mulative behavior is consistent with the isotopes acting independently. In terms of hyperconjugation, two interactions should occur simultaneously. If the more stabilizing (H rather than D) interaction were to dominate, then in the case of the trideuterio substrate we would have expected to see an isotope effect much less than half that for the hexadeuterio species. Thus, for this system the "rule of the geometric mean"[1,27] is applicable and the isotope effect can be interpreted on a "per deuterium" basis.

Conclusion

We can expect that other heterolytic decarboxylation reactions will show positive β secondary kinetic isotope effects and that reactivity will be a major determinant of the magnitude of the effect. The effect should also be additive for multiply deuterated species. Thus, for complex mechanisms in which decarboxylation is rate-determining, the isotope effect can be used to elucidate the relative magnitudes of this step and those preceding it.[26] However, knowledge of details and empirical correlations of the isotope effect as a function of structure and reactivity will require that results be obtained for many more compounds.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for support through an operating grant (R.K.) and a fellowship (M.B). We thank Professor K. T. Leffek for helpful comments.

Registry No. 1 *t*-Bu ester, 54441-66-6; 2 *t*-Bu ester, 104015-38-5; 4, 38744-73-9; 4 *t*-Bu ester, 53935-56-1; 5 *t*-Bu ester, 104034-35-7; 6 *t*-Bu ester, 104015-37-4.

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Synthesis of a C-15-Substituted Porphyrin from a b-Bilene Precursor

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The synthesis of a porphyrin substituted at C-13 with an ethoxycarbonyl residue and at C-15 with a β-(methoxycarbonyl)methyl side chain was attempted using a b-meso-substituted b-bilene-1′,8′-di-*tert*-butyl ester precursor. The latter was obtained by condensation of *tert*-butyl 3,3′-dimethyl-4-(β-acetoxyethyl)-4′-[β-(ethoxycarbonyl)ethyl]dipyrrylmethane-5-carboxylate with *tert*-butyl 3′,4-dimethyl-3-ethyl-4′-(ethoxycarbonyl)-5′-[α-oxo-β-(ethoxycarbonyl)ethyl]dipyrrylmethane-5-carboxylate. Although the b-bilene was obtained in 60% yield, its cyclization to the porphyrin using ethyl orthoformate in acid medium gave poor yields (4%), very likely due to steric interactions between the meso substituent and the ethoxycarbonyl residue.

Of the many porphyrin total syntheses which have been proposed in the recent literature only a few are useful and versatile enough to be considered as general procedures for porphyrin synthesis.[1] The use of b-bilene-1′,8′-dicarboxylates appeared to be one of them since b-bilenes could be obtained in good yields by the condensation of two pyrrylmethane halves,[2] and b-bilene-1′,8′-di-*tert*-butyl esters (see Scheme I) could be cyclized to porphyrins by treatment with trifluoroacetic acid (cleavage of the *tert*-butyl esters) followed by cyclization using trichloroacetic acid and trimethyl orthoformate as the one-carbon linking unit.[3] A b-bilene was a short-lived intermediate in the total synthesis of chlorin-e_6,[4] and a b-bilene which carried a fused cyclopenteno ring from C-13 to C-15 was also the synthetic precursor of deoxophylloerythroetioporphyrin.[5] In the latter case, however, although the synthesis of the meso-substituted b-bilene was achieved in good yields, its cyclization to the porphyrin took place in only 6% yield. This low yield was attributed to the steric factors introduced by the isocyclic ring. We therefore decided to explore the synthesis of the C-15-substituted porphyrin **4** from the b-meso-substituted b-bilene **3** (Scheme I). Porphyrin **4** (2-β-hydroxyethyl)chloroporphyrin-e_6 triester) could be regarded as a useful precursor of 2-vinylpheoporphyrin-a_5 dimethyyl ester[1a] since the cyclopentanone ring could be easily formed by a Dieckmann-type condensation, while the vinylization of the β-hydroxyethyl residue is a well-known procedure.[1g] There should be no strain in the cyclization of **3** to **4** which could be attributed to the isocyclic ring, thus eliminating what appeared to be the main hindrance in the synthesis of porphyrins which carry a cyclopentanone ring bridging the C-13 and C-15 positions.

The synthesis of the b-meso-substituted b-bilene **3** was approached by attempting the condensation of two dipyrrylmethane halves, one of which carried a β-oxopropionate residue at the C-5′ position (Scheme I). The synthesis of each dipyrrylmethane moiety required the use of extensive pyrrole chemistry which will be discussed below. The prior synthesis of dipyrrylmethane **9** was planned to obtain the dipyrrylmethane **1**, since the latter

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(2) (a) Valasinas, A.; Díaz, L.; Frydman, B.; Friedmann, H. C. *J. Org. Chem.* **1985**, *50*, 2398. (b) Díaz, L.; Valasinas, A.; Frydman, B. *Ibid.* **1981**, *46*, 864. (c) Díaz, L.; Frydman, R. B.; Valasinas, A.; Frydman, B. *Ibid.* **1979**, *101*, 2710. See also: ref 1k and references therein.

