Effect of *Meso*-Substituents on the Osmium Tetraoxide Reaction and Pinacol−Pinacolone Rearrangement of the Corresponding *vic*-Dihydroxyporphyrins

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To investigate the effects of electron-donating and electron-withdrawing substituents upon the reaction of porphyrins with osmium tetraoxide, and the pinacol−pinacolone rearrangement of the resulting diols, a series of *meso*-substituted porphyrins were prepared by total synthesis. Porphyrins with electron-donating substitutents at the *meso*-positions gave *vic*-dihydroxychlorins in which the adjacent pyrrole subunit was predominantly oxidized. No such selectivity was observed in a porphyrin containing a methoxycarbonyl as the electron-withdrawing group, whereas a formyl substituent again resulted in oxidation at the pyrrole unit adjacent to the *meso*-substituent. Under pinacol−pinacolone conditions, *vic*-dihydroxy chlorins containing 4-methoxyphenyl or 3,5-dimethoxyphenyl groups at the *meso*-position showed preferential migration of the ethyl group over the methyl group to give 8-ketochlorins, whereas the diol with an *n*-heptyl substituent under similar reaction conditions gave both 7- and 8-ketochlorins. In contrast, the diol containing a *meso*-formyl substituent produced the corresponding 7-ketochlorin exclusively. These results indicate that it is not possible to predict the reactivity of *meso*-substituted porphyrins in the osmium tetraoxide reaction nor the general substituent migratory aptitudes in the pinacol−pinacolone rearrangement based on simple electronic arguments, most likely because many parameters (e.g., *meso*-β-pyrrolic steric crowding and long-range electronic effects) ultimately determine the reactivity. The structural assignments of the porphyrin diols and the keto-analogues were confirmed by extensive ^{1}H NMR studies; some of the dihydroxychlorins and ketochlorins were found to display unusual features in their ^{1}H NMR spectra.

Introduction

In continuation of our ongoing studies, the present work describes the results of an investigation to determine the effect of substituents placed regioselectively at the *meso*-positions of the porphyrin macrocycle to generate the *vic*-dihydoxy- and the corresponding oxochlorins under appropriate reaction conditions. The oxo-derivatives of chlorins, isobacteriochlorins, and bacteriochlorins have been known for some time,[1] but their biological significance was not recognized until recently.[2] For example, the dihydroxyporphyrin structure originally proposed[3] by Barrett for heme *d* isolated from *Aerobacter aerogenes* was later reinvestigated by Timkovich et al.[4] who showed that heme *d* is in fact a derivative of 5,6-dihydroxyprotochlorin IX. It has also been reported by Sotiriou and Chang[5] that heme d_1 obtained from *Pseudomonas aeruginosa* and *Paracocis denitrificans* is a dioxoisobacteriochlorin. In recent years, some of the oxochlorins, oxobacteriochlorins, dioxobacteriochlorins, and their *vic*-dihydroxy precursors have been investigated as potential photosensitizers for the treatment of cancer using photodynamic therapy (PDT).[6] Thus, due to their biological and medicinal importance, the oxo- and their corresponding *vic*-dihydroxy derivatives have generated considerable interest.

In their studies with a variety of unsymmetrical porphyrins, Chang and Sotiriou[7] showed that unsymmetrical porphyrins (e.g., deuterioporphyrin IX dimethyl ester **1**, mesoporphyrin IX dimethyl ester **2**) upon reaction with OsO_4 gave all the possible four (ring A, B, C, and D) *vic*-dihydroxychlorins **3**, **4** without any pyrrole subunit selectivity (see Scheme 1). Acid-catalyzed pinacol−pinacolone rearrangement of the *vic*-dihydroxy compounds gave the corresponding ketones, and migratory aptitudes of hydrogen, ethyl, or alkyl groups (including the propi-

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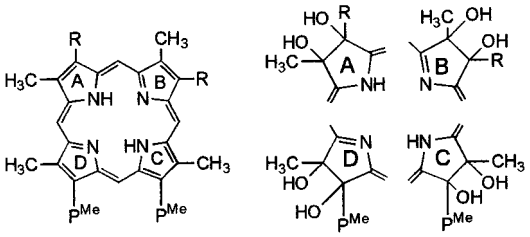
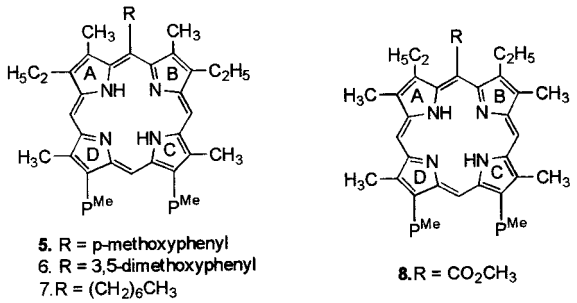
Scheme 1



1. R = H
2. R = C_2H_5

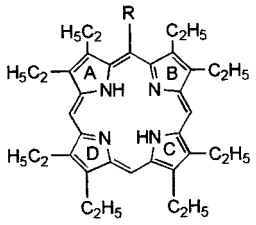
3 **(a, b, c, d).** R = H
4 (a, b, c, d). R = C_2H_5

Scheme 2



5. R = p-methoxyphenyl
6. R = 3,5-dimethoxyphenyl
7.R = $(CH_2)_6CH_3$

8.R = CO_2CH_3



9. R = H
10. R = CHO

onate side chain) over the methyl group were established.[7,8] We later extended this study to porphyrin and chlorin systems in which electron-withdrawing groups were present at peripheral positions of the macrocycle; it was shown that the regiospecificity of pyrrole subunits to OsO_4 oxidation in porphyrins is affected significantly by the presence of electron-withdrawing groups, and the pyrrole unit containing the electron-withdrawing group(s) did not undergo to oxidation.[9]Migratory aptitudes in subsequent pinacol−pinacolone rearrangements of porphyrin and pheophorbide *vic*-diol systems were likewise dependent upon the stability of the intermediate carbocation which was affected by the number of electron-withdrawing functionalities in the tetrapyrrolic ring system.[10]

In general, the syntheses of *vic*-dihydroxyporphyrins and chlorins are achieved by reacting porphyrins or chlorins with osmium tetraoxide (OsO_4). The intermediate osmate ester is then hydrolyzed reductively to give insoluble osmium salts or oxidatively to regenerate the osmium tetraoxide reagent. In either case the corresponding vicinal *cis*-diol is formed selectively in good yield. There exist several methods to hydrolyze the osmate ester,[11] but in porphyrins the reductive cleavage with hydrogen sulfide appears to give the best results. As in other alicyclic systems,[12] addition of pyridine to hydroxylation reactions led to a marked increase in the rate of formation of the intermediate osmate ester complexes. The dihydroxy derivatives, under acidic conditions, can then be converted into the corresponding keto-analogues via pinacol−pinacolone rearrangement. A notable observation is that the migratory aptitudes of side chains at the peripheral position(s) of the macrocycle generally appear to be dictated by the stability of the intermediate carbocation.

Results and Discussion

In our earlier studies, we showed that in the porphyrin system, the presence of an electron-withdrawing substituent on the pyrrole subunit deactivated that particular pyrrole unit toward the OsO_4 reaction; oxidation was achieved at the diagonally opposite pyrrole subunit which is presumably more electron-rich than the others.[9] For our present study, porphyrins **5**−**8** and **10** were used as substrates (Scheme 2). In porphyrins **5** and **7**, the electron-donating groups were regioselectively introduced at the *meso*-positions (position-5) of the macrocycle, whereas in porphyrins **6**, **8**, and **10** electron-withdrawing groups were incorporated. The basic idea for selecting these porphyrins as substrates was to address the following questions: (a) can we achieve any selectivity for the formation of the *vic*-dihydroxy analogues on reacting with osmium tetraoxide, (b) is it possible to dictate the formation of the intermediate carbocation(s) and thus the regioselective formation of 7- or 8-ketochlorins under pinacol−pinacolone conditions using electronic effects? Information derived from this study will help to establish the effect of various groups upon the regiospecificity of the oxidation reaction, and upon subsequent pinacol−pinacolone rearrangements of the intermediate diol(s) in porphyrin systems.

Porphyrins **5**−**7** were prepared in a sequence of reactions in which 2-ethoxycarbonyl-3-ethyl-4-methylpyrrole[12] was converted into dipyrromethanes **15**, **16**, and **17** in excellent yields[13] (Scheme 3). These pyrromethanes were then individually condensed with the diformyl dipyrromethane **20** under acidic conditions and the desired porphyrins obtained in 35 to 40% yield, respectively. Porphyrin **8** containing a methoxycarbonyl group at the *meso*-position was obtained by condensing the 1,9-diformyldipyrromethane **20** with dipyrromethane-1,9-dicarboxylic acid **27** under MacDonald reaction conditions[14] and was isolated in 32% yield (Scheme 3). Reaction of Ni(II) octaethylporphyrin (OEP) with Vilsmeier reagent ($POCl_3$/DMF) produced the corresponding formyl analogue in 70% yield.[15] Removal of nickel under strongly acidic conditions gave the free base porphyrin **10** in quantitative yield.

