Pinacol−Pinacolone Rearrangements in *vic*-Dihydroxychlorins and Bacteriochlorins: Effect of Substituents at the Peripheral Positions

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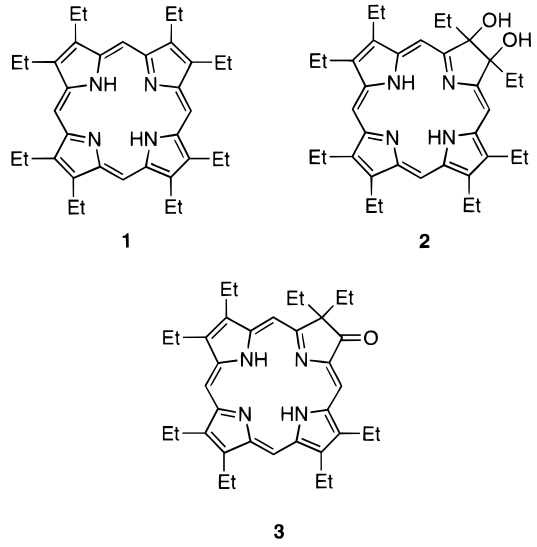
Upon reaction with osmium tetraoxide a series of porphyrins and chlorins were converted into the corresponding *vic*-dihydroxychlorins and bacteriochlorins. The presence of an electron-withdrawing substituent at a peripheral position on the porphyrins or chlorins deactivated that particular pyrrole unit toward oxidation, and also directed the oxidation regioselectively to the pyrrole ring opposite to the one bearing the electronegative group. The *vic*-dihydroxychlorins and bacteriochlorins were converted into the corresponding oxochlorins and dioxobacteriochlorins under pinacol−pinacolone reaction conditions. The migratory behavior of the various substituents were found to be quite complex, since distant conjugated peripheral substituents were able to affect the stability of the carbocation intermediates during the process; the ability to rearrange was affected not only by the intrinsic nature of the migratory group but also by steric and electronic factors operative elsewhere on the porphyrin and chlorin macrocycles. Preferential migration of the propionic ester over the methyl substituent in dioxobacteriochlorins obtained from 2,3,12,13-tetrahydroxycoproporphyrin II tetramethyl ester (IUPAC nomenclature) under pinacol−pinacolone conditions was confirmed by a single crystal X-ray study. The dioxobacteriochlorins obtained from mesoporphyrin III dimethyl ester and coproporphyrin II tetramethyl ester were converted into the corresponding dithio-analogues using Lawesson's reagent; this caused a red shift of 62 nm (compared with the dioxo compounds) affording long wavelength absorption at λ_{max} 746 nm.

Introduction

The formation of *gem*-dialkyl-*β*-oxoporphyrins with hydrogen peroxide in acidic media from alkylated porphyrins was reported by Fisher *et al.* in 1940.[1] Later, Bonnett *et al.*[2] and Inhoffen and Nolte[3] synthesized *vic*-dihydroxyoctaethylchlorin **2** by reacting octaethylporphyrin **1** with OsO_4; upon acid catalyzed pinacol−pinacolone rearrangement the oxochlorin **3** was obtained. Chang and co-workers[4] later reacted a variety of unsymmetrical porphyrins such as deuteroporphyrin IX dimethyl ester **4** with OsO_4 and, as expected, four possible vicinal dihydroxychlorins **4a**, **4b**, **4c**, and **4d** were obtained in almost equal quantity. Similar results were obtained with other unsymmetrical porphyrins such as mesoporphyrin IX dimethyl ester **5** and 3,8-(2-chloroethyl)deuteroporphyrin dimethyl ester **6**.[5] Treatment of *vic*-diols **4**, **5**, **6** (**a**, **b**, **c**, and **d**) under acidic conditions gave the ketones. The isomeric structure of the oxochlorins was confirmed by nuclear Overhauser enhancements (NOE) studies.[5]



1 **2** **3**

Studies on the migratory aptitude in generic pinacol rearrangements have been reported since 1950 in various systems.[6] Reaction rates are well documented for various alkyl and aryl groups with electron-donating and electron-withdrawing groups. It is generally accepted that the relative tendency of migration follows as aryl > alkenyl > alkyl. The reaction has been believed to proceed stepwise via a carbocation intermediate, similar to Wagner−Meerwein rearrangement.[7] According to this mechanism, pinacol rearrangement proceeds to the formation

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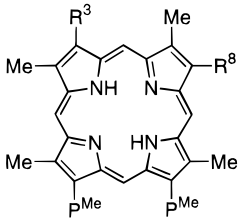
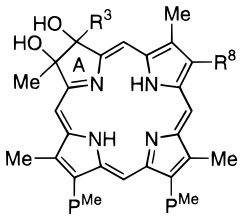
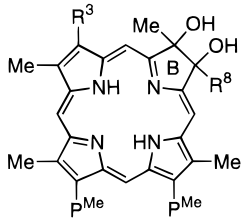


4: $R^3 = R^8 = H$
5: $R^3 = R^8 = Et$
6: $R^3 = R^8 = CH_2CH_2Cl$

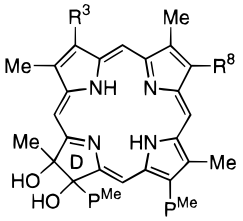
$P^{Me} = CH_2CH_2CO_2Me$



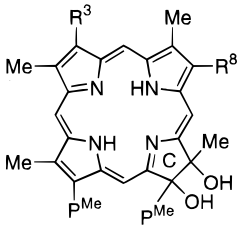
4a: $R^3 = R^8 = H$
5a: $R^3 = R^8 = Et$
6a: $R^3 = R^8 = CH_2CH_2Cl$



4b: $R^3 = R^8 = H$
5b: $R^3 = R^8 = Et$
6b: $R^3 = R^8 = CH_2CH_2Cl$



4d: $R^3 = R^8 = H$
5d: $R^3 = R^8 = Et$
6d: $R^3 = R^8 = CH_2CH_2Cl$



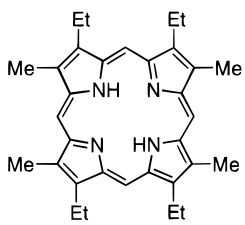
4c: $R^3 = R^8 = H$
5c: $R^3 = R^8 = Et$
6c: $R^3 = R^8 = CH_2CH_2Cl$

of a carbonyl compound via a 1,2-shift of the R group in the intermediate β-hydroxycarbocation. Recently, however, on the basis of molecular orbital calculations, Nakamura and Osamura[8] reported the possibility of a concerted mechanism without a carbocation intermediate in the pinacol rearrangement. The migratory aptitude of the hydride, methyl, vinyl, and cyclopropyl groups were calculated theoretically. The energy barriers for methyl migration and hydrogen migration were found to be 27.1 and 23.1 kcal/mol, respectively, indicating that hydrogen migration is preferred over methyl migration.

In this paper we report our studies on: (i) the synthesis of a series of porphyrins and chlorins with and without electron-withdrawing groups attached at peripheral positions, (ii) their conversion into *vic*-dihydroxychlorins, *vic*−dihydroxybacteriochlorins (in the case of oxidation of natural chlorins), and *vic*-tetrahydroxybacteriochlorins,[5b,9] and (iii) the competitive migratory reactions of the substituents during acid-catalyzed rearrangement of the vicinal diol to ketone.

