Synthesis of Bilanes of Biosynthetic Interest

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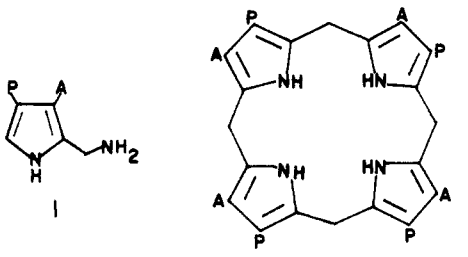
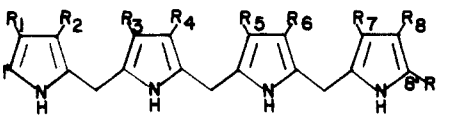
A series of bilanes of biosynthetic interest and formally derived from porphobilinogen were prepared by reduction of the corresponding *b*-bilenes. The latter were prepared by condensation of a [5'-[(*tert*-butyloxy)carbonyl]-5-formyldipyrryl]methane with dipyrrylmethane lactams and an α-unsubstituted [2-[(*tert*-butyloxy)-carbonyl]dipyrryl]methane. The *b*-bilene hydrobromides thus obtained were treated with 20% hydrogen bromide in acetic acid to cleave the (*tert*-butyloxy)carbonyl residues, and the resulting α-unsubstituted *b*-bilene hydrobromides were reduced with hydrogen over 10% Pd/C in the presence of (morpholinomethyl)polystyrene. The isomeric purity of the resulting bilanes was established by their conversion into isomerically pure uropophyrins, after saponification of the lactam rings.

The mechanism of the enzymatic polymerization of porphobilinogen (**1**) to form uroporphyrinogen III (**2**)—the precursor of all the natural porphyrins—is a source of continuous interest[1] (see Chart I). At the heart of the problem is the question whether the polymerization of porphobilinogen takes place in a "head-to-tail" sequence (each pyrrole Mannich base **1** reacts with the α-unsubstituted position of the next one), producing a bilane of type **3** which then cyclizes with rearrangement to give **2**,[2] or whether the pyrrole units join in a "head-to-head" fashion (by displacement of the 2-aminomethyl residue), thereby producing bilanes of type **4** or **5** which cyclize to **2** without any further rearrangement.[3] The synthesis of **3** made possible the study of its interactions with the enzymatic system that polymerizes **1** to **2**.[4-6] We report here that the approach which allowed us to perform the synthesis of **3**[4] was also useful to obtain the bilanes **4**–**7**.

These bilanes are expected to be unstable compounds and sensitive to acids, which will produce "scrambling" or intermolecular exchange of the pyrrole rings.[7,8] It was therefore proposed[9] that bilanes of this type should be obtained by reduction of the more stable *a,c*-biladienes or bilatrienes,[10] and this was achieved in a number of cases.[9,5,11] We found[4] that the readily obtained *b*-bilenes can serve as synthetic precursors of this type of bilane and that the *b*-bilenes are stable enough to allow the cleavage of the necessary protecting groups prior the their reduction to bilanes. The examples described in this report indicate that the obtention of bilanes from *b*-bilenes is a general method for the synthesis of the former which is far more useful than what the sporadic literature references on the reduction of *a*-bilenes[12] and *b*-bilenes[7,13-15] suggest.

Chart I





3, R=CH_2NH_2; R_1=R_3=R_5=R_7=P; R_2=R_4=R_6=R_8=A
4, R=CH_2NH_2; R_1=R_4=R_6=R_8=P; R_2=R_3=R_5=R_7=A
5, R=H ; R_1=R_4=R_6=R_8=P; R_2=R_3=R_5=R_7=A
6, R=CH_2NH_2; R_1=R_4=R_5=R_8=P; R_2=R_3=R_6=R_7=A
7, R=CH_2NH_2; R_1=R_4=R_6=R_7=P; R_2=R_3=R_5=R_8=A

P=$CH_2CH_2CO_2H$; A=CH_2CO_2H

The *b*-bilenes were prepared by condensation of a (2-formyldipyrryl)methane and α-unsubstituted dipyrrylmethanes. The former was prepared by an established sequence of reactions.[4] The dimethyl benzyl pyrrole triester **8** (Chart II) was oxidized to the acid **9**, and the latter was decarboxylated with iodine to **10**. The reduction of **10** with zinc in acetic acid[16] afforded the α-unsubstituted pyrrole **11**, which was reduced with hydrogen to the acid **12**, and the latter esterified again with *tert*-butyl alcohol in the presence of dicyclohexylcarbodiimide to the dimethyl *tert*-butyl ester **13**.