Our interest in chlorin compounds is related in part to their use in photodynamic therapy (PDT).[16,17] Chlorins in general are suitable candidates for such treatment due

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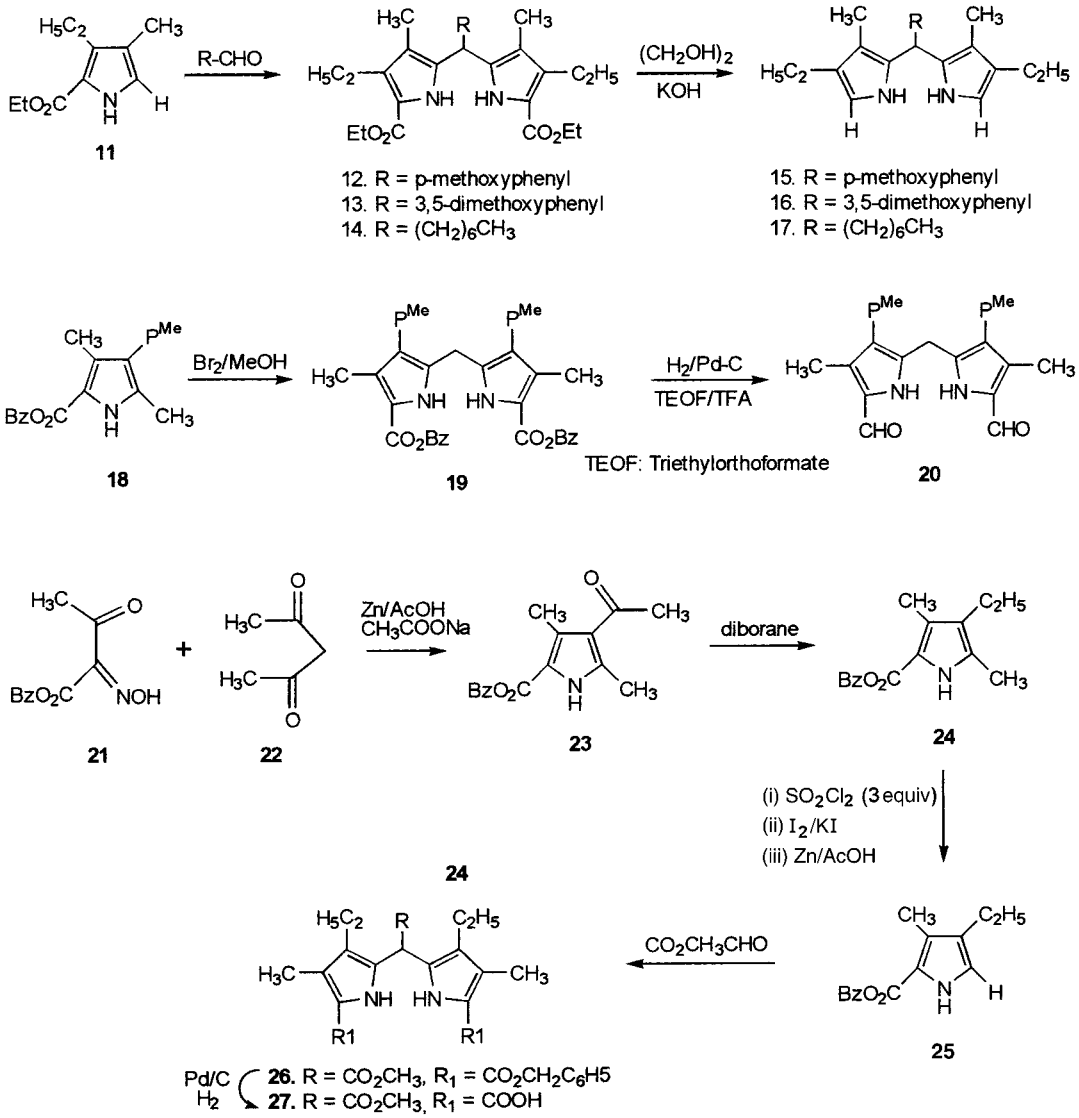
Scheme 3



to (a) their strong absorptions in the red region of the electronic absorption spectra, (b) their strong fluorescence, enabling them to be easily detected, and (c) their high singlet oxygen yield, an essential requirement for killing the tumor cells. We have recently synthesized and evaluated a series of *vic*-dihydroxy- and oxo-bacteriochlorins prepared from methyl 9-deoxy-*meso*-pyropheophorbide.[19] Among such analogues, the oxo-bacteriochlorins were found to be more effective than the corresponding *vic*-dihydroxy analogues from which they were derived.[19] In another study, among the alkyl ether analogues of various methylpheophorbides,[20] pyropheophorbides,[21] and purpurinimides,[22] we showed that altering the length of the carbon chain yielded a remarkable difference in photosensitizing efficacy. Thus, to investigate the effect(s) of the alkoxyalkyl substituents at the *meso*-position of the macrocycle on PDT efficacy, *p*-methoxyphenylporphyrin **5** was also converted into the corresponding alkyl ether derivatives with variable carbon units **29**−**31** as precursors because of interest in testing the efficacy of the corresponding dihydroxychlorins as photodynamic agents.

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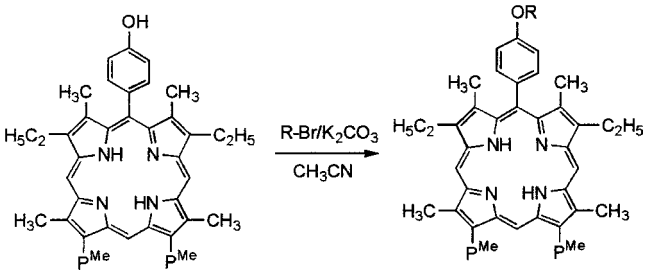
Scheme 4



28

29. R = hexyl
30. R = heptyl
31. R = decyl

As mentioned earlier, Chang and Sotiriou[5] showed that reaction of unsymmetrical porphyrins (e.g., deuterioporphyrin IX dimethyl ester **1** and mesoporphyrin IX dimethyl eser **2)** with OsO_4 produced a mixture of all four possible *vic*-dihydroxy analogues **3** and **4** (**a**,**b**,**c**,**d**), and no selectivity was observed. Under similar conditions, reaction of porphyrins **5** and **6** with 1.5 equiv of OsO_4 gave predominantly one isomer in >75% yield, along with unreacted starting material (5%). These compounds were assigned as *vic*-dihydroxyporphyrins **32** and **33** (see Scheme 5) by NMR spectroscopy. If an excess of OsO_4 is used in the reaction, the same porphyrins (e.g., **5**) produced mainly the corresponding tetrahydroxybacteriochlorins (e.g., **38**) as an isomeric mixture in which the pyrrole rings diagonal to each other were oxidized. The other diols containing *O*-hexyl- **34**, *O*-heptyl- **35**, and *O*-decyl- **36**, and *n*-heptyl group **37** were obtained from their respective porphyrins in similar yields and with similar selectivities.

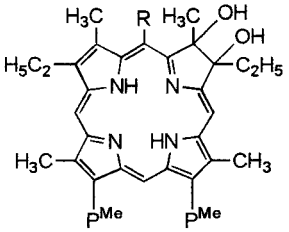
A porphyrin **8** containing a methoxycarbonyl group at 5-position, however, did not show any selectivity, the product being identified as the mixture of 7,8-dihydroxy- (**39**) and 17,18-dihydroxychlorin (**40**) in almost equal ratio and could not be separated. However, replacing the methoxy carbonyl group with a formyl group at the *meso*-position (**10**) produced a remarkable selectivity, and the 7,8-dihydroxyporphyrin **42** in which the pyrrole unit adjacent to the substituent had oxidized was isolated as a sole product. We had envisioned that porphyrins containing electron-withdrawing substituents at the *meso*-position should decrease the electron density of the adjacent pyrrole units, and thus these pyrroles should be less susceptible to oxidation than those away from such substituent. However, the experimental results were in contrast to those we had hypothesized and suggested that in porphyrin system, the site of oxidation by osmium tetraoxide does not follow the electron-withdrawing/donating ability of the *meso*-substituents. The oxidation always seems to occur at the ring adjacent to the substituent, except in the porphyrin with a *meso*-methoxycarbonyl group, where ring C was also oxidized. These results tend to suggest that the relief of strain between the *meso*- and *β*-substituents is a dominant factor in the osmium tetraoxide oxidation.