Results and Discussion

For our study, a series of porphyrins and chlorins with and without electron-withdrawing substituents were used as substrates. Etioporphyrin II **7** was prepared by following the literature procedure.[10] Mesoporphyrin III dimethyl ester (40%) **8** and coproporphyrin II tetramethyl ester (42%) **9** were prepared by reacting the diformyldipyrromethane **10**[10] with dipyrromethane dicarboxylic acids **11**[11] and **12**, respectively, under McDonald[12] conditions. 3-Acetyl- **13** and 8-acetyl-deuteroporphyrin IX



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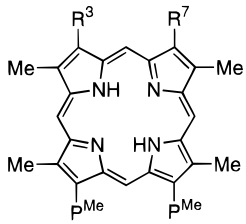
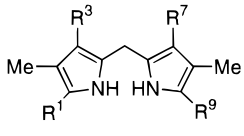
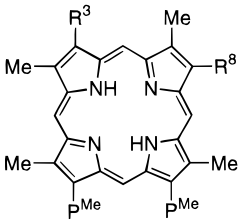


8: $R^3 = R^7 = Et$
9: $R^3 = R^7 = P^{Me}$

$P^{Me} = CH_2CH_2CO_2Me$



10: $R^3 = R^7 = P^{Me}$; $R^1 = R^9 = CHO$
11: $R^3 = R^7 = Et$; $R^1 = R^9 = CO_2H$
12: $R^3 = R^7 = P^{Me}$; $R^1 = R^9 = CO_2H$



13: $R^3 = COMe$; $R^8 = H$
14: $R^3 = H$; $R^8 = COMe$
15: $R^3 = R^8 = COMe$
16: $R^3 = R^8 = CH(OH)Me$

dimethyl ester **14** (IUPAC nomenclature) were prepared as a mixture from deuteroporphyrin IX dimethyl ester[4] by following the standard methodology reported in the literature.[13] The mixture was separated, in gram quantities, into the individual isomers either by preparative HPLC or by Chromatotron chromatography. 3,8-Diacetyldeuteroporphyrin IX dimethyl ester **15** was obtained in excellent yield by oxidation of hematoporphyrin IX dimethyl ester **16** (commercially available as the dicarboxylic acid) with tetrapropylammonium perruthenate/*N*-methylmorpholine *N*-oxide.[14]

It has been shown that octaethylporphyrin **1** can be converted into the tetrahydroxy bacteriochlorin **17** by reaction with OsO_4/H_2S; under acidic reaction conditions,[15] a mixture of two isomers **18** and **19** was obtained.

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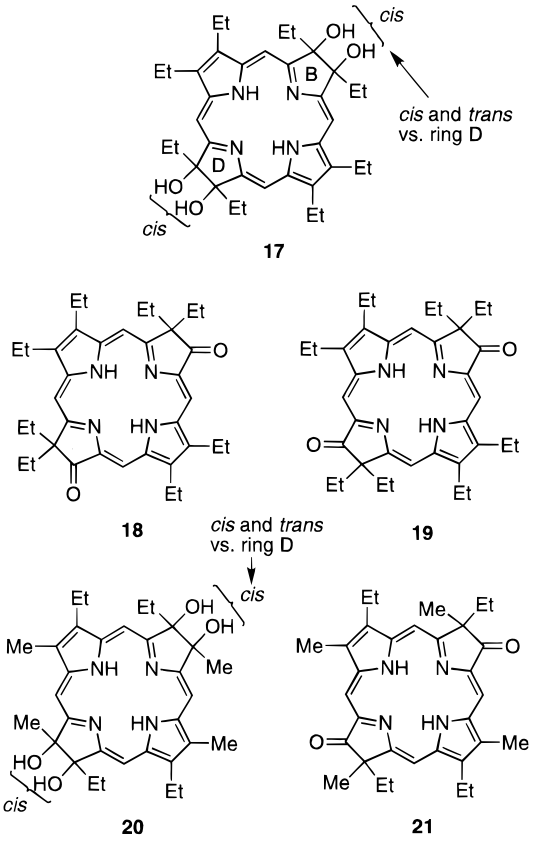
In order to understand the migratory behavior of various substituents, tetrahydroxybacteriochlorin **20** (a *cis*/*trans*



mixture of *cis*-diols), obtained from etioporphyrin II **7**, was treated with H_2SO_4, and the isomeric dioxobacteriochlorins **21** were isolated as the predominant product. Splitting of the saturated ring CH_3CH_2 group resonances in the proton NMR spectrum indicated the presence of isomeric forms in **21**, but carbon-13 NMR spectra failed to show evidence of *cis*/*trans* isomerism; NOE experiments (Figure 1A) indicated that the methyl group had migrated to give **21** as the only regioisomer. Reaction of porphyrin **8** with OsO_4 produced chlorin **22** as a major product in which a pyrrolic ring substituted with alkyl substituents (Me, Et) was transformed into the *vic*-dihydroxy derivative. Reaction of **8** with excess OsO_4 (then H_2S) gave bacteriochlorin **24** in 65% yield, along with a small amount of *vic*-dihydroxychlorin **22**. Following similar reaction conditions, coproporphyrin II tetramethyl ester **9** gave chlorin **23** and bacteriochlorin **25**, respectively. Reaction of *vic*-dihydroxychlorins **22**, **23** and bacteriochlorins **24**, **25** with H_2SO_4 under pinacol−pinacolone conditions produced oxochlorins **26** and **27**, and dioxobacteriochlorins **28a** and **30a** as major products, along with **28b** and **30b** as minor products. The isomeric structures of all the pinacolone products were confirmed by ^{1}H NMR spectroscopy. For example, due to symmetry in bacteriochlorin **30a**, the resonance for the meso protons were observed at 9.69 and 9.10 ppm, each integrating for two protons, and in dioxobacteriochlorin **30b** due to asymmetry associated with the molecule (ring "B" propionate ester group migrated over the methyl substituent, and in ring "D" the methyl group migrated over the propionic ester side chain), the meso protons were observed at 9.70, 9.60, 8.92, and 8.82 ppm, respectively. Similar results were obtained with bacteriochlorin **24**. The preferential migration of the ethyl (to give **26**

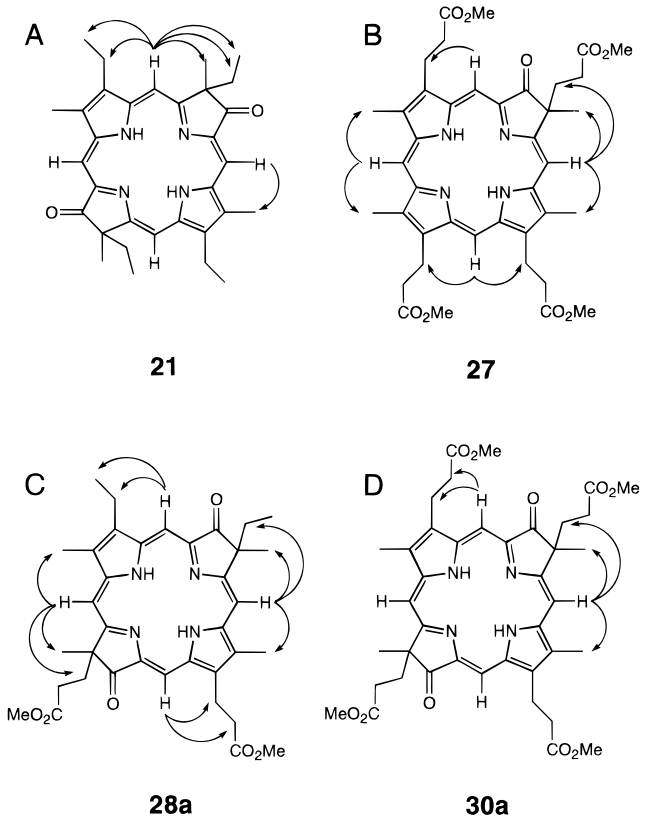


Figure 1. Nuclear Overhauser enhancement connectivities determined for A: compound **21**; B: compound **27**; C: compound **28a**; D: compound **30a**.