(3) Jackson, A. H.; Kenner, G. W.; Sach, G. S. *J. Chem. Soc. C.* **1967**, 2045. Jackson, A. H.; Kenner, G. W.; Smith, K. M. *Ibid.* **1971**, 502. Cox, M. T.; Jackson, A. H.; Kenner, G. W. *Ibid.* **1971**, 1974. See also ref 2b.

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(5) Flaugh, M. E., Rapoport, H., *J. Am. Chem. Soc.* **1968**, *90*, 6877.

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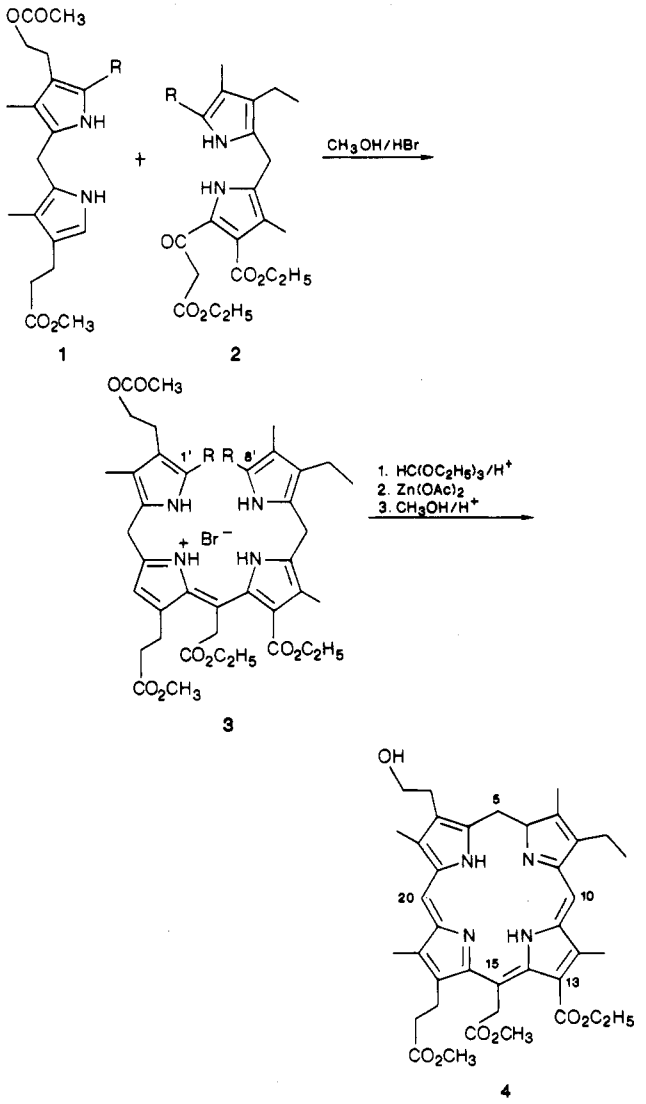
Scheme I[a]



[a] R = $CO_2C(CH_3)_3$.

could be transformed into **1** by hydrogenolysis to **10** followed by a decarboxylation step (Scheme II). Dipyrrylmethane **9** could be obtained either by condensation of pyrroles **5** and **6** or by condensation of pyrroles **7** and **8**. The experimental results indicated that both pathways were not equivalent and that the best synthesis of **9** was achieved by condensation of **7** and **8**. The synthesis of the 2-(acetoxymethyl)pyrrole **5** was known,[6] and hence a synthesis of **6** was designed. Starting with the known pyrrole **11** (Chart I) hydrogenolysis led to the carboxypyrrole **12**, which was decarboxylated with iodine to give **13**.[7] The latter was reduced with hydrogen over 10% palladium on charcoal to give **14**. The α-unsubstituted pyrrole **14** was reduced with diborane to the β-(hydroxyethyl)pyrrole **15**, which was transacetylated to give **6**. Condensation of **5** and **6** in methylene chloride in the presence of *p*-toluensulfonic acid gave a mixture of dipyrrylmethanes, one of which was **9** and the other the dimer resulting from the self-condensation of **5**. Similar results had been obtained when the condensation of **5** was attempted with other α-unsubstituted pyrroles.[6]

The synthesis of **9** by condensation of **7** and **8** was then

Scheme II

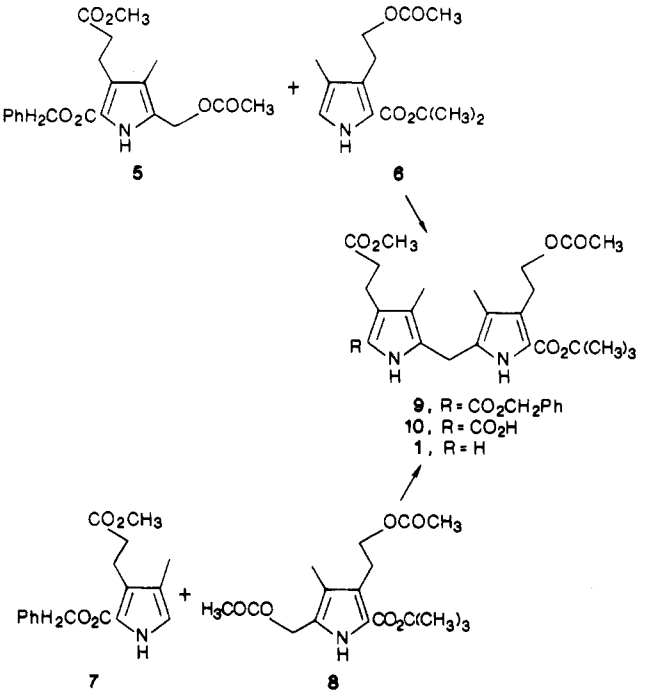
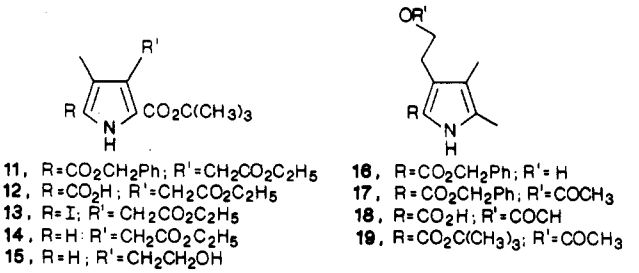