Rearrangement of the Alkyl Groups under Pinacol−Pinacolone Conditions. On treating with acid under pinacol−pinacole conditions, the *vic*-dihydroxy chlorins **32** and **33** containing a *p*-methoxyphenyl or 3,5-dimethoxy phenyl group at the *meso*-position (position-5) produced keto-chlorins **43** and **44**, respectively. In both chlorins, the ethyl group had migrated in preference to the methyl substituent. In contrast, the 5-heptyldihydroxychlorin **37** afforded a mixture of ketochlorins **45** (ethyl migrated instead of methyl) and **46** (methyl migrated instead of ethyl) in almost equal ratio with a combined yield of 60%, and the 5-*meso*-formyldihydroxychlorin **42** produced the 7-ketochlorin **47** as a single isomer. The main objective for the synthesis of chlorins **34**−**36** was to determine the effect of variable length of alkyl ether carbon chains in PDT efficacy in the presence of hydrophilic hydroxy substituents, so they were not subjected to pinacol−pinacole conditions. On the basis of these results (Scheme 7), it seems that similar to the non-*meso*-substituted porphyrin-diols, the migratory aptitude of the alkyl substituents in the corresponding *meso*-dihydroxychlorins depends in large part on the stability of the intermediate carbocation(s) formed under acidic conditions.

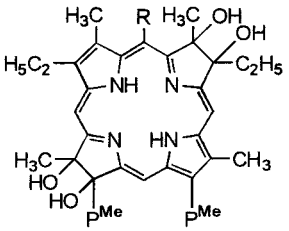
The structure of the *vic*-dihydroxychlorin **42** and the migration patterns of the ketochlorins **43**, **45**, **46**, and **47** were determined either by NOE or ROESY ^{1}H NMR studies (Figure 1). Of particular interest was the fact that no interaction between the 5-formyl and the 3-ethyl protons was observed in ketochlorin **47**. This might be due to hydrogen bonding of the 5-formyl proton with the adjacent keto-group substituted at position-7 of the macrocycle, which would orient the formyl proton away from the 3-ethyl group. Other unusual features were observed in the ^{1}H NMR spectra of porphyrins **42** and **45**. In the case of the *vic*-dihydroxychlorin **42**, there was a signal at δ 8.20, which could be assigned to an OH group of the diol based on its exchange characteristics with D_2O. This signal was shifted substantially downfield of its expected position (Figure 2). We attribute this to hydrogen bonding with the adjacent 5-formyl (CHO) group as shown in Figure 2. Furthermore, the resonances of 7-ketochlorin **46** were sharp, while those of 8-ketochlorin **45** showed substantial broadening. Addition of pyridine-d_5 to the samples was ineffective in sharpening the lines and ruled out the possibility of aggregation. However, variable temperature ^{1}H NMR 1D spectra indicated the presence of a dynamic process ($\Delta G = 68 + 2$ kJ mol^{-1}) with two species being observed at lower temperature (Figure 3). At low temperature, the *meso*-hydrogen signals indicated a ratio of 55:45. The dynamic process being observed in this system is probably due to rotation of the *meso*-alkyl group, something which has been seen in other porphyrin systems.[23] A similar effect might be present for the 7-keto isomer **46**, but not being seen because one rotamer is highly favored, the rotational barrier is lower, or the chemical shift differences are too small. The electronic absorption spectra of chlorindiols and ketochlorins in dichloromethane also showed some interesting characteristics. The diols and the related keto-analogues have similar spectra. However, compared to diols containing an electron-donating group, diols with electron-withdrawing groups (e.g., **42**) exhibited a red shift in their long wavelength absorptions (Figure 4). Among 8-keto- and 7-ketochlorins (**45** and **46**, respectively), the 8-keto isomer **45** exhibited a red shift of about 7 nm in its long wavelength absorption (Figure 5).

(23) For a recent review of ^{1}H NMR studies of dynamic process in porphyrins, see: Medforth, C. J. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: Boston, MA, 2000; Vol. 5, pp 60−74.

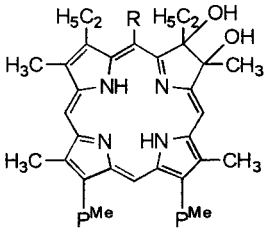
Scheme 5



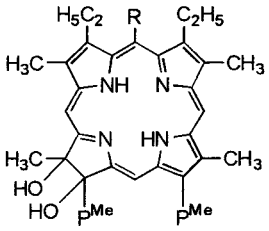
32. R = p-methoxyphenyl
33. R = 3, 5-dimethoxyphenyl
34. R = p-hexyloxyphenyl
35. R = p-heptyloxyphenyl
36. R = p-decyloxyphenyl
37. R = $(CH_2)_6CH_3$



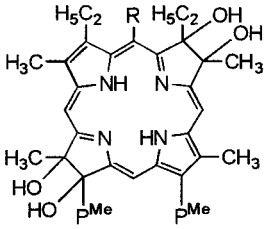
38. R = p-methoxyphenyl



39. R = CO_2CH_3

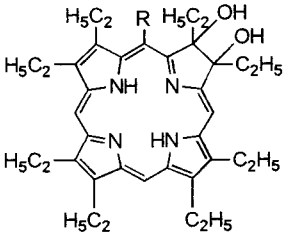


40. R = CO_2CH_3

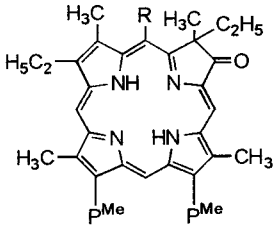


41. R = CO_2CH_3

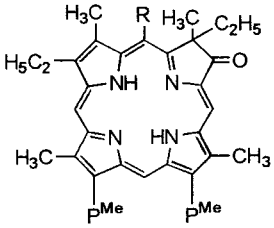
Scheme 6



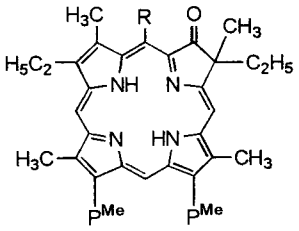
42. R = CHO



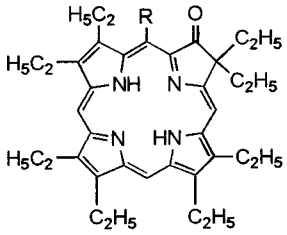
43. R = p-methoxyphenyl
44. R = 3, 5-dimethoxyphenyl



45. R = $(CH_2)_6CH_3$



46. R = $(CH_2)_6CH_3$



47. R = CHO

Experimental Section

Melting points were uncorrected and were measured on a Thomas/Bristoline microscopic hot stage apparatus. Silica gel 60 (70−230 and 230−400 mesh, Merck) or neutral alumina (Merck; usually Brockmann Grade III, i.e., deactivated with 6% water) were used for column chromatography. Preparative scale thin-layer chromatography was carried out on 20 × 20 cm glass plates coated with Merck G 254 silica gel (2 mm thick). Reactions were monitored by thin-layer chromatography and spectrophotometry, and were carried out under nitrogen and in the dark. Proton NMR spectra and NOE difference spectra were measured at 300 MHz using a General Electric QE300 or Brucker 400 MHz spectrometer. Deuteriochloroform was used as the solvent, and the chemical shifts were referenced to the residual chloroform signal at 7.258 ppm. Mass spectra were obtained at the Mass Spectrometry Facility, Michigan State University, East Lansing, and the UC San Francisco Mass Spectrometry Laboratory. Elemental analyses were obtained from Midwest Microlabs, Indianapolis, IN. Electronic absorption spectra were measured in dichloromethane using a Hewlett-Packard 8450A.