The condensation of the (2-acetoxymethyl)pyrrole **14**[4] with **13** allowed the obtention of the dipyrrylmethane **15** (62%), which was hydrogenated to the acid **16**. The latter could not be decarboxylated by heating in vacuo due to cleavage of the (*tert*-butyloxy)carbonyl group and was, therefore, decarboxylated by treatment with iodine and subsequent hydrogenolysis of the iododipyrrylmethane. The α-unsubstituted dipyrrylmethane **17** thus obtained was formylated to **18** as described elsewhere.[4]

The 2-formyldipyrrylmethane **18** was used for the synthesis of the *b*-bilenes. It was condensed with the di-

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(15) A. H. Jackson, G. W. Kenner, and K. M. Smith, *J. Chem. Soc. C*, 502 (1971).
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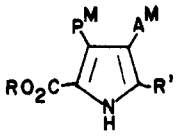
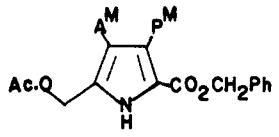
Chart II[a]



8, R=PhCH$_2$; R'=CH$_3$
9, R=PhCH$_2$; R'=CO$_2$H
10, R=PhCH$_2$; R'=I
11, R=PhCH$_2$; R'=H
12, R=R'=H
13, R=(CH$_3$)$_3$C; R'=H



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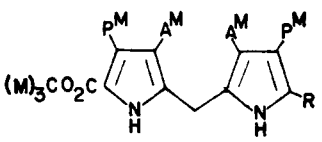
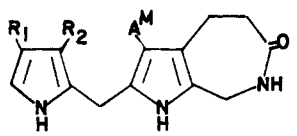
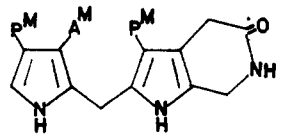


15, R=CO$_2$CH$_2$Ph
16, R=CO$_2$H
17, R=H
18, R=CHO



19, R$_1$=A^M; R$_2$=P^M
20, R$_1$=P^M; R$_2$=A^M



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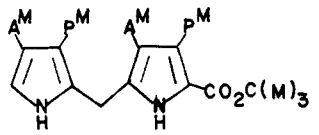

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[a] P^M = CH$_2$CH$_2$CO$_2$CH$_3$; A^M = CH$_2$CO$_2$CH$_3$; M = CH$_3$.

pyrrylmethane lactams **19–21** and with the dipyrrylmethane **22** to give the *b*-bilene hydrobromides **23–26** (Scheme I). Treatment of **23–25** with 20% hydrogen bromide in glacial acetic acid eliminated the (*tert*-butyloxy)carbonyl groups, and hydrogenation of the resulting hydrobromides over 10% Pd on charcoal in the presence of (morpholinomethyl)polystyrene gave the bilane lactams **27–29**. A similar treatment of **26** gave the bilane octamethyl ester **30**.[17]

The lactams **27–29** as well as **30** were saponified to the bilanes **4–7** by following well-established procedures,[4,18] and the resulting bilane solutions were directly used for the enzymatic studies.

Experimental Section

General Procedures. Melting points were determined on a Kofler melting point apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ on Perkin-Elmer R-12 and FT-80A spectrometers. Mass spectra were obtained with a Varian CH-7 spectrometer, and with a CVC TOF spectrometer.[19] The silica gel used in column chromatography was TLC Kieselgel (Fluka AG). TLC was performed on precoated silica gel F-254 plaques (Merck, 0.25-mm layer thickness). The substances were spotted by spraying the plaques with Ehrlich's reagent (2% *p*-(dimethylamino)benzaldehyde in 6 N HCl) or by treatment with bromine vapor which gave orange or red colors with dipyrrylmethanes and green or brown colors with bilanes.