Chart I



explored. Since pyrrole **7** was known,[8] a synthesis of **8** starting with the known pyrrole **16**[8] had to be developed. Pyrrole **16** was acetylated to give **17**, the benzyl ester of the latter was cleaved by hydrogenolysis, the resulting acid **18** was esterified to the *tert*-butyl ester **19** with *tert*-butyl alcohol and dicyclohexylcarbodiimide, and **19** was finally transformed into the 2-(acetoxymethyl)pyrrole **8** with lead tetraacetate. The condensation of **7** and **8** in acetic acid in the presence of *p*-toluensulfonic acid gave **9** in 60% yield. Hydrogenolysis of the benzyl ester of **9**, followed by decarboxylation of **10** in vacuo at 220 °C, gave the dipyrrylmethane **1** in 60% yield.

The synthesis of **2** was first planned on the assumption that the β-oxopropionate chain could be built directly from a α-carboxydipyrrylmethane such as **25** (Scheme III). The latter was easily obtained by condensation of **20**[9] with the α-unsubstituted pyrrole **21**[1j] to give **24**, which was hydrolyzed to **25** with trifluoroacetic acid. All attempts to decarboxylate **25** (heating in vacuo, treatment with iodine, acid treatments) failed to give the α-unsubstituted dipyrrylmethane. Attempts to transform **25** into its acid chloride were also unsuccesful. It was therefore decided to obtain **2** by condensation of the 2-(acetoxymethyl)-pyrrole **22** with pyrrole **23** (Scheme III).

The synthesis of **22** was easily achieved starting with pyrrole **26**, followed by reduction with diborane to **27**, and treatment of the latter with lead tetraacetate (Chart II).

(6) Díaz, L.; Buldain, G.; Frydman, B. *J. Org. Chem.* **1979**, *44*, 973.
(7) Cox, M. T.; Jackson, A. H.; Kenner, G. W.; McCombie, S. W.; Smith, K. M. *J. Chem. Soc. C* **1974**, 516.
(8) Buldain, G.; Hurst, J.; Frydman, R. B.; Frydman, B. *J. Org. Chem.* **1977**, *42*, 2953.

Scheme III

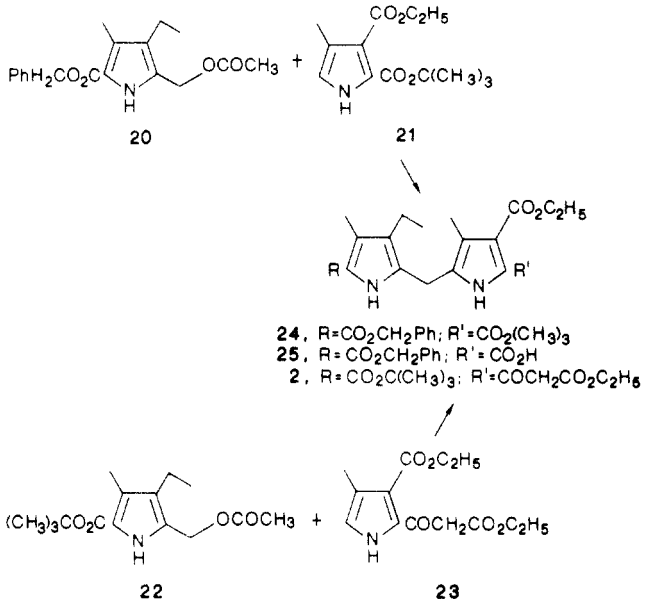
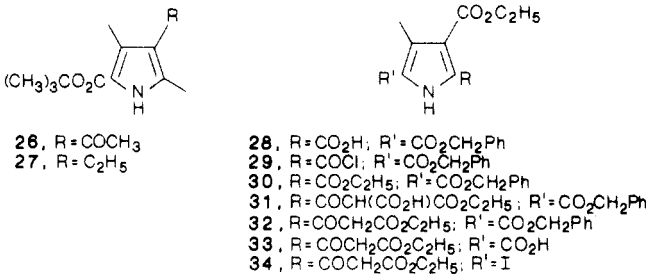