3,9-Diethyl-6-heptyl-4,8-dimethyl-2,10-diethoxycarbonyldipyrromethane (14). Pyrrole **11** (5.0 g) and octyl aldehyde (1.77 g) were dissolved in ethanol (50 mL), and *p*-toluenesulfonic acid (100 mg) was added. The reaction was refluxed overnight under nitrogen and was monitored by analytical TLC. It was then diluted with dichloromethane (200 mL) and washed with aqueous sodium bicarbonate and finally with water. The organic layer was then dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue which was chromatographed over silica column eluted with 1% methanol/dichloromethane. Appropriate eluates were collected and combined. Evaporation of the solvent gave the title compound as a yellow colored viscous oil. ^{1}H NMR (400 MHz,

Scheme 7

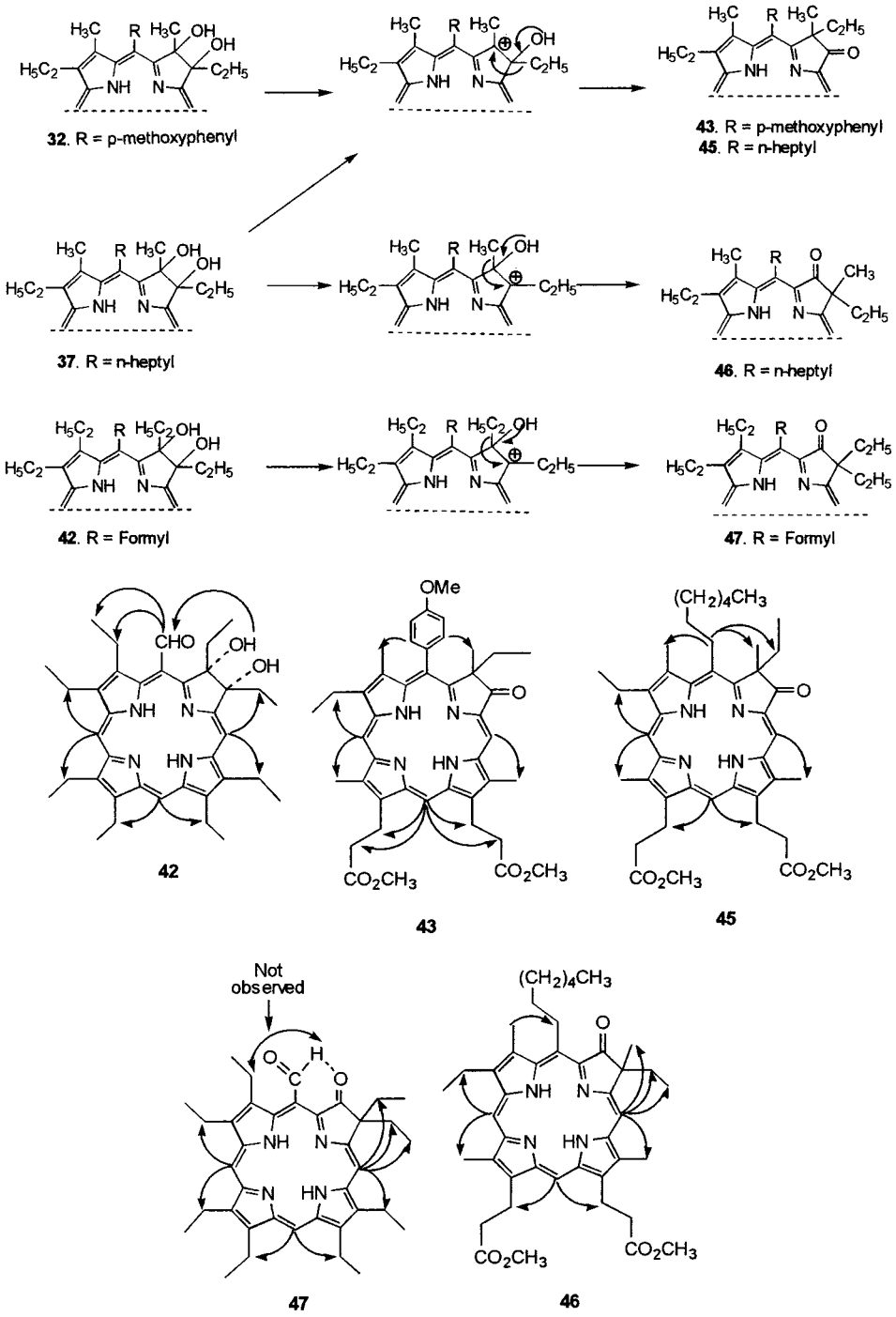


Figure 1. Interactions observed by NOE and 2D ROESY ^{1}H NMR studies.

$CDCl_3$): δ 9.30 (s, 2H, 2 NH); 4.25 (m, 5H, 2 × CO_2CH_2 CH_3 and bridge CH); 2.75 (m, 4H, 2 × CH_2 CH_3); 2.10 (m, 2H, CH_2-$(CH_2)_5$ CH_3); 1.90 (s, 6H, 2 × CH_3); 1.25 (m, 10H, $CH_2(CH_2)_5$ CH_3); 1.12 (t, 6H, 2 × CH_2 CH_3); 0.80 (t, 3H, $(CH_2)_5CH_3$. HRMS for $C_{28}H_{44}N_2O_4$: 472.3297. Found: 472.3290.

3,9-Diethyl-6-heptyl-4,8-dimethyl-2,10-dipyrromethane (17). The foregoing diethoxycarbonyl dipyrromethane (1.0 g) was dissolved in ethylene glycol. Sodium hydroxide (1.0 g) was added, and the reaction mixture was refluxed for 1 h. It was then cooled, diluted with dichloromethane (300 mL), and washed with water (3 × 250 mL). The dichloromethane layer was dried over anhydrous sodium sulfate. The residue obtained after evaporating the solvent was chromatographed over silica column eluted with chloroform. The appropriate eluates were combined, the solvent was evaporated, and the desired dipyrromethane was obtained in 50% yield (347 mg) as a light yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (s, 2H, 2 × NH); 6.50 (d, 2H, α-pyrrolic H); 4.00 (br s, 1H, bridge CH); 2.40 (m, 4H, 2 × CH_2CH_3); 2.00 (s merged

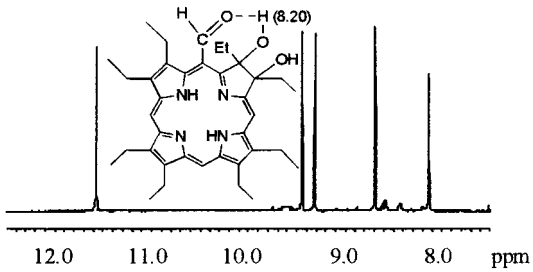


Figure 2. Partial 400 MHz ^{1}H NMR spectrum (in $CDCl_3$) of chlorin 42, showing downfield shift of the 7-OH proton.

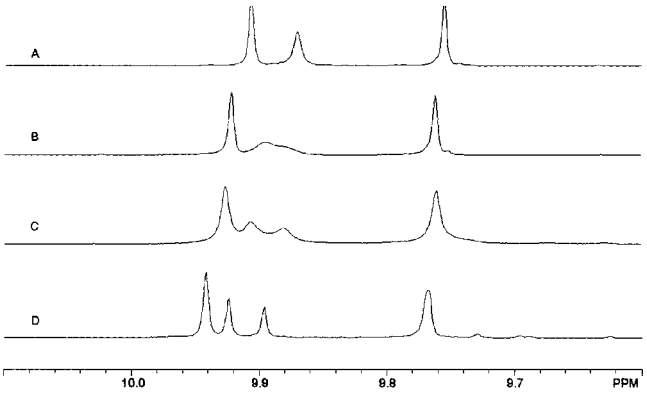


Figure 3. 400 MHz H NMR spectra of 5-heptyl-8-ketochlorin 45 at 323 K (A); 303 K (B); 293 K (C); and 278 K (D). At low temperature, one *meso*-hydrogen shows the presence of two forms with an equilibrium distribution of 55:45 ($\Delta G = 0.4$ kJ mol^{-1}).

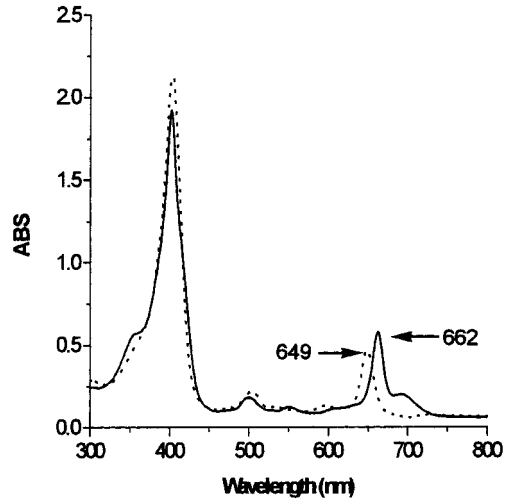


Figure 4. Electronic absorption spectra (CH_2Cl_2) of compound **37** (- - -) and **42** (—) at the same concentration (17.0 μM).

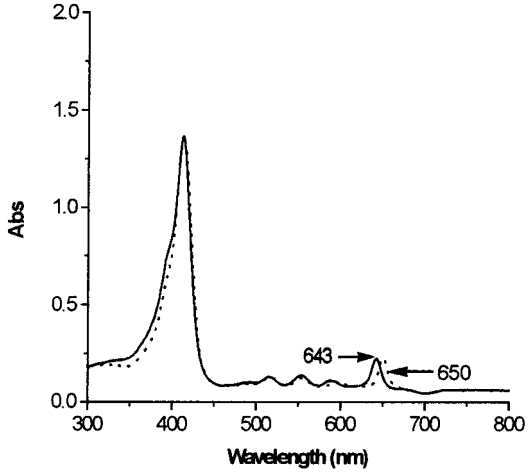


Figure 5. Electronic absorption spectra (CH_2Cl_2) of compound **45** (- - -) and **46** (—) at the same concentration (8.6 μM).

with m, 2 × CH_3, 4 × CH_2 of $(CH_2)_5$ CH_3; 1.25 (m, 10H, 2 × $(CH_2)_5$ CH_3);1.20 (t, 6H, 2 × CH_2CH_3); 0.80 (3H, t, $(CH_2)_6CH_3$. Mass calcd for $C_{22}H_{36}N_2$: 328.2875. Found (FAB): *m/e* 329 (M + 1).