Benzyl 2-Carboxy-3-[(methoxycarbonyl))methyl]-4-[β-(methoxycarbonyl)ethyl]-5-pyrrolecarboxylate (9). Dimethyl benzyl pyrrole triester 8[20] (10 g) dissolved in 100 mL of dry methylene chloride was treated with 7 mL of sulfuryl chloride at 20 °C during 1 h. The solution was evaporated to dryness in vacuo, and the oily residue was treated with a boiling solution of 20 g of sodium acetate in 200 mL of water during 5 min. Solid sodium bicarbonate was added to the cooled mixture, the latter was extracted with ether (2 × 100 mL), and the aqueous solution was adjusted to pH 4 with concentrated hydrochloric acid to give 8.6 g (80%) of **9**, mp 181–183 °C (from ethanol). Anal. Calcd for $C_{20}H_{21}NO_8$: C, 59.55; H, 5.21; N, 3.47. Found: C, 59.43; H, 5.18; N, 3.78.

Benzyl 2-Iodo-3[(methoxycarbonyl)methyl]-4-[β-(methoxycarbonyl)ethyl]-5-pyrrolecarboxylate (10). The acid **9** (8.6 g), dissolved in a solution of 16 g of sodium bicarbonate in 120 mL of water, was added to a solution of 16 g of potassium iodide and 8 g of iodine in 120 mL of water. The mixture was heated and stirred at 75 °C during 1 h, cooled, and filtered, and the residue was crystallized from methanol–water to give **10**: 8.1 g (72%); mp 102–103 °C. Anal. Calcd for $C_{19}H_{20}INO_6$: C, 47.01; H, 4.12; N, 2.88; I, 26.18. Found; C, 47.05; H, 4.19; N, 2.90; I, 26.20.

Benzyl 3-[β-(Methoxycarbonyl)ethyl]-4-[(methoxycarbonyl)methyl]-2-pyrrolecarboxylate (11). A solution of the 2-iodopyrrole **10** (8 g) in 80 mL of glacial acetic acid was heated at 140 °C, and 16 g of zinc powder was added in small portions during 3 h with continuous stirring. The mixture was then filtered while hot, and the filtrate was cooled to 20 °C, adjusted to pH 2 with concentrated hydrochloric acid, and poured over 500 mL of cold water. The precipitate was filtered, dried, and crystallized from benzene–cyclohexane: 4.8 g (80%); mp 61–63 °C; NMR δ 2.8 (m, 4 H, CH_2CH_2), 3.5 (s, 2 H, CH_2CO), 3.60, 3.65 (2 s, 3 H each, OCH_3), 5.3 (s, 2 H, CH_2Ph), 6.8 (br, 1 H, H-5), 7.4 (2 s, Ph). Anal. Calcd for $C_{19}H_{21}NO_6$: C, 63.51; H, 5.84; N, 3.89. Found: C, 63.41; H, 5.71, N, 3.80.

***tert*-Butyl 3-[β-(Methoxycarbonyl)ethyl)-4-[(methoxycarbonyl)methyl]-2-pyrrolecarboxylate (13).** A solution of 4 g of **11** in 200 mL of methanol was reduced with hydrogen over 700 mg of 10% Pd on charcoal at 50 psi of H_2 during 1 h. The solution was evaporated to dryness in vacuo after the catalyst was filtered. The crystalline acid **12** was redissolved in 20 mL of anhydrous *tert*-butyl alcohol and 18 mL of dry tetrahydrofuran,

(17) By treatment of the *b*-bilene **26** with trichloroacetic acid and triethyl orthoformate in dry methylene chloride it was cyclized to pure uroporphyrin III (**2**, as a porphyrin) in 20% yield. The synthesis of the latter from the *b*-bilene is thus comparable to its synthesis from two dipyrrylmethane halves.[20]

(18) A. Valasinas, E. S. Levy, and B. Frydman, *J. Org. Chem.*, **39**, 2872 (1974).

(19) The spectra on the CH-7 were performed by UMYMFOR (Buenos Aires) and those on the TOF by Dr. Randall Winans (Argonne National Laboratory) whose help we gratefully acknowledge.