Chart II

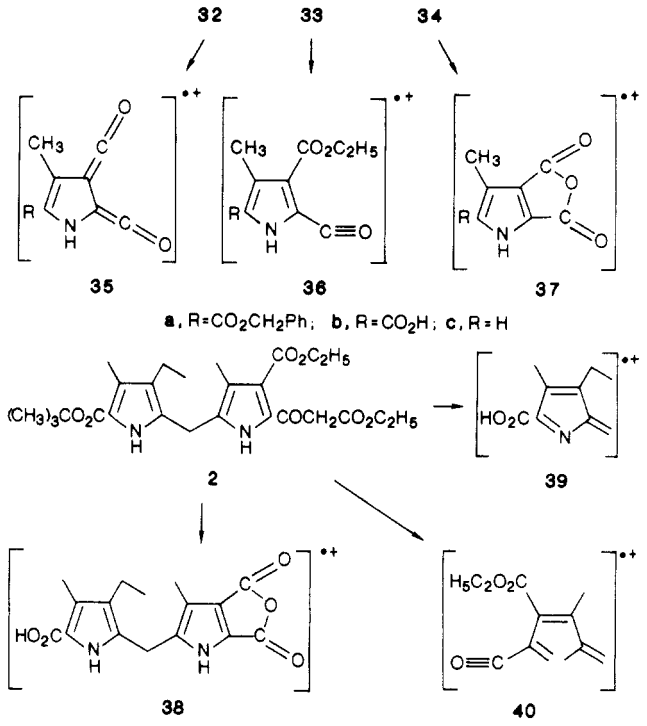


The synthesis of **23** started with the known[1j] pyrrole acid **28** which was transformed into its chloride **29** in very good yield. The attempted condensation of **29** with the magnesium salt of *tert*-butyl ethyl malonate to build up the β-oxopropionate chain ended in failure since the diethyl ester **30** was always the main reaction product. The condensation was successfully carried out by using the magnesium salt of the acid ethyl malonate ester[10] to give first the acid intermediate **31** which was easily decarboxylated with trifluoracetic acid to **32**. The NMR spectra of the β-keto ester **32** showed that the latter was always in an equilibrium with its enol form, and both forms could be distinguished by TLC analysis. Its mass spectrum gave the typical fragmentation pattern[1j] of the α,β-dicarbonylpyrroles (Chart III). Treatment of **32** with hydrogen over 10% Pd on charcoal gave the acid **33**, which was decarboxylated with iodine to give **34** and the latter was reduced with hydrogen to give **23**.

The condensation of **22** and **23** gave the dipyrrylmethane **2** in 70% yield. Condensation of the latter with **1** in the presence of methanol–hydrobromic acid gave the b-bilene **3** in 60% yield. However, when **3** was cyclized with ethyl orthoformate in the presence of zinc acetate to the porphyrin **4**, the latter was obtained in very low yield (4%). Therefore, the synthesis of a C-15-substituted porphyrin when an ethoxycarbonyl substituent is sited at C-13 using meso-substituted 1′,8′-bis[(*tert*-butyloxy)carbonyl]-b-bilene is not practical, very likely due to the steric interactions

(9) Cavaleiro, J. A. S.; Rocha Goncalvez, A. M. D'A.; Kenner, G. W.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2471.
(10) Bram, G.; Vilkas, M. *Bull. Soc. Chim. Fr.* **1964**, 945.

Chart III



between the meso substituent and the ethoxycarbonyl residue, which are apparently present even in the absence of an isocyclic ring. The synthetic strategy which we now favor for the synthesis of the asymmetric porphyrin **4** is based on the use of the copper(II)-catalyzed cyclization of the 1′,8′-dimethyl-a,c-biladienes.[1h]

Experimental Section

General Procedures. Melting points were determined on a Kofler melting point apparatus and are uncorrected, and NMR spectra were recorded in $CDCl_3$ on a FT-80A spectrometer. Mass spectra were obtained with a Varian CH-7 spectrometer. The silica gel used in column chromatography was TLC Kieselgel (Merck). TLC was performed on precoated silica gel F-254 plates (Merck, 0.25-mm layer thickness). The substances were spotted by spraying the plates 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 the dipyrrylmethanes.

***tert*-Butyl 3-((Ethoxycarbonyl)methyl)-4-methyl-2-pyrrolecarboxylate (14).** Pyrrole **13**[7] (8 g) dissolved in 200 mL of ethanol containing 8 g of anhydrous sodium acetate was reduced with hydrogen at 40 psi over 1.5 g of 10% Pd on charcoal during 2 h. The catalyst was filtered off, the solution was evaporated to dryness, the residue was dissolved in chloroform, and the latter was washed twice with water, dried (Na_2SO_4), and evaporated to dryness in vacuo. The pyrrole **14** was crystallized from benzene–hexane; 2.4 g (93%): mp 68–70 °C; ^{13}C NMR δ 170.99 (CH_2CO_2-), 161.29 (CO_2-), 125.10, 121.03, 120.51, 120.26 (pyrrole-C), 59.10 (CH_2CH_3), 31.00 (CH_2CO_2-), 28.50 ($C(CH_3)_3$), 14.00 (CH_2CH_3), 9.87 (4-CH_3). Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.92; H, 7.86; N, 5.24. Found: C, 62.86; H, 7.28; N, 5.20.