2,8-Diethyl-13,17-bis(2-methoxycarbonylethyl)-5-(4′-methoxyphenyl)-3,7,12,18-tetramethylporphyrin (5). Diformyl dipyrromethane **20** (1.03 g) and dipyrromethane **15** (1.14 g) were dissolved in dichloromethane (250 mL). *p*-Toluenesulfonic acid (3.0 g) dissolved in methanol (50 mL) was added, and the reaction mixture was stirred at room-temperature overnight under nitrogen atmosphere. A saturated solution of zinc acetate/methanol (100 mL) was added, and the reaction was stirred for a further 12 h. It was then diluted with dichloromethane and washed with water, and the organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue, which was treated with trifluoroacetic acid (30 mL) for 1 h. The zinc-free porphyrin thus obtained after the standard workup was chromatographed over a short Grade III Alumina column, eluted with dichloromethane. The major band was collected, and the solvent evaporated. The residue was crystallized from dichloromethane/hexane in 42% yield (750 mg), mp >300 °C. UV/vis (λ_{max}, ϵ): 403 (140 000); 500 (20 000); 536 (16 000); 569 (14 000); 620 (12 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.20 (s, 2H, 2 × meso H); 9.90 (s, 1H, meso H); 7.88 and 7.25 [each d, 2H, C_6H_4 (OCH_3)]; 4.40 (t, 4H, 2 × CH_2 CH_2 CO_2CH_3); 4.12 (s, 3H, OCH_3); 4.02 (q, 4H, 2 × CH_2CH_3); 3.62 (s, 12H, 2 × CH_2CH_2 CO_2CH_3, and 2 × ring CH_3); 3.25 (t, 4H, 2 × CH_2CH_2 CO_2-CH_3); 2.52 (s, 6H, 2 × ring CH_3); 1.75 (t, 6H, 2 × CH_2CH_3); −3.22 and −3.27 (each s, 1H, 2 × NH). Anal. Calcd for $C_{43}H_{48}N_4O_5$: C, 73.69; H, 6.90; N, 7.99. Found: C, 73.45; H, 6.93; N, 7.95.

2,8-Diethyl-13,17-bis(2-methoxycarbonylethyl)-5-(3′,5′-dimethoxyphenyl)-3,7,12,18-tetramethylporphyrin (6). Diformyl dipyrromethane **20** was reacted with pyrromethane **16** (937 mg) by following the method discussed for the preparation of porphyrin **5** and was obtained in 30% yield (560 mg), mp 300 °C. UV/vis [CH_2Cl_2, λ_{max}, (ϵ)]: 403 (136 000); 500 (20 700); 536 (15 000); 569 (15 000); 623 (12 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.18 (s, 2H, 2 × meso H); 9.97 (s, 1H, meso H); 7. 39 (s, 2H, 2 × H of $C_6H_3(OCH_3)_2$ and 7.08 [s, 1H, C_6H_3-$(OCH_3)_2$]; 4.41 (t, 4H, 2 × CH_2 CH_2 CO_2CH_3); 4.12 (s, 6H, 2 × OCH_3); 4.02 (q, 4H, 2 × CH_2CH_3); 3.66 (s, 12H, 2 × CH_2CH_2 CO_2CH_3, and 2 × ring CH_3); 3.31 (t, 4H, 2 × CH_2CH_2 CO_2-CH_3); 2.54 (s, 6H, 2 × ring 3, 7- CH_3); 1.80 (t, 6H, 2 × CH_2CH_3); −3.22 and −3.24 (each s, 1H, 2 × NH). Anal. Calcd for $C_{44}H_{50}N_4O_6$: C, 72.31; H, 6.90; N, 7.67. Found: C, 71.78; H, 6.87; N, 7.47.

2,8-Diethyl-5-heptyl-13,17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylporphyrin (7). Dipyrromethane **17** (260 mg) was condensed with diformyl dipyrromethane **20** (460 mg) following the procedure discussed for the preparation of porphyrin **5**. After purification, the residue was crystallized from CH_2Cl_2/hexane. Yield: 108 mg (20%), mp 155−158 °C, UV/vis [CH_2Cl_2, λ_{max} (ϵ)]: 404 (161 000); 502 (15 000); 535 (6 000); 574 (6 000); 620 (3 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 2H, 2 × meso H); 9.81 (s, 1H, meso H); 4.36 (t, 4H, 2 × $CH_2CH_2CO_2CH_3$); 4.11 (br q, 4H, 2 × CH_2CH_3); 3.60−3.67 (merged signals, 18H, 2 × $CH_2CH_2CO_2CH_3$ and 4 × ring CH_3); 3.27 (t, 4H, 2 × CH_2CH_2 CO_2CH_3); 1.81 (t, 6H, 2 × CH_2CH_3), 5.15, 2.07. 1.38, 1.31 [m, 12H, $(CH_2)_6$ CH_3]; 0.88 [t, 3H, $(CH_2)_6$ CH_3]; −2.88 and −2.96 (each s, 1H, 2 × NH). MS for $C_{43}H_{56}N_4O_4$: 692.43. Found (FAB): *m/e* 693.50 (M + 1).

3,7-Diethyl-5-methoxycarbonyl-13,17-bis(2-methoxycarbonylethyl)-2,8,12,18-tetramethylporphyrin (8). Dipyrromethane dicarboxylic acid **27** (210 mg) was condensed with diformyl dipyrromethane **20** (225 mg) following the method discussed for porphyrin **5** and was isolated in 55% (200 mg) yield as a fluffy deep red solid, mp > 300 °C. UV/vis [CH_2Cl_2, λ_{max}, (ϵ)]: 399 (115 600); 499 (15 200); 535 (11 400); 571 (9 700), 675 (8 200). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 2H, 2 × meso H); 9.97 (s. 1H, meso H); 4.51 (s, 3H, meso CO_2-CH_3); 4.36 (t, 4H, 2 × $CH_2CH_2CO_2CH_3$); 3.77 (q, 4H, 2 × CH_2-CH_3); 3.62 and 3.52 (s merged, 18 H, 2 × $CH_2CH_2CO_2CH_3$ and 4 × ring CH_3); 3.26 (t, 4H, 2 × CH_2CH_2 CO_2CH_3); 1.67 (t, 6H, 2 × CH_2CH_3); −3.50 and −3.54 (each s, 1H,2 × NH). Anal. Calcd for $C_{38}H_{44}N_4O_6$: C, 69.92; H, 6.79; N, 8.58. Found: C, 69.02; H, 6 69; N, 8.42.

5-Formyl-2,3,7,8,12,13,18,19-octaethylporphyrin (10). Octaethylporphyrin (500 mg) was dissolved in *o*-xylene (200 mL), and nickel acetylacetonate (500 mg) was added. The reaction mixture was refluxed for 30 min, and after the standard workup the corresponding Ni(II) complex was ob-

tained in 100% (553 mg) yield. It was then reacted with Vilsmeier reagent prepared from $POCl_3$ (3.5 mL) and DMF (5 mL) for 1 h at 0 °C. The reaction was monitored by analytical TLC. The intermediate iminium salt was hydrolyzed overnight with aqueous sodium carbonate (pH > 10). After the standard workup, the Ni(II**)** formyloctaethylporphyrin that was isolated in quantitative yield on treating with concentrated H_2SO_4 produced the title compound in 93% (489 mg) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.77(s, 1H, CHO); 10.06 (2H, 2 × meso H); 9.94 (1H, meso H), 4.1−3.8(m, 16 H 8 × CH_2CH$_3$), 1.95−1.47 (m, 24H 8 × CH$_2$CH_3**).** mp 254−255 °C, reported: 255 °C.[15]

