 4.01 (each s, 3H, Me and OMe), 10.03, 10.05, 10.08 (each s, 1H, 1H, 2H, meso-H); vis:  $\lambda$  max 408 nm ( $\epsilon$  154,400), 498 (14,600), 532 (11,600), 568 (6800), and 622 (5100).

*Anal.* Calcd. for C<sub>36</sub>H<sub>40</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>·H<sub>2</sub>O: C, 63.43; H, 6.16; N, 8.22. Found: C, 63.81; H, 6.00; N, 8.11.

2,4-Di-(2-chloroethyl)-5,7-di-(2-methoxycarbonylethyl)-1,3,6,8-tetramethylporphyrin (**19**).

The a,c-biladiene dihydrobromide **18** (195 mg) was treated with copper(II) chloride (800 mg) in dimethylformamide as described above. After demetalation the product was crystallized from dichloromethane/hexane to give 78 mg (51%) with mp 140-142°; nmr:  $\delta$ , ppm, -3.75 (s, 2H, NH), 3.25-3.28 and 4.32-4.56 (each m, 16H, CH<sub>2</sub>), 3.60-3.69 (overlapping s, each 3H, Me and OMe), 10.04, 10.07, 10.09, 10.11 (each s, 1H, meso-H); vis:  $\lambda$  max, 408 nm ( $\epsilon$  156,000), 498 (15,000), 532 (11,900), 568 (7100) and 622 (5300).

*Anal.* Calcd. for C<sub>36</sub>H<sub>40</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>·H<sub>2</sub>O: C, 63.43; H, 6.16; N, 8.22. Found: C, 63.21; H, 5.83; N, 7.91.

2,4-Di-(2-chloroethyl)-6,8-di-(2-methoxycarbonylethyl)-1,3,5,7-tetramethylporphyrin (**16**).

The a,c-biladiene dihydrobromide **15** (174 mg) was likewise cyclized

using copper(II) chloride (720 mg) in dimethylformamide (15 ml) to give 80 mg (58%) of the porphyrin, mp 230-232° (lit [9] mp 233-235°); nmr:  $\delta$ , ppm, -3.73 (s, 2H, NH), 3.26-3.30 and 4.31-4.57 (each m, 16H, CH<sub>2</sub>), 3.60-3.69 (overlapping s, 18H, Me and OMe), 10.04, 10.06, 10.10, 10.12 (each s, 1H, meso-H); vis:  $\lambda$  max, 404 nm ( $\epsilon$  165,500), 498 (17,900), 532 (9200), 568 (7100) and 622 (5600).

Anal. Calcd. for C<sub>36</sub>H<sub>40</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>: C, 65.15; H, 6.03; N, 8.44. Found: C, 64.87; H, 6.04; N, 8.15.

5,8-Di-(2-methoxycarbonylethyl)-1,3,6,7-tetramethyl-2,4-divinylporphyrin (2), "Protoporphyrin-XI Dimethyl Ester".

The di-(2-chloroethyl)-porphyrin **11** (73 mg) in degassed pyridine (50 ml) was refluxed for 5 minutes before addition of degassed water (6 ml) and degassed 3% aqueous sodium hydroxide (15 ml). After addition of 25% aqueous acetic acid (15 ml) the mixture was then refluxed and stirred for a further 2.5 hours before evaporation of the solvents (using a toluene chaser). Water was then added and the precipitate was filtered off, dried under vacuum and then dissolved in 5% sulfuric acid in methanol (50 ml) and set aside overnight in the dark. The mixture was poured into aqueous sodium acetate, extracted with dichloromethane (50 ml), washed with aqueous sodium bicarbonate, then water, and dried. Evaporation gave a red residue which was chromatographed on alumina (Brockmann Grade III, elution with dichloromethane), and the appropriate eluates were evaporated to give 46 mg (70%) after recrystallization from dichloromethane/hexane, mp 212-214°, (lit [14] mp 213-214°); nmr:  $\delta$  ppm, -3.62 (s, 2H, NH), 3.26 and 4.37 (each t, 4H, CH<sub>2</sub>CH<sub>2</sub>CO), 3.61, 3.64, 3.65, 3.70, 3.72, 3.74 (each s, 3H, Me and OMe), 6.19-6.43 and 8.28-8.32 (each m, 4H, 2H, vinyl CH<sub>2</sub>=CH), 10.06, 10.11, 10.18, 10.27 (each s, 1H, meso-H); vis:  $\lambda$  max, 420 nm ( $\epsilon$  148,000), 504 (14,000), 540 (9000), 576 (6500) and 630 (4500).

Anal. Calcd. for C<sub>38</sub>H<sub>38</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.20; H, 6.48; N, 9.48. Found: C, 72.97; H, 6.48; N, 9.39.

6,8-Di-(2-methoxycarbonylethyl)-1,3,5,7-tetramethyl-2,4-divinylporphyrin (3), "Protoporphyrin-I Dimethyl Ester".

This porphyrin was similarly prepared from the di-(2-chloroethyl)porphyrin **16** (73 mg) and gave 47 mg (72%), mp 207-208°, (Lit [15] mp 206-208°); nmr:  $\delta$  ppm, -3.66 (s, 2H, NH), 3.24 and 4.40 (each t, 4H, CH<sub>2</sub>CH<sub>2</sub>CO), 3.62, 3.65, 3.68, 3.69, 3.72 and 3.73 (each s, 3H, Me and OMe), 6.17-6.42 and 8.25-8.35 (each m, 4H, 2H, vinyl CH<sub>2</sub>=CH), 10.03, 10.09, 10.18, 10.25 (each s, 1H, meso-H); vis:  $\lambda$  max, 414 nm ( $\epsilon$  150,000), 504 (14,500), 540 (10,700), 576 (6500), 630 (4800).

Anal. Calcd. for C<sub>38</sub>H<sub>38</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.20; H, 6.48; N, 9.48. Found: C, 72.99; H, 6.38; N, 9.35.

5,7-Di-(2-methoxycarbonylethyl)-1,3,6,8-tetramethyl-2,4-divinylporphyrin (4), "Protoporphyrin-XIV Dimethyl Ester".

This porphyrin was likewise prepared from the di-(2-chloroethyl)porphyrin **19** (73 mg) and gave 44 mg (68%), mp 189-190°, (Lit [14] mp

189-192°); nmr:  $\delta$  ppm, -3.66 (s, 2H, NH), 3.23 and 4.37 (each t, 4H, CH<sub>2</sub>CH<sub>2</sub>CO), 3.64 and 3.69 (each s, 6H, Me), 3.73 (s, 6H, OMe); 6.18-6.43 and 8.26-8.35 (each m, 4H, 2H, vinyl CH<sub>2</sub>=CH), 10.02, 10.09, 10.17, 10.25 (each s, 1H, meso-H); vis:  $\lambda$  max, 420 nm ( $\epsilon$  148,500), 506 (14,300), 540 (10,700), 576 (6600) and 630 (4900).

Anal. Calcd. for C<sub>38</sub>H<sub>38</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.20; H, 6.48; N, 9.48. Found: C, 72.93; H, 6.48; N, 9.25.

Acknowledgement.

This work was supported by a grant from the National Institutes of Health (HL 22252).

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