***tert*-Butyl 3-(β-Acetoxyethyl)-4-methyl-2-pyrrolecarboxylate (6).** A stream of nitrogen carrying diborane liberated from a mixture of 40 mL of borontrifluoride etherate and 12 g of sodium borohydride in 40 mL of diglyme was slowly bubbled through a solution of 2 g of **14** in dry tetrahydrofuran during 4 h. Methanol was then added to the mixture, which was evaporated to dryness, the residue was dissolved in chloroform, and the latter was washed with dilute hydrochloric acid and then with water, dried (Na_2SO_4), and evaporated to dryness in vacuo. The pyrrole **15** (1.5 g, 77%) was obtained as an oil (^1H NMR δ 9.35 (b, 1, NH), 6.70 (b, 1, H_5), 3.72 (t, 2, CH_2CH_2OH), 2.68 (t, 2, CH_2CH_2OH), 2.32 (s, 1, OH), 2.25 (s, 3, CH_3), 1.58 (s, 9, $C(CH_3)_3$)); it was dissolved in 45 mL of dry pyridine, 9 mL of acetic anhydride were

added, and the mixture was kept at 5 °C during 3 h. It was then poured over ice–water, and the precipitate was filtered and recrystallized from ethanol: 1.1 g (65%) of **6** were obtained; mp 67–69 °C; ^{13}C NMR δ 171.58 (-OO*C*CH$_3$), 161.67 (*C*O$_2$R), 125.62, 121.52, 121.14, 120.60 (pyrrole-C), 80.00 (*C*(CH$_3$)$_3$), 65.25 (CH$_2$-*C*H$_2$O-), 29.02 (C(*C*H$_3$)$_3$), 25.21 (OOC*C*H$_3$), 21.51 (*C*H$_2$CH$_2$OR), 10.38 (CH$_3$). Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.92; H, 7.86; N, 5.24. Found: C, 62.90; H, 7.38; N, 5.20.

Benzyl 3-(β-Acetoxyethyl)-4,5-dimethyl-2-pyrrolecarboxylate (17). Acetic anhydride (5 mL) was added at 5 °C to a solution of 3 g of pyrrole **16**[8] in 25 mL of dry pyridine, and the mixture was kept at 20 °C during 3 h. It was then poured over ice water, and the precipitate was filtered, dried, and recrystallized from benzene–cyclohexane; 1.44 g (46%): mp 74–75 °C; ^{13}C NMR δ 169.25 (O*C*OCH$_3$), 159.28 (*C*O$_2$-), 134.59; 126.73, 126.32 (*C*$_6$H$_5$), 128.75, 125.56, 115.73, 114.72 (pyrrole-C), 63.85 (*C*H$_2$Ph), 62.82 (*C*H$_2$CH$_2$O-), 23.08 (*C*H$_2$CH$_2$O-), 19.20 (OCO*C*H$_3$), 9.57 (CH$_3$-4), 6.89 (CH$_3$-5). Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.57; H, 6.66; N, 4.44. Found: C, 68.50; H, 6.58; N, 4.40.

***tert*-Butyl 3-(β-Acetoxyethyl)-4,5-dimethyl-2-pyrrolecarboxylate (19).** A solution of 1.4 g of **17** in 200 mL of ethanol was reduced with hydrogen at 50 psi over 0.7 g of 10% Pd on charcoal during 2 h. The catalyst was filtered, the solvent was evaporated to dryness at reduced pressure, and the acid **18** thus obtained was dissolved in a mixture of 15 mL of dry tetrahydrofuran, 15 mL of anhydrous *tert*-butyl alcohol, and 200 mg of dicyclohexylcarbodiimide. The solution was left at 20 °C during 18 h, the precipitate was filtered, the solution was evaporated to dryness, the residue was stirred with a small volume of dry benzene (5 mL), the suspension was filtered again, and the filtrate was applied to a TLC silica gel column (3 × 20 cm) packed under slight pressure and previously washed with 2% methanol in benzene. The ester **19** was eluted with the latter solvent (monitoring of the eluates was made with TLC), the eluates were evaporated to dryness, and the residue was recrystallized from cyclohexane; 568 mg (45%): mp 79–81 °C; ^{13}C NMR δ 171.09 (O*C*OCH$_3$), 160.90 (*C*O$_2$-), 129.07, 125.89, 118.28, 117.12 (pyrrole-C), 80.40 (*C*(CH$_3$)$_3$), 67.78 (*C*H$_2$CH$_2$O-), 28.47 (C(*C*H$_3$)$_3$), 24.90 (OCO*C*H$_3$), 21.05 (*C*H$_2$CH$_2$O-), 11.41 (CH$_3$-5), 8.71 (CH$_3$-4). Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.05; H, 8.18; N, 4.98. Found: C, 64.00; H, 8.09; N, 4.85.

***tert*-Butyl 3-(β-Acetoxyethyl)-4-methyl-5-(acetoxymethyl)-2-pyrrolecarboxylate (8).** Lead tetraacetate (1 g) was added in small portions over 1 h to a solution of 500 mg of **19** in 10 mL of glacial acetic acid. The mixture was stirred and kept at 20 °C during 18 h; it was then poured over a large volume of ice water and the precipitate was filtered, dried, and recrystallized from methanol–water: 270 mg (45%); mp 74–75 °C. Anal. Calcd for $C_{17}H_{25}NO_6$: C, 60.17; H, 7.37; N, 4.12. Found: C, 60.10; H, 7.35; N, 4.08.