2,8-Diethyl-5-(4′-hydroxyphenyl)-13,17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylporphyrin (28). The 4-methoxyphenylporphyrin **5** (200 mg) was dissolved in dry dichloromethane (25 mL) and placed in a round-bottom flask equipped with a nitrogen inlet. The solution was cooled to −40 °C with CH_3CN−dry ice slush bath. Boron tribromide (1 mL) was added, and the solution was then allowed to warm to room temperature. The reaction mixture was diluted with dichloromethane (100 mL). The excess of BBr_3 was quenched by cautious dropwise addition of methanol (Caution! Violently exothermic!). An aqueous solution (10% w/v) of sodium bicarbonate (50 mL) was then added and the solution stirred for 30 min. The organic layer was separated and dried under high vacuum. The solid so obtained was redissolved in 5% methanol/CH_3Cl (10 mL) and passed through a 1 cm × 25 cm silica column using 5% MeOH/$CHCl_3$ eluent. The slow major band was collected and evaporated to yield the title compound in 77% (150 mg) yield, mp 300 °C. UV/Vis [CH_2Cl_2, λ_{max} (ϵ)]: 405 (177, 800), 503 (14, 000), 537 (4, 500), 571 (5, 200); 623 (1, 500). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 2H, 2 meso H); 9.90 (s, 1H, meso H); 7.78 and 7.12 (each m, 2H, phenyl H); 4.20 (m, 4H, 2 × CH_2 CH$_2$CO$_2$CH$_3$); 4.00 (q, 2H, 2 × CH_2CH$_3$); 3.62 (m, 12H, 2 × CH$_2$CH$_2$CO$_2$CH_3 and 2 × ring CH$_3$); 2.50 (s, 6H, 2 × ring CH$_3$); 1.75 (m, 6H, 2 × CH$_2$ CH_3); −2.22 (br s, 2H, 2x NH). HRMS Calcd for $C_{42}H_{46}N_4O_5$: 686. 3468; Found: 686.3450. Anal. Calcd for $C_{42}H_{46}N_4O_5$: C, 73.45; H, 6.75; N, 8.16. Found: C, 73.26; H, 6.61; N, 7.85.

General Procedure for the Synthesis of Porphyrins 29, 30. Porphyrin **28** (100 mg) was dissolved in acetonitrile (40 mL), and the related 1-bromoalkane (1-bromohexane for **29**, 1-bromoheptane for **30**) (1.5 mL) was added along with anhydrous potassium carbonate (200 mg). The reaction mixture was refluxed under nitrogen for 48 h. It was then diluted with dichloromethane and washed with water, and the organic layer separated and dried over anhydrous sulfate. Evaporation of the solvent gave a residue which was chromatographed over an alumina (Grade III) column eluted with dichloromethane. The major band was collected, and the residue obtained after evaporating the solvent was crystallized from CH_2Cl_2/hexane as fluffy light red solid.

Compound **29** was isolated in 89% (100 mg) yield, mp 263−266 °C. UV/vis [CH_2Cl_2, λ_{max} (ϵ): 402 (110 000); 502 (16 700), 535 (11 700); 625 (8 700)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.06 (s, 2H, 2 × meso H); 10.00 (s, 1H, meso H); 7.80 and 7.30 (each d, 2H, phenyl); 4.40 (m. 4H, CH_2 CH$_2$CO$_2$CH$_3$); 4.30 (t, 2H, OCH$_2$); 4.10 (m, 4H, CH_2 CH$_3$); 3.70 (m, 12H, 2 × CH$_3$ and 2 × CH$_2$CH$_2$CO$_2$CH_3); 3.25 (q, 4H, CH$_2$CH_2 CO$_2$CH$_3$); 2.52 (s, 6H, 2 × ring CH$_3$); 0.78, 0.98−2.01 (several m, total 11H, (CH$_2$ (CH_2)$_4$ CH_3); 1.10 (t, 6H, 2 × CH$_2$ CH_3); −3.21 and −3.31 (each s, 1H, 2 × NH). Anal. Calcd for $C_{48}H_{58}N_4O_5$: C, 74.78; H, 7.58; N, 7.27. Found: C, 73.90; H, 7.76; N, 6.83.

Compound **30**: mp. 268−270. UV/vis (ϵ): 402 (112 000); 502 (17 700), 535 (12 700); 625 (9 000)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 2H, 2 × meso H); 9.95 (s, 1H, meso H); 7.90 and 7.26 (each d, 2H, phenyl); 4.40 (m. 4H, *C*H_2 CH$_2$CO$_2$CH$_3$); 4.26 (t, 2H, OCH$_2$); 4.06 (m, 4H, *C*H_2 CH$_3$); 3.67 (12H, 2 × CH$_3$ and 2 × CH$_2$CH$_2$CO$_2$CH_3); 3.30 (q, 4H, CH$_2$CH_2 CO$_2$CH$_3$); 2.52 (s, 6H, 2 × ring CH$_3$); 0.72, 0.98−2.01 (several m, total 13H, (CH$_2$ *(CH$_2$)$_5$CH$_3$*); 1.08 (t, 6H, 2 × CH$_2$ *CH$_3$*); −3.21 and −3.31 (each s, 1H, 2 × NH). HRMS calcd for $C_{49}H_{60}N_4O_5$: 784. 4557. Found 785. 4560 (M + 1).

2,8-Diethyl-7,8-*vic*-dihydroxy-13,17-bis(2-methoxycarbonylethyl)-5-(4′-methoxyphenyl)-3,7,12,18-tetramethylporphyrin (32) and 2,8-Diethyl-7,8,17,18-tetrahydroxy-13,17-bis(2-methoxycarbonylethyl)-5-(4′-methoxyphenyl)-3,7,12,18-tetramethylporphyrin(38). The methoxyphenylporphyrin **5** (100 mg) was dissolved in dichloromethane, and a few drops of pyridine were added. OsO_4 (100 mg) dissolved in ether (2 mL) was added, and the reaction mixture was stirred at room-temperature overnight. The reaction was diluted with dichloromethane (50 mL), and hydrogen sulfide gas was bubbled through the solution. It was then filtered, and the solvent was evaporated. The crude product was purified by preparative plates, using 5% methanol/dichloromethane as a solvent; three bands were separated and identified as follows: (a) the faster moving band (minor amount) was characterized as the starting porphyrin, the middle band [major product, 50 mg (48%)] was identified as dihydoxychlorin **32**. UV/vis [CH_2Cl_2, λ_{max} (ϵ): 399 (100 300); 499 (31 000); 592 (26 000); 646 (40 000)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90, 9.62, 9.22 (each s, 1H, 3 × meso H); 7.90, 7.70 (each d, H, phenyl H) and 7.20 (m, 2H, phenyl H); 4.30 and 4.25 (each t, 2H, 2 × CH_2 CH$_2$CO$_2$CH$_3$), 4.10 (s, 3H, OCH$_3$); 4.00 (q, 2H, ring A CH_2 CH$_3$); 3.69, 3.68 (each s, 3H, CH$_2$CH$_2$CO$_2$CH_3); 3.46, 3.48 (each s, 3H, 2 × ring CH$_3$); 3.20 (m, 4H, 2 × CH$_2$CH_2 CO$_2$CH$_3$); 2.40 (q merged with s, 5H, ring B CHCH and 3-CH$_3$); 1.70 (t, 3H, ring A CH$_2$CH_3); 1.50 (s, 3H, ring B CH$_3$); 0.50 (t, 3H, 8-CH$_2$CH_3); −2.38 (s, 2H, 2NH). HRMS calcd for $C_{43}H_{50}N_4O_7$: 734. 3679; Found: 734. 3670. Anal. Calcd for $C_{43}H_{50}N_4O_7$: C, 70.28, H, 6.86, N, 7.62. Found: C, 69.71, H, 6.80, N, 7.99.

The most polar band was isolated in minor amount (10 mg) and was characterized as dihydroxybacteriochlorin **38** as an isomeric mixture. UV/vis [CH_2Cl_2, λ max (ϵ)]: 379 (121 000); 478 (11 000); 508 (24 000); 712 (55 000). HRMS calcd for $C_{43}H_{52}N_4O_9$: 768.3628 − 18 (H_2O) = 750.3628; Found 750.3594. Anal. Calcd for $C_{43}H_{52}N_4O_9$: C, 67.12; H, 6.82; N, 7.29. Found: C, 67.32; H, 6.74, N, 7.39.