and **28a**) and the 2-(methoxycarbonyl)ethyl groups (to give **27** and **30a**, respectively) over methyl substituents was initially confirmed by NOE studies; typical NOE connectivities for compounds **27**, **28a**, and **30a** are shown in Figure 1B,C,D, respectively. Unambiguous proof of the structure of one crystalline isomer and its specific regiochemistry was obtained from a single crystal X-ray analysis. Figure 2 shows a view of the molecular structure of bacteriochlorin **30a**.[16a] The structure shows the typical geometrical characteristics of a bacteriochlorin.[16b] The C(3)−O(5) bond length, at 1.238(9) Å, is typical for the oxo-form. However, a slight inequivalency is found between the bond lengths of C(1)−C(2) at 1.525(10) Å and C(3)−C(4) at 1.471(10) Å, indicating some degree of participation by the carbonyl group in the conjugation via the latter bond. As is typical for hydroporphyrins, the compound shows an enlarged core with different center−nitrogen distances of 2.10 Å for the nitrogen in the reduced (oxo-modified) ring and 2.07 Å for the pyrrole nitrogen. The macrocycle shows slight deviations from planarity, the macrocyclic atoms deviating on average by 0.053 Å from their least-squares planes. Individual displacements of up to 0.2 Å are observed for some C_β-positions.

Bacteriochlorin **30b** had a strong long wavelength absorption at 684 nm (ϵ 90000). Conversion of oxo-(C=O)

(16) (a) The authors have deposited atomic coordinates and a full structure description for **30a** with the Cambridge Crystallographic Data Center. The structure can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK. (b) Barkigia, K. M.; Fajer, J.; Chang, C. K.; Young, R. *J. Am. Chem. Soc.* **1984**, *106*, 6457. Barkigia, K. M.; Gottfried, D. S.; Boxer, S. G.; Fajer, J. *J. Am. Chem. Soc.* **1989**, *111*, 6444.

(17) Cava, M. P.; Levinson, M. I. *Tetrahedron* **1985**, *41*, 5061.

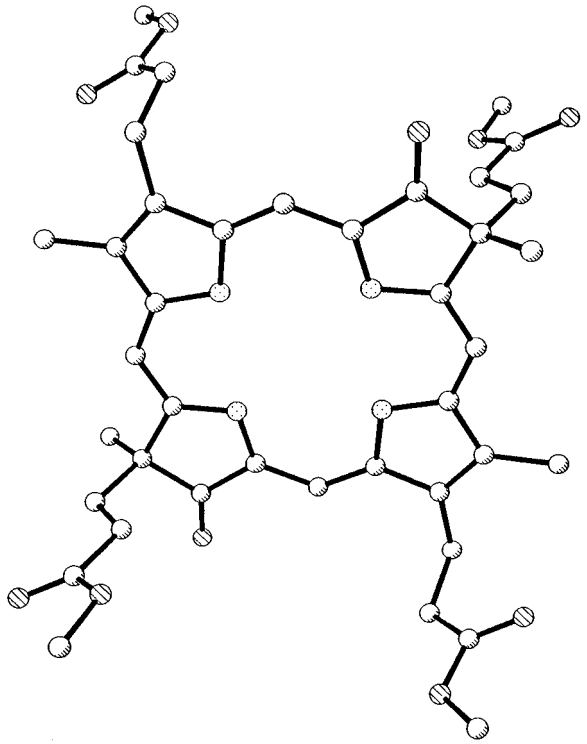
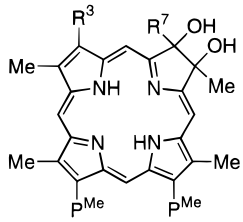


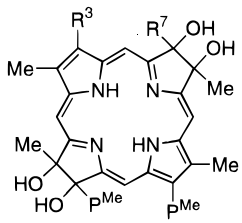
Figure 2. Crystal structure determination of dioxobacteriochlorin **30a**. Hydrogen atoms have been omitted for clarity.

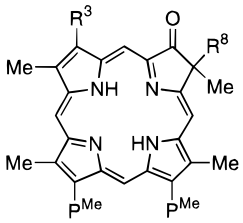
groups to thiono-(C═S) **31b** by reaction with Lawesson's reagent[17] gave a red shift of 62 nm, affording a strong absorption maximum at 746 nm. By following a similar approach, dithono derivative **29a** was prepared from the corresponding dioxo analogue **28a**. Osmium tetraoxide reactions with porphyrins **13**, **14** (in which the electron-withdrawing groups are present at position-3 or -8 of the macrocycle) under similar reaction conditions produced as major products the *vic*-dihydroxychlorin **32** and **34**, respectively, in which the hydroxylation occurred at the pyrrole rings opposite to the electron-withdrawing substituted pyrroles. These results suggest that in porphyrins, the electron-withdrawing groups deactivate both the pyrrole units to which they are attached and those immediately adjacent, and a regioselective synthesis of dihydroxy chlorins can therefore be achieved. Similarly 3,8-diacetyldeuteroporphyrin IX dimethyl ester **15** produced a mixture of dihydroxychlorins **37** and **38** which were separated into the individual isomers by preparative chromatography on silica gel. Pinacol−pinacolone rearrangement of *vic*-dihydroxychlorin **32** produced mainly the oxochlorin **33** in which the (2-(methoxycarbonyl)ethyl) group had migrated in preference to the methyl substituent. Surprisingly, *vic*-dihydroxychlorin **34** under pinacol−pinacolone conditions afforded a mixture of oxochlorins **35** and **36.** Chlorin **38** (structure was confirmed by NOE studies), upon treatment with acid, also gave a mixture of oxochlorins **39** and **40**. These compounds were not studied as their individual isomers. The structures of chlorins **32** and **34** were confirmed by NOE studies,[18] and also by preparation of the respective spirolactones **41** and **43**, following the methodology of Sotiriou and Chang.[5] The intramolecular lactonization was found to be a general base-catalyzed reaction. The formation of *cis*-lactones **41** and **43** were accomplished easily by



22: $R^3 = R^7 = Et$
23: $R^3 = R^7 = P^{Me}$

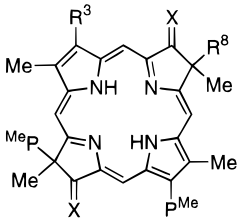
$P^{Me} = CH_2CH_2CO_2Me$

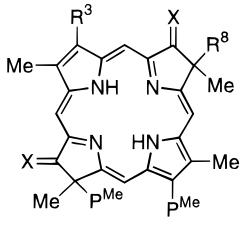




24: $R^3 = R^7 = Et$
25: $R^3 = R^7 = P^{Me}$
cis/*trans*, ring B vs. D

26: $R^3 = R^8 = Et$
27: $R^3 = R^8 = P^{Me}$





a: Major product >90%

b: Minor product ~5%

28: $R^3 = R^8 = Et$; X = O
29: $R^3 = R^8 = Et$; X = S
30: $R^3 = R^8 = P^{Me}$; X = O
31: $R^3 = R^8 = P^{Me}$; X = S

cis/*trans*, ring B vs. D

refluxing the respective diol with methanolic sodium acetate, while the *trans*-lactones **42** and **44** were obtained by epimerization of the corresponding *cis*- lactones with silica gel. The most obvious feature exhibited by the ^1H NMR spectra of the lactones is the disappearence of one methyl singlet due to the formation of the spirolactone from the OH group and the pyrroline propionic ester side chain. No methylene protons appear below 3.06 ppm in the ^1H NMR spectra. Almost the same pattern of ^1H NMR peaks was observed for the lactone **41** derived from 8-acetyl-17,18-dihydroxydeuterochlorin IX dimethyl ester, **32**, as well as lactones **43** obtained from 3-acetylporphyrin **34**. The spirolactone methylene proton signals overlapped with methyl peaks making further analysis difficult.