***tert*-Butyl 3,5-Dimethyl-4-acetyl-2-pyrrolecarboxylate (26).** A solution of 70 g of sodium nitrite in 250 mL of water was slowly added to a solution of 160 g of *tert*-butyl acetate in 300 mL of acetic acid kept below 5 °C with constant stirring. After the addition was complete, the solution was kept at 5 °C during 18 h, and it was then slowly added to a stirred mixture of 110 g of 2,4-pentanedione, 200 g of zinc powder, and 200 g of anhydrous sodium acetate in 200 mL of acetic acid. After the addition was complete, the mixture was heated at 75 °C during 1 h; it was then poured in a large volume of ice water, the precipitate was filtered, redissolved in methanol, filtered again to separate zinc dust, and enough water was added to the filtrate to precipitate the pyrrole **26**. The latter was filtered, dried, and recrystallized from ethanol, 16 g (67%); mp 129–130 °C. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.82; H, 8.01; N, 5.90. Found: C, 65.80; H, 7.95; N, 5.70.

***tert*-Butyl 3,5-Dimethyl-4-ethyl-2-pyrrolecarboxylate (27).** Boron trifluoride etherate (40 mL) was slowly added over 1 h to a stirred mixture of 6 g of sodium borohydride and 16 g of β-acetylpyrrole **26** in 160 mL of tetrahydrofuran kept under a nitrogen atmosphere. After the addition was complete, the mixture was stirred for 1 h, after which 200 mL of 5% hydrochloric acid were added, the solution was extracted with chloroform, the organic layer was washed with water, dried (Na_2SO_4), evaporated to dryness, and the residue was crystallized from methanol; 13 g (84%): mp 96–97 °C; ^{13}C NMR δ 162.06 (*C*O$_2$-), 129.20, 125.76, 123.56, 118.25 (pyrrole-C), 79.86 (*C*(CH$_3$)$_3$), 28.66 ((*C*H$_3$)$_3$), 17.34 (*C*H$_2$CH$_3$), 15.47 (CH$_2$*C*H$_3$), 11.26 (CH$_3$-5), 10.73 (CH$_3$-3). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 69.95; H, 9.41; N, 6.27. Found: C, 69.90; H, 9.35; N, 5.89.

***tert*-Butyl 3-Methyl-4-ethyl-5-(acetoxymethyl)-2-pyrrolecarboxylate (22).** Lead tetraacetate (4 g) was added in small portions over 1 h to a solution of 2 g of **27** in 40 mL of glacial acetic acid. The mixture was stirred during 2 h at 20 °C and then poured over a large volume of ice water; the precipitate of **22** was filtered and recrystallized from acetone–water; mp 70–71 °C. Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.05; H, 8.18; N, 4.98. Found: C, 63.95: H, 8.10; N, 4.90.

Benzyl 3-Methyl-4-(ethoxycarbonyl)-5-(α-oxo-β-(ethoxycarbonyl)ethyl)-2-pyrrolecarboxylate (32). The carboxypyrrole **28** (8 g) was dissolved in 100 mL of freshly distilled thionyl chloride and the solution was heated under reflux for 2 h. The solution was then evaporated to dryness in vacuo and the residue was dissolved in dry benzene and evaporated to dryness again. The acid chloride **29** thus obtained was dissolved in 40 mL of dry tetrahydrofuran and used as described below. Magnesium turnings (12 g) were added to a solution of 50 g of isopropyl bromide in 400 mL of tetrahydrofuran and the mixture was stirred at 20 °C until total dissolution of the turnings. The resulting solution was cooled to 5 °C and was slowly added to 26 g of acid ethyl malonate in 200 mL of dry tetrahydroduran at 5 °C. The resulting solution was heated under reflux during 5 min and cooled to 5 °C, and the solution of the acid chloride **29** in tetrahydrofuran was then added. The mixture was then heated under reflux for 1.5 h, cooled, and concentrated in vacuo to 150 mL, and 30 mL of trifluoroacetic acid was then added to the concentrate at 20 °C. After 10 min the decarboxylation of **31** was complete, the solution was poured over a large volume of water, the aqueous layer was extracted with chloroform, and the pooled extracts were washed with water, dried (Na_2SO_4), and then evaporated to dryness in vacuo. The oily residue was finally heated at 80 °C and 0.1 torr to eliminate all volatile components. The residual oil was dissolved in a small volume of 1% methanol in benzene and the solution was applied to a TLC silica gel column (3 × 20 cm) packed under pressure and prewashed with the same solvent. The keto ester **32** was eluted from the column with the same solvent by applying a slight pressure. The eluates containing **32** (as monitored by TLC using the same solvent; it showed two spots with similar R_f corresponding to the keto and enol forms) were evaporated to dryness leaving behind 4 g (60%) of oily **32**; ^{13}C NMR δ 180.00 (*C*H$_2$CO), 170.10 (*C*H$_2$*C*O$_2$-), 160.22 (*C*O$_2$-), 158.78 (=*C*OH), 135.44, 128.56, 128.37, 128.19 (*C*$_6$H$_5$), 130.20, 126.00, 121.25, 120.00 (pyrrole-C), 97.00 (=CH), 66.54 (-*C*O$_2$*C*H$_2$*C*$_6$H$_5$), 60.92, 60.00 (*C*O$_2$*C*H$_2$CH$_3$), 48.88 (*C*H$_2$CO), 14.05, 13.92 (OCH$_2$-*C*H$_3$), 10.80 (CH$_3$-3); ^{1}H NMR δ 5.2 (d, C*H*-COH), 3.4 (s, CH$_2$CO), 1.7 (s, 1, =COH); mass spectrum, *m/e* (relative intensity) 401 (M$^+$, 38), 285 (**37a**, 76), 269 (**35a**, 90), 194 (**37a** - C$_6$H$_5$, 84), 178 (**35a** - C$_6$H$_5$, 92), 314 (**36a**, 82).