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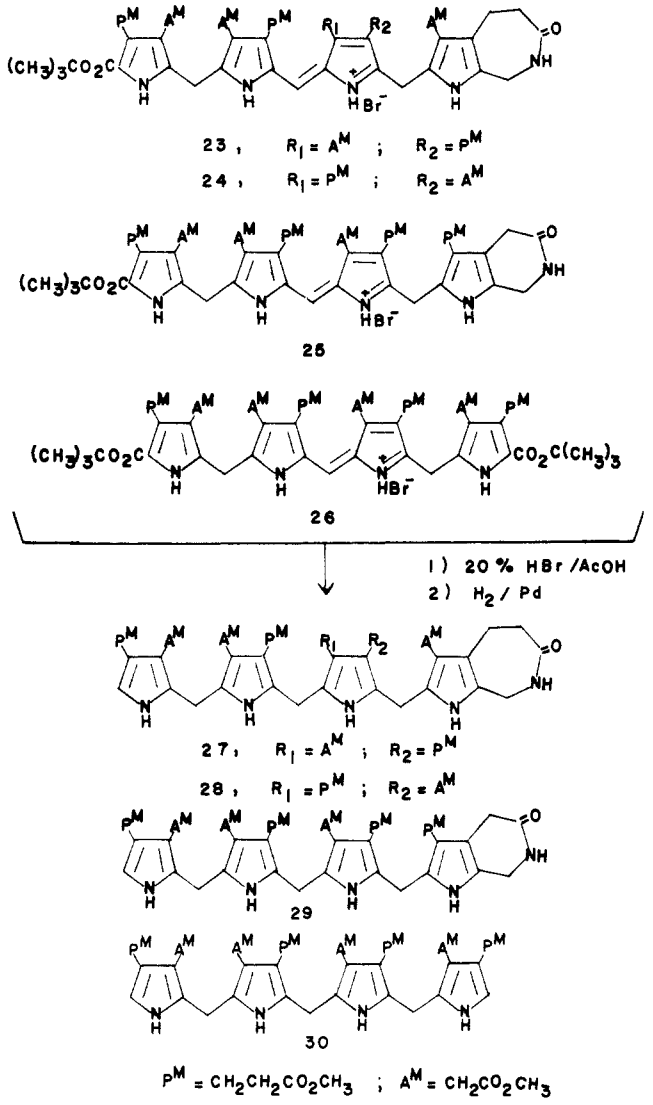
Scheme I



and 2 g of dicyclohexylcarbodiimide was added to the solution. The latter was then stirred at 20 °C during 17 h, the precipitate of dicyclohexylurea was filtered, the filtrate was evaporated to dryness, and the oily residue was purified by column chromatography on TLC silica gel with 2% methanol in benzene as a solvent: yield 1.7 g; mass spectrum, *m/e* (relative intensity) 325 (M^+, 30); NMR δ 1.5 (s, 9 H, $C(CH_3)_3$), 2.75 (m, 4 H, CH_2CH_2), 3.45 (s, 2 H, CH_2CO), 3.65, 3.70 (2 s, 3 H each, OCH_3), 6.8 (br 1 H, H_5).

***tert*-Butyl 3,3'-Bis[(methoxycarbonyl)methyl]-4,4'-bis-[β-(methoxycarbonyl)ethyl]-5-[(benzyloxy)carbonyl]dipyrrylmethane-5-carboxylate (15).** A solution of 1.2 g (3.7 mmol) of pyrrole **13**, 1.6 g (3.4 mmol) of the acetate **14**,[4] and 70 mg of *p*-toluenesulfonic acid in 70 mL of dry methylene chloride was heated at 41 °C during 5 h while being stirred with a stream of nitrogen. The solution was poured into 100 mL of water, the organic layer was separated, the aqueous layer was extracted with chloroform (3 × 50 mL), and the pooled organic solvents were washed with a saturated soldium bicarbonate solution and then with water, dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was crystallized from methanol–water: 1.6 g (62%); mp 105–106 °C; NMR δ 1.5 (s, 9 H, $C(CH_3)_3$), 2.8 (m, 8 H, CH_2CH_2), 3.6, 3.8 (both br, 16 H, OCH_3, CH_2CO), 3.95 (s, 2 H, pyrr–CH_2–pyrr), 5.25 (s, 2 H, CH_2Ph), 7.4 (br, 5 H, Ph); mass spectrum, *m/e* (relative intensity) 696 (M^+, 5). Anal. Calcd for $C_{36}H_{44}N_2O_{12}$: C, 62.06; H, 6.32; N, 4.03. Found: C, 62.00; H, 6.22; N, 3.96.