The procedure of Sotiriou and Chang[5] was followed in the conversion of the *cis*-isomer to the *trans*-isomer. The lactones **41** and **43** were loaded separately onto silica gel plates and then left inside the developing tank overnight (eluting with 3% methanol/dichloromethane); this gave compounds **42** and **44**, respectively, as the sole products. Stirring the lactones **41** and **43** with silica gel G overnight produced the same result; there were no significant changes in the R_f values before and after exposure to silica gel. The only difference observed in the ^1H NMR

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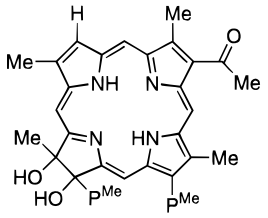
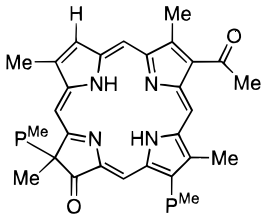
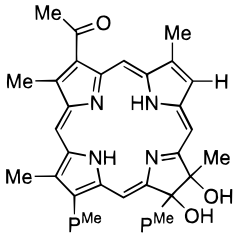


32

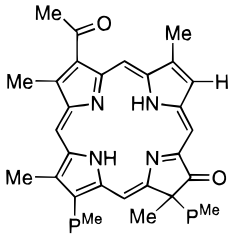


33

$P^{Me} = CH_2CH_2CO_2Me$



34



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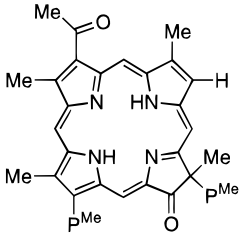
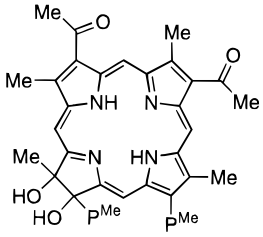
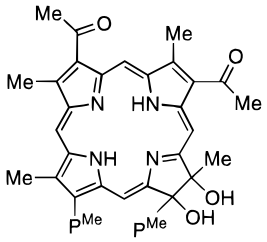


36



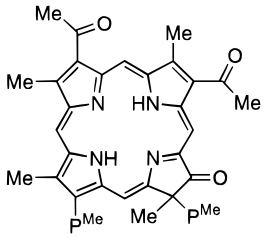
37



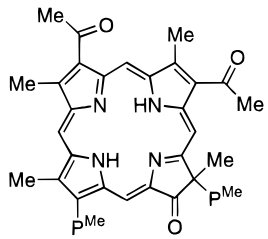
38

spectra (for example of compounds **43** and **44**) is the chemical shift pattern of the methyl resonances. Overlapping peaks in the region where the methylene signals appear make other assignments difficult. Currently, efforts are being made to grow good crystals for confirmatory X-ray studies.

In order to understand the effect of electron-withdrawing substituents upon the migratory behavior of alkyl substituents in the chlorin series, methyl mesopyropheophorbide-a **47**, methyl 3-formylpyropheophorbide-a **46**, methyl 3-de(1-hydroxyethyl)-3-acetylbacteriopheophorbide-d **50** [obtained from **49** by oxidation of the 3-substituent with tetra-*n*-propylammonium perruthenate/*N*-methylmorpholine *N*-oxide (NMO)], mesochlorin e_6 trimethyl ester **52**, and 3-formylchlorin e_6 trimethyl ester **53** were used as substrates. Methyl mesopyropheophorbide-a **47** and mesochlorin e_6 trimethyl ester **52** were obtained in quantitative yield by catalytic hydrogenation of methyl pyropheophorbide-a **45** and chlorin e_6 trimethyl ester **51**, respectively. Formyl derivatives **46** and **53** were prepared (in 80 and 75% yields, respectively) by reacting

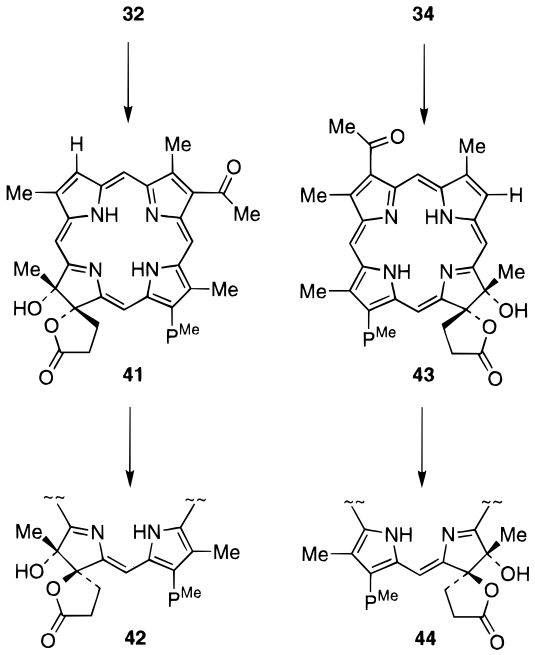


39



40

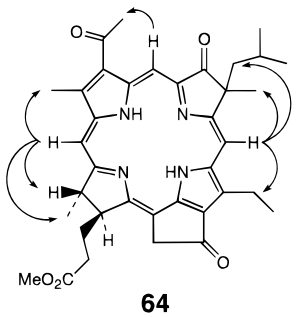
$P^{Me} = CH_2CH_2CO_2Me$



32 34 41 43 42 44

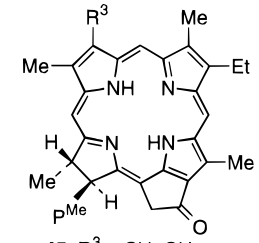
methyl pyropheophorbide-a **45** and chlorin e_6 trimethyl ester **51** with $OsO_4/NaIO_4$.

Reaction of methyl mesopyropheophorbide-a **47** with OsO_4/pyridine gave the dihydroxy bacteriochlorin **54** with *cis*-vicinal hydroxyl pairs either up or down (relative to ring D). When subjected to acid treatment, diol **54** gave the oxobacteriochlorin **61** in which the migrating group was ethyl (NOE studies). By following a similar approach, mesochlorin e_6 trimethyl ester **52** was converted into *vic*-dihydroxy bacteriochlorins **59**, which, under pinacol−pinacolone reaction conditions gave oxochlorin isomers **65**. Similarly **57**, obtained by OsO_4 oxidation of methyl 3-de(1-hydroxyethyl)-3-acetylbacteriopheophorbide−d **50** (prepared from bacteriopheophorbide-d **49** by oxidation with tetra-*n*-propylammonium perruthenate/

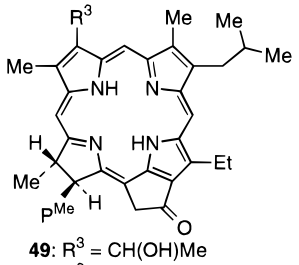


64

Figure 3. Nuclear Overhauser enhancement connectivities determined for compound **64**.