2,8-Diethyl-7,8-*vic*-dihydroxy-13,17-bis(2-methoxycarbonylethyl)-5-(3,5-dimethoxyphenyl)-3,7,12,18-tetramethylporphyrin (33). The dimethoxyphenylporphyrin **6** (100 mg) was dissolved in CH_2Cl_2 (20 mL) and pyridine (0.25 mL) and reacted with OsO_4 (90 mg) in ether (2 mL) for 6 h. The major band was isolated after the standard workup described for **32**, and the desired product was isolated in 55% (57 mg) yield as a green solid, mp 237−240 °C. UV/vis: [CH_2Cl_2, λ_{max} (ϵ)] 396 (100, 300); 499 (31, 000); 592 (25, 000); 646 (39, 900)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.87, 9.63, 9.23 (each s, 1H, 3 × meso H), 7.26, 6.98, 6.85 (each s, 1H, phenyl H); 4.28, 4.17 (each t, 2H, 2 × CH_2 CH$_2$CO$_2$CH$_2$); 4.00 (q, ring A CH$_2$); 3.98, 3.89, 3.69, 3.66, 3.49, 3.45, 2.52 (each s, 3H, 2 × CH$_2$CH$_2$-CO$_2$CH_3 and 2 × OCH$_3$ and 3 × ring CH$_3$); 3.17 (m, 4H, 2 × CH$_2$CH_2 CO$_2$CH$_3$); 2.38 (q, 2H, ring 8-CH$_2$CH_3); 1.60 (s, 3H, ring B CH$_3$); 0.55 (t, 3H, ring B CH$_2$CH_3); −2.33 (s, 2H, 2 × NH). Anal.Calcd. for $C_{44}H_{52}N_4O_8$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.72; H, 6.79; H, 7.22**.**

2,8-Diethyl-5-(4′-hexyloxylphenyl)-7,8-dihydroxy-13,-17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylporphyrin (34). The title compound was prepared by reacting porphyrin **29** (50 mg) with osmium tetraoxide (50 mg), following the procedure discussed for the foregoing dihydroxy analogue, and was obtained in 70% (36 mg) yield, mp 122−124 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 398 (134 500); 500 (14 000); 646 (34 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86, 9.63, 9.22 (each s, 1H, 3 × meso H); 7.90, 7.65, 7.25, 7.15 (each dd, 1H, 4 phenyl H); 4.32 (t, 2H, OCH$_2$); 4.15 (m, 4H, 2 × CH_2CH$_2$-COOCH$_3$); 3.95 (m, 2H, 2-CH_2CH$_3$); 3.68 (s, 3H), 3.66 (s, 3H), 3.48 (3H), 3.44 (s, 3H) (2 × COOCH_3, 2 × ring CH_3); 3.17 (q, 4H, 2 × CH$_2$CH_2CO$_2$CH$_3$); 2.4 (s, 3H, ring-CH_3); 2.36 (m, 2H, 8-CH_2CH$_3$); 1.48 (s, 3H, 7-CH_3); 1.95, 1.68−1.25, 0.92 (several m, 8H, OCH$_2$(CH_2)$_4$CH$_3$, 6H, 2 × CH$_2$CH_3); 0.55 (t, 3H, O(CH)$_5$CH_3). HRMS calcd for $C_{48}H_{60}N_4O_7$: 804.4540. Found (FAB): *m/e* 805.4554 (M + 1).

2, 8-Diethyl-5-(4′-heptyloxylphenyl)-7,8-dihydroxy-13,-17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylporphyrin (35). Reaction of porphyrin **30** (40 mg) with osmium tetraoxide (40 mg) afforded the title compound in 68% (28 mg) yield, mp 132−134 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 398 (134 000); 500 (14 500); 646 (34 500). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86,

9.64, 9.22 (each s, 1H, 3 × meso H); 7.92, 7.66, 7.25, 7.16 (each dd, 1H, 4-phenyl H); 4.32 (t, 2H, OCH_2); 4.20 (m, 4H, 2 × CH_2-CH_2COOCH_3); 3.95 (m, 2H, 2-CH_2CH_3); 3.68 (s, 3H), 3.66 (s, 3H), 3.48 (3H), 3.44 (s, 3H) (2 × $COOCH_3$, 2 × ring CH_3); 3.18 (q, 4H, 2 × $CH_2CH_2COOCH_3$); 2.41 (s, 3H, 3-CH_3); 2.36 (m, 2H, 8-CH_2CH_3); 1.50 (s, 3H, ring-CH_3); 1.95, 1.70−1.27, 0.95 (several m, 10H, $OCH_2(CH_2)_5CH_3$, 6H, 2 × CH_2CH_3); 0.5 (t, 3H, $O(CH_2)_5CH_3$). HRMS calcd for $C_{49}H_{62}N_4O_7$: 818.4611. Found: 818.4622.

2, 8-Diethyl-5-(4′-decyloxylphenyl)-7,8-dihydroxy-13,-17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylporphyrin (36). Porphyrin **31** (60 mg), prepared by reacting the hydroxyphenylporphyrin (65 mg) **29** with 1-iododecane (1 mL), was treated with osmium tetraoxide (60 mg) by following the method discussed for the preparation of the related heptyl analogue **35** and was obtained in 72% (63 mg) yield, mp 135−137 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 398 (133 500); 500 (13 200); 646 (33 500). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86, 9.64, 9.22 (each s, 1H, 3 × meso H); 7.92, 7.66, 7.25, 7.16 (each dd, 1H, phenyl H); 4.30 (t, 2H, OCH_2); 4.20 (m, 4H, 2 × CH_2CH_2-$COOCH_3$); 3.95 (m, 2H, 2-CH_2CH_3); 3.68 (s, 3H), 3.66 (s, 3H), 3.48(3H), 3.44 (s, 3H) (2 × $COOCH_3$, 2 × ring CH_3); 3.18 (q, 4H, 2 × $CH_2CH_2COOCH_3$); 2.41 (s, 3H, 3-CH_3); 2.36 (m, 2H, 8-CH_2CH_3); 2.18, 2,12, 2.0−0.84 (several m, 16H, $OCH_2(CH_2)_8$-CH_3, 6H, 2 × CH_2CH_3, 3H, 7-CH_3); 0.5 (t, 3H, $O(CH)_5CH_3$). HRMS calcd for $C_{52}H_{68}N_4O_7$: 861.5166. Found: 861.5146

7,8-*vic*-Dihydroxy-3,8-diethyl-5-heptyl-17,18-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylchlorin (37). Porphyrin **7** (200 mg) was reacted with O_sO_4 (150 mg) by following the methodology discussed for the synthesis of the other diols. The product obtained after the standard workup was purified by silica column chromatography eluting with 5% methanol/dichloromethane. The title compound was obtained in 65% (136 mg) yield, mp 155−159 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 402 (130 000); 504 (13 250); 648 (29 500). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.75, 9.56, 0.9.00 (each s, 1H, 3 × meso H); 4.65 (m, 2H, $CH_2(CH_2)_5CH_3$); 4.25 (m, 2H, CH_2CH_2 $COOCH_3$); 4.15 (m, 2H, $CH_2CH_2CO_2CH_3$); 4.02 (m, 2H, 3-CH_2CH_3); 3.68, 3.64, 3.52, 3.45, 3.41 (each s, 2 × $COOCH_3$, 3 × ring CH_3); 3.15 (m, 4H, 2 × $CH_2CH_2COOCH_3$); 1.9−0.75 (several m, 3H, CH_3, 6H, 2 × CH_2CH_3, 2H, CH_2CH_3, 13H, $CH_2(CH_2)_5CH_3$). HRMS Calcd for $C_{43}H_{58}N_4O_6$: 726.4434 Found (FAB): *m/e* 727.4458 (M + 1).

3,7-Diethyl-7,8-dihydroxy- (39), 3,7-diethyl-17,18-dihydroxy- (40), and 7,8,17,18-tetrahydroxy-5-methoxycarbonyl-13,17-(2-methoxycarbonylethyl)-2,8,12,18-tetramethylchlorin (41). Porphyrin **8** (100 mg) was reacted with OsO_4 (100 mg) by following the procedure as discussed above. Two major bands were isolated: the less polar band was found to be a mixture of dihydroxychlorins **39** and **40** and could not be purified to individual isomer. The ^{1}H NMR spectrum of the mixture was quite complex, and it was difficult to assign the resonances of all the protons. HRMS calcd for $C_{38}H_{46}N_4O_7$ − H_2O = $C_{38}H_{44}N_4O_6$ = 668.3210. Found 668.3194. The most polar band was characterized as one of the possible isomers of tetrahydroxybacteriochlorin **41**, mp > 300 nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91. 8.10, 8.09 (each s, 1H, 3 × *meso*-H); 3.80 (t, 2H, ring C, $CH_2CH_2CO_2CH_3$); 4.28 (s, 3H, CO_2CH_3); 3.66, 3.48, 3.30, 3.01 (each s, 3H, 2 × $CH_2CH_2CO_2CH_3$ and 2 × ring CH_3); 2.90 (t, 2H, ring C, CH_2CH_2 CO_2CH_3); 3.60 (q, 2H, ring A CH_2CH_3); 2.40−2.60 (4 h, ring D $CH_2CH_2CO_2CH_3$); 2.38 (q, 2H, ring B CH_2CH_3); 2.34 and 2.13 (each s, 3H, ring B and ring D CH_3); 1.51 (t, 3H, ring A CH_2CH_3); −0.40 (t, 3H, ring B CH_2CH_3); -2.27 and −2.32 (each s, 1H, 2 × NH). Anal. Calcd for $C_{38}H_{48}N_4O_{10}$: C, 63.30, H, 6.71; N, 7.77. Found: C, 63.94; H, 6.64; N, 7.92.