***tert*-Butyl 3,3'-Bis[(methoxycarbonyl)methyl]-4,4'-bis-[β-(methoxycarbonyl)ethyl]-5'-carboxydipyrrylmethane-5-carboxylate (16).** Dipyrrylmethane **15** (1.6 g) dissolved in 100 mL of ethanol was reduced with hydrogen at 50 psi during 2 h over 0.8 g of 10% Pd on charcoal. The solution was evaporated to dryness after filtration of the catalyst. The residue was purified by LC on a TLC silica gel column (4 × 30 cm) with 5% methanol in chloroform as a solvent. The acid **16** (800 mg, 57%) was crystallized from ethanol–water: mp 148–150 °C; NMR δ 1.5 (s, 9 H, $C(CH_3)_3$), 2.8 (m, 8 H, CH_2CH_2), 3.6 (br 4 H, CH_2CO), 3.65, 3.75 (2 s, 12 H, OCH_3), 3.9 (br 2 H, pyrr–CH_2–pyrr). Anal. Calcd for $C_{29}H_{38}N_2O_{12}$: C, 57.42; H, 6.27; N, 4.62. Found: C, 57.38; H, 6.20; N, 4.60.

tert-Butyl 3,3'-Bis[(methoxycarbonyl)methyl]-4,4'-bis-[β-(methoxycarbonyl)ethyl]dipyrrylmethane-5-carboxylate (17). A solution of carboxydipyrrylmethane **16** (800 mg) in 32 mL of 50% ethanol containing 800 mg of sodium bicarbonate was cooled to 5 °C, while 640 mg of iodine dissolved in 32 mL of ethanol was slowly added. The stirred mixture was then kept for 30 min at 20 °C, after which an equal volume of water was added, the excess iodine was destroyed with 3% sodium thiosulfate, and the solution was extracted with chloroform (2 × 50 mL). The extracts were dried (Na_2SO_4) and evaporated to dryness, and the residue was redissolved in 100 mL of ethanol containing 1 g of sodium acetate and reduced with hydrogen at 50 psi over 500 mg of 10% Pd/C during 2 h. The catalyst was then filtered, the solution was evaporated to dryness, the residue was dissolved in 20 mL of water and extracted with chloroform (2 × 30 mL), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purifed by LC on TLC silica gel with 2% methanol in benzene. The oily residue of **17** (420 mg, 57%) had the following NMR: δ 1.50 (s, 9 H, $C(CH_3)_3$), 2.70 (m, 8 H, CH_2CH_2), 3.75 (br, 16 H, OCH_3, CH_2CO), 3.90 (pyrr–CH_2–pyrr), 6.35 (m, 1 H, H_5); mass spectrum, *m/e* (relative intensity) 562 (M^+, 13), 505 (M^+ – isobutylene, 46).

***tert*-Butyl 3,3'-Bis[(methoxycarbonyl)methyl]-4,4'-bis-[β-(methoxycarbonyl)ethyl]-5'-formyldipyrrylmethane-5-carboxylate (18).** A solution of 420 mg of dipyrrylmethane **17** in 2.8 mL of dimethylformamide was kept at 5 °C, and 0.42 mL of benzoyl chloride was added in one portion. The mixture was kept under moisture-exclusion conditions at 20 °C during 1 h and was then diluted with 20 mL of ethyl ether. The solution was extracted with ether (3 × 5 mL), and the aqueous extracts were in turn reextracted with ether (2 × 5 mL). The aqueous solution was ajusted to pH 8 with sodium carbonate and kept at 20 °C during 4 h. After the solution was cooled at 5 °C, it was filtered and the product crystallized from ethanol: 265 mg (60%); mp 100–101 °C; NMR δ 1.5 (br, 9 H, $(CH_3)_3C$), 2.8 (m, 8 H, CH_2CH_2), 3.55, 3.65 (both br, 12 H, OCH_3), 3.75 (br, 4 H, CH_2CO), 3.8 (br, 2 H, pyrr–CH_2–pyrr), 9.7 (s, 1 H, CHO). Anal. Calcd for $C_{29}H_{38}N_2O_{11}$: C, 58.98; H, 6.44; N, 4.74. Found: C, 58.90; H, 6.40; N, 4.70.