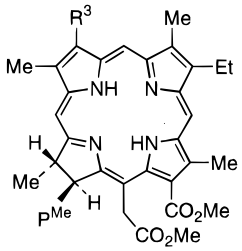


45: R^3 = CH=CH_2
46: R^3 = CHO
47: R^3 = Et
48: R^3 = CH(O-n-hexyl)Me

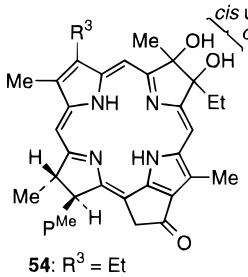


49: R^3 = CH(OH)Me
50: R^3 = COMe

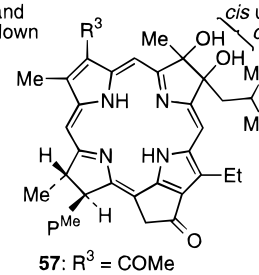
P^{Me} = $CH_2CH_2CO_2Me$



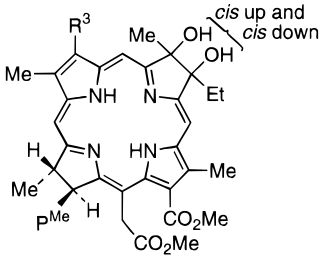
51: R^3 = CH=CH_2
52: R^3 = Et
53: R^3 = CHO



54: R^3 = Et
55: R^3 = CHO
56: R^3 = CH(O-n-hexyl)Me



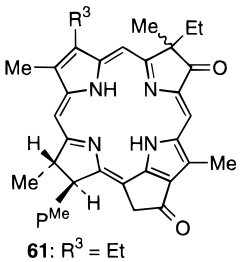
57: R^3 = COMe
58: R^3 = CH(OH)Me



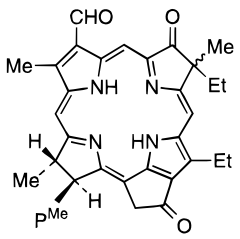
59: R^3 = Et
60: R^3 = CHO

NMO) gave *cis*/*trans* oxobacteriochlorins **64** as the sole regioisomer after reaction with H_2SO_4. Figure 3 shows the NOE connectivities observed in the proton NMR spectrum of **64**. Interestingly, under similar pinacol−pinacolone reaction conditions, the *vic*-dihydroxy bacteriochlorin **55** and **60** (obtained from methyl 3-devinyl-3-formylpyropheophorbide-a **46** and formylchlorin e_6 trimethyl ester **53**, respectively) produced a mixture of oxobacteriochlorins isomeric pairs **62**, **63** (from **55**) and **66**, **67** (from **60**).

Our study reveals that in porphyrin and chlorin systems the regioselective oxidation of pyrrole subunits in porphyrins by OsO_4 is significantly affected by the presence of electron-withdrawing groups at various points on the macrocycles. Migratory behavior of the substituents in subsequent pinacol−pinacolone rearrangements also depends upon the position and the number of the electron-withdrawing substituents present.

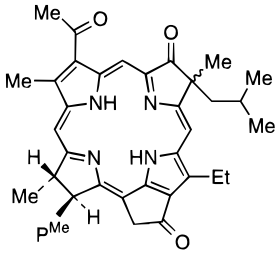


61: R^3 = Et
62: R^3 = CHO

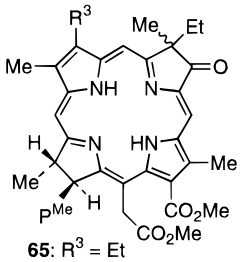


63

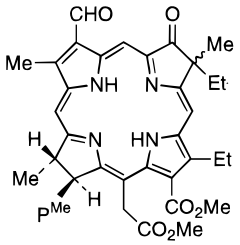
P^{Me} = $CH_2CH_2CO_2Me$



64



65: R^3 = Et
66: R^3 = CHO



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Experimental Section

General details are as previously described.[19] Carbon-13 NMR spectra were measured on a GE QE 300 spectrometer, at 75 MHz. Mass spectra were measured at the Mass Spectrometry Facility, University of California, San Francisco.

Crystal Structure Analysis of 30a. Crystals suitable for X-ray analysis could only be grown with difficulty due to the presence of a mixture of *cis*/*trans* isomers. Very small black parallelpipeds were finally obtained by slow evaporation of a solution of the compound in dichloromethane/methanol. Crystal data at 130 K (Cu Kα radiation, λ = 1.54178, $2\Theta_{max}$ = 108.5°), monoclinic, space group $P2_1/n$, a = 12.248(6) Å, b = 6.2720(10) Å, c = 24.113(5) Å, β = 90.62(3)°, V = 1852.3(10) Å^3, Z = 2, R = 0.092, R_w = 0.124 for 1517 reflections with $F > 3.0\sigma(F)$ and 244 parameters.

Methyl 3-Devinyl-3-formylpyropheophorbide-a (46). Methyl pyropheophorbide-a **45** (250 mg) [in tetrahydrofuran (60 mL)], sodium periodate (600 mg) [in water (15 mL) and dioxane (25 mL)], and osmium tetraoxide (45 mg) [in carbon tetrachloride (2 mL)] were mixed and then stirred at room temperature for 2 h. Progress of the reaction was monitored by spectrophotometry. The mixture was diluted with dichloromethane (200 mL) and washed with 2% aqueous sodium acetate, and again with water until pH 7. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue which was chromatographed on alumina (elution with dichloromethane). The major band was collected, and after evaporating the solvent the title compound was crystallized from CH_2Cl_2/hexane to give 200 mg (80% yield), mp 188−191 °C. λ_{max}: 386 nm (ϵ 61 000), 428 (69 500), 521

(19) Wallace, D. M.; Leung, S. H.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1993**, *58*, 7245.

(16 500), 554 (17 000), 632 (13 000), 695 (56 000). ^{1}H NMR (δ): 11.42 (s, 1H), 10.13, 9.43, 8.76 (each s, 1H), 5.16−5.29 (q, 2H), 4.53 (m, 1H), 4.33 (m, 1H), 3.74 (q, 2H), 3.70 (s, 3H), 3.69, 3.59, 3.20 (each s, 3H), 2.66 (m, 1H), 2.33 (m, 1H), 2.56 (m, 1H), 2.29 (m, 1H), 1.83 (d, 3H), 1.64 (t, 3H), −2.20 (br s, 2H). HRMS: Calcd for $C_{33}H_{34}N_4O_4$: 550.2580. Found: 550.2578. Anal. Calcd for $C_{33}H_{34}N_4O_4$: C, 71.98; H, 6.22; N, 10.17. Found: C, 71.84; N, 6.18; N, 10.12.

3-Devinyl-3-formylchlorin e$_6$ Trimethyl Ester (53). Chlorin e$_6$ trimethyl ester **51** (225 mg) was reacted with OsO_4 (50 mg) and $NaIO_4$ (900 mg) by following the procedure discussed for the foregoing compound; the title product was isolated in 80% yield (180 mg), mp 257−260 °C. λ_{max}: 417 nm (ϵ 49 000), 513 (4800), 546 (5200), 633 (2800), 690 (26 900). ^{1}H NMR (δ): 11.52 (s, 1H), 10.26, 9.62, 8.88 (each s, 1H), 5.25−5.48 (q, 2H), 4.5 (q, 1H), 4.32 (m, 1H), 3.80 (q, 2H), 4.25, 3.75, 3.72, 3.65, 3.60, 3.40 (each s, 3H), 2.66 and 2.29 (m, each 2H), 1.80 (t, 6H), −1.60 and −1.80 (each s, 1H). Anal. Calcd for: $C_{35}H_{40}N_4O_7$: C, 66.86; H, 6.41; N, 8.91. Found: C, 66.89; H, 6.28; N, 8.53.