7,8-*vic*-Dihydroxy-5-formyl-2,3,7,8,12,13,17,18-octaethylchlorin (42). 5-Formyloctaethylporphyrin **10** (200 mg) was reacted with OsO_4 (150 mg) for 16 h, and the title compound was isolated in 63% (134 mg) yield, mp 255−258 °C. UV−vis, [CH_2Cl_2, λ_{max}, (ϵ)]: 403 (114 700); 501 (12 000); 550 (10 000); 663 (33 000); 693 (18 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.65 (s, 1H, C*H*O); 9.45, 9.32, 8.70 (each s, 1H, 3 × meso H); 8.13 (s, 1H, O*H*); 3.96−3.62 (m, 12H, CH_2CH_3); 2.68−2.32 (m, 4H, CH_2CH_3); 1.82−1.68 (m, 18H, CH_2CH_3); 1.15 (t, 3H, CH_2CH_3); 0.52 (t, 3H, CH_2CH_3). Anal. Calcd for $C_{37}H_{48}N_4O_3$: C, 74.46; H, 8.10; N, 9.38. Found: C, 74.26; H, 8.36; N, 8.68.

2,7-Diethyl-13,17-(2-methoxycarbonylethyl)-5-(4-methoxyphenyl)-3,7,12,18-tetramethyl-8-ketochlorin (43). The *vic*-dihydroxy porphyrin **32** (100 mg) was treated with concentrated H_2SO_4 (10 mL) for 30 min at room temperature under a nitrogen atmosphere. The reaction mixture was poured in ice-cold water and extracted with dichloromethane. The dichloromethane layer was washed with aqueous sodium bicarbonate and again with water. The organic layer was dried over anhydrous sodium sulfate. The crude residue obtained after evaporating the solvent was purified by preparative plates using 5% methanol/dichloromethane as eluting solvents. The title product was crystallized from dichloromethane/hexane as a green powder. Yield: 40% (39 mg), mp 255−258 °C. UV/vis [$CHCl_2$, λ_{max} (ϵ): 408 (180 000); 511 (17 500); 550 (16 600); 589 (13 200); 646 (33 900)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.00, 9.98, and 9.80 (each s, 1H, 3 × meso H); 7.82, 7.12 (each m, 4H phenyl); 4.37 and 4.25 (each t, 2H, 2 × CH_2-$CH_2CO_2CH_3$); 4.20 (s, 3H, OCH_3); 4.12 (q, 2H, 2-CH_2CH_3); 3.75, 3.73, 3.67, 3.52, 2.40 (each s, 3H, 2 × $CH_2CH_2CO_2CH_3$ and 3 × ring CH_3); 3.25 (m, 4 h, 2 × $CH_2CH_2CO_2CH_3$); 2.38 (q, 2H, 7-CH_2CH_3); 1.60 (s, 3H, 7-CH_3); 0.50 (t, 3H, 7-CH_2CH_3); −2.17 and −2.75 (each s, 1H, 2 × NH). HRMS Calcd for $C_{43}H_{48}N_4O_6$: 716.3573; Found: 716. 3555.

2,7-Diethyl-13,17-(2-methoxycarbonylethyl)-5-(3,5-dimethoxyphenyl)-3,7,12,18-tetramethyl-8-ketochlorin (44). The *vic*-dihydroxy porphyrin **33** (100 mg) was treated with concentrated H_2SO_4 by following the methodology described for ketochlorin **43**, and the title compound was obtained in 42% (41 mg) yield. mp 245−250 °C. UV/vis [$CHCl_2$, λ_{max} (ϵ): 410 (185 000); 510 (17 000); 550 (16 500); 590 (13 000); 645 (34 000)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.99, 9.98, and 9.86 (each s, 1H, 3 × meso H); 7.16, 7.12, and 6.87 (each s, 1H, phenyl); 4.37 and 4.23 (each t, 2H, 2 × $CH_2CH_2CO_2CH_3$); 4.03 (q, 2H, 2-CH_2CH_3); 3.92 (s, 6H, 2 × OCH_3); 3.67, 3.66, 3.61, 3.49, 2.56 (each s, 3H, 2 × CH_2CH_2 CO_2CH_3 and 3 × ring CH_3); 3.25 (m, 4H, 2 × CH_2CH_2 CO_2CH_3); 2.40 (q, 2H, 7-CH_2CH_3); 1.76 (s, 3H, 7-CH_3); 0.30 (t, 3H, 7-CH_2CH_3); −2.18 and −2.78 (each s, 1H, 2 × NH). HRMS calcd for $C_{44}H_{50}N_4O_7$: 746.3673; Found: 746.3565.

3,7-Diethyl-5-heptyl-8-keto-13,17-bis(2-methoxycarbonylethyl)-3,7,12,18-tetramethylchlorin (45) and 2,8-Diethyl-5-heptyl-7-keto-13,17-bis(2-methoxycarbonylethyl)-3,8,12,18-tetramethylchlorin (46). The *vic*-dihydroxy porphyrin **37** (40 mg) was treated with 93% H_2SO_4 (10.0 mL) for 50 min at room temperature and under nitrogen atmosphere. The two isomers **45** and **46** were isolated in 46% (18.0 mg) and 36% (14.0 mg) yields, respectively.

Compound 45. mp 133−136 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 413 (154 600); 516 (14 500); 650 (26 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (s, 1H, 20-meso H); 9.88 (s, 1H, 10-meso H); 9.76 (s, 1H, 15-meso H); 4.92 (m, 2H, $CH_2(CH_2)_5CH_3$); 4.36 (t, 2H, $CH_2CH_2CO_2CH_3$), 4.22 (t, 2H, $CH_2CH_2COOCH_3$), 4.12 (m, 2H, CH_2CH_3); 3.67, 3.65, 3.60, 3.58, 3.48 (each s, 3H, 3 × CH_3, 2 × CH_2CH_2 CO_2CH_3); 3.22 (m, 4H, 2 × $CH_2CH_2COOCH_3$); 2.76 (m, 2H, CH_2CH_3); 2.25−0.80, 0.3 (several m, 16 H, 7-CH_3, 3H, 2-CH_2CH_3, $CH_2(CH_2)_5CH_3$); 0.92 (t, 3H, 7-CH_2CH_3); −2.2, −2.7 (each s, 1H, 2 × N*H*). Anal .Calcd for $C_{43}H_{56}N_4O_5$: C, 72.85; H, 7.96; N, 7.90. Found: C, 72.39; H, 8.44; N, 7.75.

Compound 46. mp 123−126 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 412 (176 000); 515 (14 500); 642 (26 400). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H, 10- H); 9.57 (s, 1H, 15- H); 8.98 (s, 1H, 20-H); 5.48 (m, 1H, CH_2 $(CH_2)_5CH_3$); 4.56 (m, 1H, $CH_2(CH_2)_5$-CH_3); 4.32 and 4.18 (t, 2H each, $CH_2CH_2COOCH_3$); 4.08 (m, 2H, 2-CH_2CH_3); 3.72 (s, 6H, 2 × $CH_2CH_2CO_2CH_3$); 3.60, 3.52, 3.46 (each s, 3H, 3 ring CH_3); 3.24, 3.19 (each t, 2H, 2 × $CH_2CH_2CO_2CH_3$); 2.70 (2H, 8-CH_2CH_3); 1.77 (t, 3H, 8-CH_2CH_3); 1.54, 1.38 (two m, 13H, $CH_2(CH_2)_5CH_3$ and 8-CH_3); 0.92 (t, 3H, 8-CH_2CH_3); 0.35 (t, 3H, $CH_2(CH_2)_5CH_3$); −2.00, −2.32 (each s, 1H, 2 × N*H*). Anal. Calcd for $C_{43}H_{56}N_4O_5$: C, 72.85; H, 7.96; N, 7.90. Found: C, 72.95; H, 8.54; N, 8.15.

5-Formyl-7-ketooctaethylchlorin (47). The *vic*-dihydroxy porphyrin **42** (40 mg) was treated with 93% H_2SO_4 (10 mL) for 50 min at room temperature under a nitrogen atmosphere.

After the standard workup, the title compound was obtained in quantitative yield (39 mg), mp 257−259 °C. UV−vis [CH_2Cl_2, λ_{max} (ϵ)]: 412 (211 800); 515 (17 100); 553 (18 500); 590 (13 300); 644 (41 000). ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.56 (s, 1H C*H*O); 10.04, 9.84 (each s, 1H, 15, 20-meso H); 9.16 (s, 1H, 10-H); 4.07−3.82 (m, 10H, 5 × CH_2CH$_3$); 3.76 (q, 2H, CH_2-CH$_3$); 2.72 (q, 4H, 2 × CH$_2$CH$_3$); 1.9−1.79 (m, 15H, 5 × CH$_2$CH_3); 1.65 (t, 3H, CH$_2$CH_3); 0.42 (t, 6H, 2 × CH$_2$CH_3). Anal. Calcd for $C_{37}H_{46}N_4O_2$: C, 76.78; H, 8.01; N, 9.68. Found: C, 76.56; H, 8.21; N, 9.47.

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