1,4,6,8-Tris[β-(methoxycarbonyl)ethyl]-2,3,5,7-tetrakis-[(methoxycarbonyl)methyl]-8-(β-carboxyethyl)-8'-(aminomethyl)bilane Lactam (27). A mixture of 84 mg (0.14 mmol) of aldehyde **18** and 60 mg (0.13 mmol) of dipyrrylmethane lactam **19**[18] were dissolved in 4 mL of anhydrous methanol, and 0.3 mL of 48% HBr was added. The solution was kept at 20 °C during 15 min and was then poured over a column (1.5 × 20 cm) of deactivated alumina (prepared by suspending Merck grade I alumina in methanol, filtering, and drying in air) prewashed with chloroform. The bilene (yellow band) was eluted with the same solvent, the latter was evaporated to dryness at room temperature, the residue [NMR δ 1.5 (br, 9 H, $(CH_3)_3C$), 7.8 (br, 1 H, CH=)] was dissolved in 3 mL of 20% HBr in glacial acetic acid, and the solution was kept at 20 °C during 90 min and was finally freeze-dried. The residue was dissolved in a mixture of 40 mL of chloroform and 20 mL of methanol and was reduced with hydrogen at 40 psi during 1 h over 150 mg of 10% Pd on charcoal and 400 mg of (morpholinomethyl)polystyrene (Fluka AG). The catalyst and resin were then filtered, the solution was evaporated to dryness, and the residue was purifed by filtration through a TLC silica gel column (2 × 30 cm) packed and eluted with 4% methanol in chloroform. The fractions containing the bilane (bromine vapor was used for visualization) were combined and evaporated to dryness: 18 mg (12%); mass spectrum,[21] *m/e*

(21) See ref 4 for the fragmentation pattern of this type of bilane.

(relative intensity) 933, (M^+, 16), 475 (100), 471 (40), 462 (60), 459 (compound **19**, 53), 222 (50); NMR δ 2.79 (br, 12 H, $CH_2CH_2CO_2$), 3.09 (br, 4 H, CH_2CH_2CONH), 3.46, 3.52, 3.55, 3.66 (4 s, 29 H, CH_2, OCH_3), 3.70 (m, 6 H, pyrr–CH_2–pyrr), 4.17 (m, 2 H, CH_2NH), 6.21 (br, 1 H, NHCO), 6.37 (br, 1 H, H-1'), 8.65, 8.89, 8.91 (2 s, 3 H, NH). The bilane **27** was pure when examined by TLC (4% methanol in chloroform). When it was saponified to give **4** and the latter was heated at pH 7.4 and 37 °C as described elsewhere,[4] it gave 20% yield of **2** (98% pure), indicating that no rearrangement of the bilane chain took place during the condensation.

1,4,5-Tris[β-(methoxycarbonyl)ethyl]-2,3,6,7-tetrakis-[(methylcarbonyl)methyl]-8-(β-carboxyethyl)-8'-(aminomethyl)bilane Lactam (28). It was prepared following the procedure described for **27**. The condensation of 84 mg of the aldehyde **18** and 60 mg of the dipyrrylmethane lactam **20**[18] gave 10 mg (15%) of the bilane lactam **28**: mass spectrum (TOF), *m/e* 933 (M^+); mass spectrum, *m/e* (relative intensity) 933 (M^+, 25), 475 (100), 471 (30), 459 (compound **20**, 63), 222 (60); NMR δ 2.79 (br, 12 H, CH_2CH_2CO), 3.05 (br, 4 H, CH_2CH_2CONH), 3.43, 3.52, 3.63 (br s, 35 H, CH_2CO_2, OCH_3), 3.69 (m, 6 H, pyrr–CH_2–pyrr), 4.18 (m, 2 H, CH_2NH), 6.13 (br, 1 H, NHCO), 6.36 (br, 1 H, H-1'). The bilane **28** was pure when examined by TLC (4% methanol in chloroform). When it was saponified to give **6** and the latter was heated at pH 7.4 and 37 °C as described elsewhere,[4] it gave a 15–18% yield of uroporphyrinogen II (98% pure), indicating that no rearrangement of bilane chain took place during the condensation.