Mesoporphyrin II Dimethyl Ester (8). Dipyrromethane-1,9-dicarboxylic acid **11** (1.1 g) and 1,9-diformyldipyrromethane **10** (1.26 g) were dissolved in dichloromethane (250 mL). *p*-Toluenesulfonic acid (4.0 g) dissolved in methanol (50 mL) was added, and the reaction mixture was stirred overnight under a nitrogen atmosphere. Zinc(II) acetate (4.0 g) dissolved in methanol (100 mL) was added, and the reaction mixture was stirred further for 12 h while a slow stream of air was bubbled through the solution. The dichloromethane layer was washed with water, aqueous sodium bicarbonate and again with water. The organic layer was separated and dried over anhydrous sodium sulfate, and the residue obtained after evaporating the solvent was treated with TFA (20 mL) for 1 h under an inert atmosphere. After the standard workup the residue was chromatographed on alumina (elution with dichloromethane). The major band was collected, and the solvent was evaporated. The title compound was crystallized from CH_2Cl_2/hexane, to give 620 mg (33%), mp 233 °C (lit.[20] 233 °C). ^{1}H NMR (δ): 10.08 and 10.06 (each s, 2H), 4.40 (t, 4H), 4.07 (q, 4H) ; 3.66 (s, 6H), 3.65, 3.62 (each s, 6H), 3.32 (t, 4H), 1.89 (t, 6H), −3.77 (s, 2H).

Coproporphyrin II Tetramethyl Ester (9). 1,9-Diformyldipyrromethane **10** (1.20 g) was condensed with dipyrromethane-1,9-dicarboxylic acid **12** (1.30 g) following the method discussed above for the foregoing porphyrin; the title porphyrin was obtained in 30% yield (630 mg), mp 285 °C (lit.[21] 286−289 °C). ^{1}H NMR (δ): 10.08 and 10.06 (each s, 2H), 4.46 (t, 8H), 3.70−3.75 (s, 24 H), 3.25 (t, 8H), −3.85 (s, 2H).

Methyl 3-De(1-hydroxyethyl)-3-acetyl-12-ethyl-8-isobutylbacteriopheophorbide-d (50). 12-Ethylbacteriopheophorbide-d **49** (200 mg) was dissolved in dichloromethane (200 mL), before addition of tetrapropylammonium perruthenate (20 mg) and *N*-methylmorpholine *N*-oxide (450 mg). The reaction mixture was stirred for 20 min (monitored by TLC). It was then diluted with dichloromethane and washed with water, and the organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to give a residue, which was chromatographed on a short column of alumina (elution with dichloromethane). The major band was collected. Evaporation of the solvent gave a residue which was crystallized from CH_2Cl_2/hexane to give the title compound (180 mg, 90%), mp 174−176 °C. ^{1}H NMR (δ): 9.98, 9.60, 8.76 (each s, 1H), 5.21 (q, 2H), 4.56 (q, 1H), 4.35 (m, 1H), 4.17 (q, 2H), 3.65, 3.62 (each s, 3H), 3.56 (d, 2H), 3.29, 3.28 (each s, 3H), 2.70−2.20 (m, 5H), 1.96 (t, 3H), 1.81 (d, 3H), 1.21 (d, 6H); 0.00 and −1.97 (each s, 1H). Anal. Calcd for $C_{37}H_{42}N_4O_4$: C, 73.24; H, 6.97; N, 9.23. Found: C, 73.04; H, 7.13; N, 9.29.

General Procedure for OsO_4 Reaction. The porphyrin or chlorin substrate was dissolved in dichloromethane. A few drops of pyridine were added, and OsO_4 dissolved in ether was added. The reaction mixture was stirred overnight in a sealed flask. The reaction was monitored by analytical TLC and spectrophotometry. H_2S gas was then bubbled through the solution for 2−3 min, and the mixture was diluted with dichloromethane. It was then filtered, the black precipitate was washed several times with dichloromethane, and the combined eluates were evaporated. The residue was chromatographed on a silica gel column (elution with 5% methanol/dichloromethane). The major band was collected. After evaporating the solvent the product was crystallized.

3-Acetyl-12,13-dihydroxydeuterochlorin IX Dimethyl Ester (34). 3-Acetyldeuteroporphyrin IX dimethyl ester **13** (100 mg) was dissolved in dichloromethane (300 mL), reacted with OsO_4 (98 mg, 0.385 mmol) in ether (2 mL) and 15 drops of pyridine, and stirred ovenight. The mixture was worked up by following the general method discussed above. The major brownish green band was collected from the column and crystallized from dichloromethane/*n*-hexane to give 71 mg (68%) of the title compound and 12 mg of starting porphyrin. Compound **34** had mp 109−110 °C. λ_{max}, 410 nm (ϵ 158 600), 508 (12 300), 542 (10 700), 580 (8300), 632 (26 700). ^{1}H-NMR (δ): 10.00 (s, 1H), 9.41 (s, 1H), 8.90 (s, 2H), 8.52 (s, 1H), 4.52 (br s, 2H), 4.05 (t, 2H), 3.71 (s, 3H), 3.52 (s, 3H), 3.40, 3.34 (each s, 6H), 3.27 (s, 3H), 3.01 (t, 2H), 2.89 (s, 3H), 2.75 (m, 2H), 2.61 (m. 2H), 2.12 (s, 3H), −2.51 (br s, 2H). HRMS: Calcd for $C_{34}H_{38}N_4O_7 \cdot H_2O$: 596.2629. Found: 596.2648 (38%, M − H_2O) and 520.2489 (100%). Anal. Calcd for $C_{34}H_{38}N_4O_7$: C, 66.44; H, 6.23; N, 9.11. Found: C, 66.23; H, 6.18; N, 9.19.

8-Acetyl-17,18-dihydroxydeuterochlorin-IX Dimethyl Ester (32). The same procedure as above was followed for *cis*-hydroxylation of 8-acetyldeuteroporphyrin-IX dimethyl ester **14** to give the desired dihydroxychlorin in 60% yield along with 10% of recovered starting compound. Mp 208−209 °C. λ_{max}: 412 nm (ϵ 141 700), 508 (12 600), 546 (12 200), 582 (10 000), 634 (28 400). ^{1}H-NMR (δ): 10.33 (s, 1H,), 9.69 (s, 1H), 9.02, 8.98 (each s, 1H), 8.89 (1H, s), 4.39 (br s, 2H), 4.11 (t, 2H), 3.69, 3.61, 3.40 (each s, 3H), 3.55, 3.50 (each s, 3H), 3.12 (t, 2H), 3.12 (s, 3H), 2.82 (m, 2H), 2.621 (m, 2H), 2.24 (3H, s), −2.16, −2.42 (each br s, 1H). HRMS: Calcd for $C_{34}H_{38}N_4O_7 \cdot H_2O$: 596.2629. Found: 596.2613 (100%, M − H_2O), 520.245782 (82%). Anal. Calcd for $C_{34}H_{38}N_4O_7$: C, 66.44; H, 6.23; N, 9.11. Found: C, 66.61; H, 6.18; N, 8.91.