Ethyl 2-(α-Oxo-β-(ethoxycarbonyl)ethyl)-4-methyl-5-carboxy-3-pyrrolecarboxylate (33). A solution of 4 g of the ester **32** in 200 mL of ethanol was reduced with hydrogen over 1.5 g of 10% Pd on charcoal at 50 psi during 3 h. The catalyst was filtered off, the solvent was evaporated to dryness, and the residue was dissolved in a small volume of 5% methanol in chloroform and was filtered through a TLC silica gel column as described above; 1.5 g (54%): mp 150–151 °C (ethanol–water); ^{1}H NMR δ 5.1 (d, 1, *C*H=COH), 3.3 (s, 0.8, CH$_2$CO); mass spectrum, *m/e* (relative intensity) 312 (M$^+$, 18), 195 (**37b**, 90) 179 (**35b**, 90), 224 (**36b**, 81). Anal. Calcd for $C_{14}H_{17}O_7N$: C, 54.01; H, 5.46; N, 4.50. Found: C, 53.98; H, 5.40; N, 3.45.

Ethyl 2-(α-Oxo-β-(ethoxycarbonyl)ethyl)-4-methyl-3-pyrrolecarboxylate (23). A solution of 1.5 g of **33** and 0.3 g of sodium bicarbonate in 15 mL of water was added to a solution of 0.9 g of iodine and 1.9 g of potassium iodide in 15 mL of water. The mixture was stirred at 75–80 °C during 1 h, it was then poured over a large volume of water, the aqueous solution was extracted with chloroform, and the chloroform extracts were washed with 5% sodium thiosulfate, dried (Na_2SO_4), and evaporated to dryness. The residue of 0.78 g (61%) of **34** was dissolved in 100 mL of ethanol, 1.5 g of sodium acetate and 0.25 g of 10% Pd on charcoal were added, and the mixture was reduced with hydrogen during 2 h at 40 psi. The catalyst was filtered, the solvent was evaporated to dryness, the residue was partitioned between water and

chloroform, and the chloroform layer was separated, dried (Na_2SO_4), and evaporated to dryness. The oily residue of **23** was purified by filtration through a TLC silica gel column packed and eluted as described above using 2% methanol in benzene; 160 mg (60%): 1H NMR δ 6.5 (s, 1, H-5), 5.1 (d, 1, C*H*=COH), 3.3 (s, 0.7, CH_2CO); mass spectrum, *m/e* (relative intensity) 267 (M^+, 27), 135 (**35c**, 40), 151 (**37c**, 100), 180 (**36c**, 54).

Benzyl 3,3′-Dimethyl-4-[β-(ethoxycarbonyl)ethyl]-4′-(β-acetoxyethyl)-5′-[(*tert*-butyloxy)carbonyl]dipyrrylmethane-5-carboxylate (9). A solution of 210 mg of the 2-(acetoxymethyl)pyrrole **8** and 240 mg of the α-unsubstituted pyrrole **7** in 15 mL of glacial acetic acid containing 30 mg of *p*-toluensulfonic acid was heated at 40 °C during 4 h. It was then poured over a large excess of ice water, the aqueous solution was extracted with chloroform, and the organic layer was washed with water, then with 5% sodium bicarbonate, again with water, dried (Na_2SO_4), and evaporated to dryness. The residue was purified by filtration through a TLC silica gel column prepared as described above, using 2% methanol in benzene, as eluant; 240 mg of oily **9** (60%) were obtained: 1H NMR δ 7.19 (b, 5, C_6H_5), 5.14 (s, 2, $CH_2C_6H_5$), 4.20 (t, 2, CH_2CH_2O-), 3.72 (s, 2, pyrr-CH_2-pyrr), 3.49 (s, 3, CO_2CH_3), 2.91–2.82 (m, 4, CH_2CH_2O-, CH_2CH_2-), 2.45–2.25 (m, 2, $CH_2CH_2CO_2$-), 1.90, 1.87, 1.85 (s, s, s, 3, 3, 3, CH_3-3, CH_3-3′, $COCH_3$), 1.40 (s, 9, $(CH_3)_3$); mass spectrum, *m/e* (relative intensity) 580 (M^+, 16).