1,4,6,7-Tetrakis[β-(methoxycarbonyl)ethyl]-2,3,5-tris-[(methoxycarbonyl)methyl]-8-(carboxymethyl)-8'-(aminomethyl)bilane Lactam (29). This compound was obtained by following the procedure described for **27**. The condensation of 100 mg (0.17 nmol) of aldehyde **18** and 72 mg (0.16 mmol) of dipyrrylmethane lactam **21**[22] afforded the *b*-bilene **25** [mass spectrum (TOF), *m/e* 1032 (M^+)], which was reduced to the bilane **29**: 28 mg (17%); mass spectrum (TOF), *m/e* 933 (M^+); mass spectrum, *m/e* (relative intensity) 933 (M^+, 100), 475 (15), 471 (10), 222 (51); NMR δ 2.50 (m, 8, P-α-CH_2), 2.78 (m, 8 H, P-β-CH_2), 3.55, 3.60 (2 s, 6 H, CH_2CO_2), 3.63, 3.65 (both br, 21 H, OCH_3), 3.70 (br, 2 H, CH_2CONH), 3.75 (br, 6 H, pyrr–CH_2–pyrr), 4.35 (m, 2 H, CH_2NH), 6.10 (m, 1 H, NHCO), 6.40 (m, 1 H, H-1'), 8.71, 8.89, 9.01 (br, br, m, and br, 4 H, NH).

Di-*tert*-butyl 1,4,6,8-tetrakis[β-(methoxycarbonyl)-ethyl]-2,3,5,7-tetrakis[(methoxycarbonyl)ethyl]-*b*-bilene-1',8'-dicarboxylate Hydrobromide (26). It was obtained by the condensation of 80 mg (0.14 nmol) of aldehyde **18** and 75 mg (0.13 nmol) of dipyrrylmethane **22**.[4] The residue obtained after elution from the alumina column was dissolved in 1 mL of glacial acetic acid, 0.3 mL of 40% HBr in acetic acid were added, and the mixture was immediately freeze-dried. The hydrobromide **26** thus obtained was crystallized by treatment with petroleum ether: 125 mg (76%); mp 95–93 °C; mass spectrum (TOF), *m/e* 1135 (M^+ – HBr); NMR δ 1.52 (s, 18 H, $C(CH_3)_3$), 2.74 (br, 16 H, $CH_2CH_2CO_2$), 3.55, 3.64 (2 s, 8 H, CH_2CO_2), 3.65, 3.69 (both br, 24 H, OCH_3), 4.45 (br, 4 H, pyrr–CH_2–pyrr), 7.60 (br, 1 H, CH=).

1,4,6,8-Tetrakis[β-(methoxycarbonyl)ethyl]-2,3,5,7-tetrakis[(methoxycarbonyl)methyl]bilane (30). This compound was obtained from the hydrobromide **26** (100 mg) by treatment with 20% HBr in acetic acid followed by hydrogenation, according to the procedure described in the preparation of **27**. The crystalline bilane **30** (23 mg, 28%) had the following: mass spectrum, *m/e* (relative intensity) 936 (M^+, 11), 711 (5), 462 (100); NMR δ 2.35 (br, 8 H, P-α-CH_2), 2.83 (br, 8 H, P-β-CH_2), 3.37, 3.46, 3.50 (all br, 8 H, CH_2CO_2), 3.63, 3.65, 3.70 (all s, 24 H, OCH_3), 3.75 (br, 6 H, pyrr–CH_2–pyrr), 6.36 (br, 2 H, H-1, H-8'), 8.78, 9.06 (both br, 4 H, NH). The bilane **30** was pure when examined by TLC (4% methanol in chloroform). It has also been prepared by reduction of a bilitriene.[9]

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