Reaction of 3,8-Diacetyldeuteroporphyrin IX Dimethyl Ester with OsO_4. 3,8-Diacetyldeuteroporphyrin IX dimethyl ester **15** (250 mg) was reacted with OsO_4 (250 mg) by following the general procedure. After the standard workup two separate bands were isolated by preparative chromatography. Band A: *3,8-Diacetyl-17,18-dihydroxydeuterochlorin-IX dimethyl ester* ***37***, mp 205−208 °C. λ_{max}: 368 nm (ϵ 31 300), 420 (106 800), 514 (13 200), 548 (7800), 596 (8100), 650 (28 300). ^{1}H-NMR (δ): 10.04, 9.63 (each s, 1H), 9.43, 8.92 (each s, 1H), 4.82 (br s, 2H), 4.12 (m, 2H), 3.75, 3.49, 3.26 (each s, 3H), 3.43 (s, 6H), 3.13 (t, 2H), 3.03, 2.92 (each s, 3H), 2.80 (m, 2H), 2.40 (m, 2H), 2.34 (s, 3H), −1.84 (br s, 2H). HRMS: Calcd for $C_{36}H_{40}N_4O_8$: 656.2846. Found: 656.2870. Anal. Calcd for $C_{36}H_{40}N_4O_8$: C, 65.02; H, 6.14; N, 8.53. Found: C, 65.26; H, 6.43; N, 8.13. Band B: *3,8-Diacetyl-12,13-dihydroxydeuterochlorin-IX dimethyl ester* ***38***, mp 105−106 °C. λ_{max}: 354 nm (ϵ 29 100), 422 (125 100), 516 (14 000), 552 (10 200), 600 (9300), 652 (31 000). ^{1}H-NMR (δ): 10.15 (s, 2H), 9.00, 8.96 (each s, 1H), 4.50 (br s, 2H), 4.25 (m, 2H), 3.69, 3.54, 3.35 (each s, 3H), 3.50, 3.45 (each s, 3H), 3.10 (t, 2H), 3.06 (s, 6H), 2.75 (m, 2H), 2.60 (m, 2H), 2.24 (s, 3H), −2.25 (br s, 2H). HRMS: Calcd for $C_{36}H_{40}N_4O_8$: 656.2846. Found: 656.2814.

Methyl *cis*-7,8-Dihydroxymesopyropheophorbide-a (54) (Isomeric Pair). Methyl mesopyropheophorbide-a **47** was dihydroxylated in 60% yield following the same procedure as for 3-acetyldeuteroporphyrin-IX dimethyl ester. The title product had mp 145−146 °C. λ_{max}: 358 nm (ϵ 96 000), 371 (69 900), 484 (13 400), 514 (30 800), 636 (16 800), 694 (28 900). ^{1}H-NMR (δ): 8.31, 8.27, 7.90 (each s, 1H), 4.86−4.56 (q, 2H,), 4.03 (q, 1H), 3.82 (m, 1H), 3.61 (s, 3H), 3.53 (q, 2H), 3.18 (s, 3H), 3.04 (s, 3H), 2.47−2.19 (m, 4H), 1.86 (s, 3H), 1.80 (d, 3H), 1.59 (m, 2H), 1.33 (t, 3H), 1.22 (t, 3H), 0.21, 0.11 (each s, 1H). Anal. Calcd for $C_{34}H_{40}N_4O_5$: C, 69.84; H, 6.90; N, 9.59. Found: C, 69.94; H, 6.93; N, 9.32.

(20) Fischer, H.; Orth, H. *Die Chemie des Pyrrols*; Akademische Verlag: Leipzig, 1937; Vol. 2, part 1, p 436.

(21) Fischer, H.; Orth, H. *Die Chemie des Pyrrols*; Akademische Verlag: Leipzig, 1937; Vol. 2, part 1, p 489.

Methyl 3-Devinyl-3-formyl-7,8-dihydroxybacteriopyropheophorbide-a (55) (1:1 Diastereomeric Mixture of *cis*-Diols). Methyl 3-formylpyropheophorbide-a **46** (100 mg) was reacted with OsO_4 by following the general procedure, and the *vic*-dihydroxybacteriochlorin **55** was isolated in 74% yield (70 mg), mp 215−217 °C. λ_{max}: 368 nm (ϵ 76 600), 506 (9200), 542 (32 400), 688 (10 600), 754 (70 500). ^{1}H NMR (δ): 11.42 (s, 2H,), 8.74, 8.73, 8.94, 8.91, 8.67, 8.66 (each s, 1H), 5.0−5.20 (q, 4H), 4.41 (q, 2H), 4.23 (m, 2H), 3.65, 3.64 (each s, 6H), 3.53, 3.51 (each s, 3H), 2.40−2.67 (m, 8H), 2.36, 2.27 (s, 3H), 1.84, 1.80 (each d, 3H), 1.16, 1.01 (each t, 3H), 0.10 and 0.00 (each s, 1H), −1.22 (s, 2H). Anal. Calcd for $C_{33}H_{36}N_4O_6$: C, 67.79; H, 6.21; N, 9.58. Found: C, 67.92; H, 5.91, H, 9.73.

7,8-Dihydroxy-mesobacteriochlorin e_6 Trimethyl Ester (59) (Almost 1:1 Diastereomeric Mixture of *cis*-Diols). Mesochlorin e_6 trimethyl ester **52** (120 mg) was reacted with OsO_4 by following the general method, and after the chromatographic purification the title compound was isolated in 63% yield (80 mg), mp 155−158 °C. λ_{max}: 358 nm (ϵ 86 000), 448 (7500), 478 (9600), 508 (26 500), 652 (11 300), 718 (38 500). ^{1}H NMR (δ): 8.66, 8.47, 8.29 (each s, 1H, major isomer), 5.02 (q, 2H), 4.05−4.30 (m, 2H), 4.17, 3.72, 3.62, 3.30, 3.18 (each s, 3H), 3.70 (q, 2H), 2.1−2.5 (m, 4H), 2.06 (s, 3H), 1.66 (d, 3H), 1.65 (q, 2H), 0.98, 0.82 (each t, 3H) 0.66 and −0.38 (each s, 1H). Anal. Calcd for $C_{37}H_{46}N_4O_8$: C, 65.86; H, 6.87; N, 8.30. Found: C, 65.74; H, 6.92, H, 8.16. HRMS: Calcd for $C_{37}H_{46}N_4O_8 \cdot H_2O$: 674.3315. Found: 674.3323.

3-Devinyl-3-formyl-7,8-dihydroxychlorin e_6 Trimethyl Ester (60) (3:2 Diastereomeric Mixture of *cis*-Diols). 3-Formylchlorin e_6 trimethyl ester **53** (100 mg) was converted into the title compound in 62% yield upon reaction with OsO_4 by following the general method. The product had mp 143−146 °C. λ_{max}: 369 nm (ϵ 82 300), 528 (31 400), 690 (11 600), 750 (70 100). ^{1}H NMR (δ): 11.06 (s, 1H, major isomer), 10.91 (s, 1H, minor isomer), 9.32, 8.82, 8.53 (each s, 1H, major), 9.38, 8.56 and 8.48 (each s, 1H, minor), 5.25 (q, 4H), 4.22, 3.75, 3.67, 3.52, 3.43 (each s, 3H, major), 1.60−1.70 (m, 4H, minor and major), 4.22, 3.77, 3.64, 3.36, 3.25 (each s, 3H, minor), 1.98−2.70 (m, 8H), 2.25 (s, 3H, major), 2.20 (s, 3H, minor), 1.70 (d, 3H, major), 1.60 (d, 3H, minor), 0.70 (t, 3H, minor), 0.42 (t, 3H, major), −0.70, −0.85, −0.90 and −1.00 (each s, 1H). HRMS: Calcd for $C_{36}H_{42}N_4O_9$: 674.2945. Found: 674.2930.