***tert*-Butyl 3,3′-Dimethyl-4-(β-acetoxyethyl)-4′-[β-(ethoxycarbonyl)ethyl]dipyrrylmethane-5-carboxylate (1).** A solution of 220 mg of dipyrrylmethane **9** in 50 mL of ethanol was reduced with hydrogen at 50 psi during 2 h over 100 mg of 10% Pd on charcoal. The catalyst was filtered off, the solvent was evaporated to dryness in vacuo, and the residue was dissolved in a small volume of 5% methanol in chloroform and was filtered through a TLC silica gel column as described above using the same solvent for elution. The acid dipyrrylmethane **10** (120 mg, 64%) was thus obtained and was decarboxylated by heating at 220 °C and 0.050 torr during 2 min in a nitrogen atmosphere. The decarboxylated product was finally purified by filtration through a TLC silica gel column (2 × 20 cm), packed, and eluted with 2% methanol in benzene; 70 mg (60%) of oily **1** were recovered from the eluates: 1H NMR δ 6.30 (b, 1, H-5), 6.30 (b, 1, H-5′), 4.25 (t, 2, CH_2CH_2O-), 3.70 (s, 2, -CH_2-), 3.48 (s, 3, CO_2CH_3), 2.90–2.80 (m, 4, CH_2CH_2O-, $CH_2CH_2CO_2$-), 2.31 (m, 2, $CH_2CH_2CO_2$-), 1.90, 1.82, 1.80 (s, s, s, 3, 3, 3, $COCH_3$, CH_3-3′, CH_3-3), 1.35 (s, 9, $C(CH_3)_3$); mass spectrum, *m/e* (relative intensity) 446 (M^+, 17).

***tert*-Butyl 3′,4-dimethyl-3-ethyl-4′-(ethoxycarbonyl)-5′-[α-oxo-β-(ethoxycarbonyl)ethyl]dipyrrylmethane-5-carboxylate (2)** was obtained by condensation of 130 mg of 2-(acetoxymethyl)pyrrole **22** and 130 mg of pyrrole β-keto ester **23** following the procedure described for the synthesis of **9**. The product was purified through a TLC silica gel column as described for **9** and 170 mg (71%) of **2** were obtained: 1H NMR δ 4.00–4.60 (m, 4, OCH_2CH_3), 3.80 (s, 2, pyrr-CH_2-pyrr), 3.40 (s, 2, $COCH_2CO_2$-), 2.60–2.20 (b, 5, CH_3-3′, CH_2CH_3), 2.10 (s, 3, CH_3-4), 1.70 (s, 9, $(CH_3)_3$), 1.50–0.90 (m, 9, OCH_2CH_3); mass spectrum, *m/e* (relative intensity) 488 (M^+, 18), 316 (**38**, 50), 192 (**40**, 80), 165 (**39**, 70).

Ethyl 2,7,12,18-Tetramethyl-3-(β-hydroxyethyl)-8-ethyl-15-[(methoxycarbonyl)methyl]-17-[β-(methoxycarbonyl)ethyl]porphyrin-13-carboxylate (4). A mixture of 60 mg (0.12 mM) of **2** and 45 mg (0.10 mM) of the α-unsubstituted dipyrrylmethane **1** was dissolved in 1 mL of anhydrous methanol and 0.1 mL of 48% HBr was added. The solution was kept at 20 °C during 50 min and was then poured over a column (15 × 20 cm) of deactivated alumina (prepared by suspending Merck grade I alumina in methanol, filtering, and drying in air) prewashed with chloroform. The bilene **3** (deep orange band) was eluted with the same solvent, the latter was evaporated to dryness at 20 °C, the residue [53 mg (60%); 1H NMR δ 1.5 (b, 18, $(CH_3)_3C$), 3.93 (s, 2, -C-CH_2CO_2-)] was dissolved in 2 mL of glacial acetic acid and 0.4 mL of 40% HBr in glacial acetic acid were added, and the solution was kept during 15 min at 20 °C and was finally freeze-dried. The amorphous residue was dissolved in 20 mL of dry methylene chloride, 500 mg of dry trichloracetic acid and 0.15 mL of triethyl orthoformate were added, and the solution was kept during 24 h at 20 °C in the dark. Methanol saturated with zinc acetate (10 mL) was then added, and the mixture was kept for further 72 h at 20 °C. It was then evaporated to dryness, the residue was dissolved in 20 mL of 5% sulfuric acid in methanol, the solution was kept at 20 °C during 24 h, it was then diluted with chloroform (100 mL), the mixture was washed with water and then 5% sodium bicarbonate, dried (Na_2SO_4), and evaporated to dryness, and the porphyrin was purified by preparative TLC on silica gel using 2% methanol in benzene as solvent; 3.3 mg of the oily product was obtained: 1H NMR δ 10.72 (s, 1, H-10), 9.60, 9.53 (25, 1, 1, H-20 and H-5), 5.35 (s, 2, -C-CH_2CO_2-), 4.85 (q, 2, OCH_2CH_3), 4.29, 4.20 (m, 4, $CH_2CH_2CO_2$-, CH_2CH_2OH), 3.91 (q, 2, CH_2CH_3), 3.75, 3.68, 3.63, 3.60, 3.38 (5s, 3, 3, 3, 6, 3, pyrr-CH_3, OCH_3), 3.20, 3.10 (CH_2OH, $CH_2CH_2CO_2$-), 1.80, 1.76 (m, 6, CH_2CH_3, OCH_2CH_3); mass spectrum, *m/e* (relative intensity) 668 (M^+, 50).

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