Reaction of Methyl 3-De(2-hydroxyethyl)-3-acetyl-12-ethyl-8-isobutylpheophorbide-d with OsO_4 (1:1 Diastereomeric Mixture of *cis*-Diols). Methyl 3-de(1-hydroxyethyl)-3-acetyl-12-ethyl-8-isobutylpheophorbide-d **50** (80 mg) was treated with OsO_4 (50 mg) as discussed for the preparation of other *cis*-dihydroxybacteriopheophorbides, and the title compound was obtained in 59% yield (50 mg), mp: 224−227 °C. λ_{max}: 363 nm (ϵ 97 400), 536 (31 800), 652 (12 600), 746 (56 300). ^{1}H NMR (δ): 9.18, 9.15, 8.78, 8.72, 8.46, 8.44 (each s, 1H), 4.99 (q, 4H), 4.14 (m, 2H), 4.30 (m, 2H), 3.84 (q, 4H), 3.63, 3.62, 3.47, 3.46, 3.15, 3.13 (each s, 3H,), 2.00−2.52 (m, 10H); 1.86 [d, 2H], 1.83 (t merged, 6H), 1.56 (s, 6H), 1.02, 0.93, 0.88 and 0.70 (each d, 3H); 0.39, 0.25, −0.96 and −1.06 (each s, 1H). HRMS Calcd for $C_{37}H_{44}N_4O_6$: 596.2629. Found: 596.2620.

Methyl 3-(1-Hexyloxyethyl)-*vic*-7,8-dihydroxybacteriopheophorbide-a (56). Methyl 3-devinyl-3-[1-(hexyloxy)-ethyl]pyropheophorbide-a **48** (200 mg) was reacted with OsO_4 (200 mg) by following the general procedure discussed above, and the title compound was isolated in 70% yield (147 mg), mp 119−122 °C. λ_{max}: 359 nm (ϵ 94 000), 458 (9000), 486 (13 300), 518 (31 700), 644 (16 900), 704 (32 400). ^{1}H NMR: Due to the presence of four isomers the NMR spectrum was complicated, and it was difficult to assign all peaks. However, the meso region was well resolved; the meso ^{1}H assignments and CH(*O*-hexyl)CH_3 were as follows: 8.72, 8.42, and 8.06 (each s, 2H), 8.70, 8.68, 8.39, 8.38, 8.04, 8.02 (each s, 1H), 5.65 (m, 4H). Other assignments: 4.80 (m, 8H), 4.15 (m, 4H), 3.95 (m, 4H), 3.0−3.65 (several s, 3H); 2.48, 2.18 (each m, 8H), 1.1−2.00 (multiple peaks); 0.80 (m, 12H), −0.08 to −0.23 (m, 8H). Anal. Calcd for $C_{40}H_{52}N_4O_6$: C, 70.15; H, 7.65; N, 8.18. Found: 70.43; H, 7.75; N, 7.93.

Pinacol−Pinacolone Rearrangement: General Procedure. The *cis*-dihydroxychlorins or bacteriochlorins (typically 50 mg) were treated with concd H_2SO_4 (typically 10 mL) for 30 min at rt and under a nitrogen atmosphere. The reaction mixture was poured into ice cold water and extracted with dichloromethane, and the organic layer was washed with aqueous sodium bicarbonate and then with water. It was then dried over anhydrous sodium sulfate, evaporated to dryness, and the crude residue was purified using preparative silica gel plates (elution with 2% methanol in dichloromethane), or by column chromatography (silica gel or alumina; typically eluted with up to 2% methanol in dichloromethane). Most of the oxochlorins or dioxobacteriochlorins were crystallized from dichloromethane/hexane.

8,18-Dioxo Derivative of Etioporphyrin II (21). Etioporphyrin II **7** (200 mg) was reacted with OsO_4 (400 mg) in pyridine (0.5 mL); the 7,8,17,18-tetrahydroxybacteriochlorin **20** so obtained was not characterized, and was immediately treated with concd H_2SO_4 as described above. After the standard workup the title compound was purified by preparative plates, to give 75 mg (43%), mp 336−338 °C. λ_{max}: 400 nm (ϵ 178 500), 408 (197 700), 484 (9000), 510 (11 400), 552 (14 700), 622 (10 500), 622 (10 500), 650 (12 000), 684 (104 300). ^{1}H NMR (δ): 9.72, 9.05 (each s, 2H), 3.95 (q, 4H), 3.51 (s, 6H), 2.72 (q, 4H), 2.00 (s, 6H), 1.77 (t, 6H), 0.45 (t, 6H), −2.71 (s, 2H). ^{13}C NMR:(no evidence of *cis*/*trans* isomerism) δ, ppm, 210.4, 163.3, 146.1, 138.4, 135.9, 135.5, 132.8, 93.9, 93.7, 54.7, 32.0, 23.1, 19.5, 17.3, 11.1, 8.8. HRMS: Calcd for $C_{32}H_{38}N_4O_2$: 510.2994. Found: 510.3012. Anal. Calcd for $C_{32}H_{38}N_4O_2$: C, 72.26; H, 7.50, N, 10.97. Found: C, 72.05, H, 7.48, N, 10.86.

3,8-Diethyl-7,17-dioxo-13,18-bis[2-(methoxycarbonyl)ethyl]-2,8,12,18-tetramethylbacteriochlorin (28a) (Mixture of *cis* and *trans* Isomers). Mesoporphyrin II dimethyl ester **8** (120 mg) was reacted with OsO_4 (240 mg). After the standard workup, the tetrahydroxy analogue **24** was purified by silica gel column chromatography (elution with 10% methanol/dichloromethane). After evaporating the solvent, the product was crystallized from dichloromethane/hexane in 60% yield (150 mg). It was not characterized, but was treated immediately with H_2SO_4 as described in the general procedure to give the title compound in 62% yield (125 mg), mp 188−190 °C. λ_{max}: 410 nm (ϵ 180 000), 480 (10 000), 510 (12 000), 550 (17 000), 586 (13 000), 640 (35 000). ^{1}H NMR (δ): 9.71, 9.67, 9.07 and 9.06 (each s, 1H), 4.31 (t, 2H), 3.98 (q, 2H), 3.76, 3.52, 3.49 and 3.33 (each s, 3H), 3.22 (t, 2H), 3.03 (t, 2H), 2.72 (q, 2H), 2.08, 1.52 (each m, 1H), 2.03, 2.00 (each s, 3H), 1.77 (t, 3H), 0.46 (t, 3H), −2.73 and −2.79 (each s, 1H). ^{13}C NMR: (no evidence of *cis*/*trans* isomerism) δ, ppm, 210.2, 173.1, 173.0, 163.5, 162.4, 146.7, 145.6, 140.1, 137.0, 136.4, 135.6, 135.1, 134.2, 132.5, 131.9, 94.5, 94.0, 93.6, 93.6, 54.6, 53.1, 51.8, 51.3, 36.6, 33.1, 32.0, 28.9, 23.2, 23.2, 21.4, 19.3, 17.2, 11.3, 11.2, 8.8. HRMS: Calcd for $C_{36}H_{42}N_4O_6$: 626.3096. Found: 626.3092.

3,8-Diethyl-13,18-bis[2-(methoxycarbonyl)ethyl]-2,8,12,18-tetramethyl-7,17-dithionobacteriochlorin (29a). The foregoing dioxobacteriochlorin **28a** (30 mg) was dissolved in dry toluene (50 mL), and Lawesson's reagent (120 mg) was added in portions. The reaction mixture was refluxed under nitrogen for 1 h while being monitored by spectrophotometry. The solvent was evaporated, and the product was chromatographed on alumina (elution with dichloromethane). The major band was collected, and evaporation of the solvent gave a residue which was crystallized from dichloromethane/hexane to give the title compound in 65% yield (20 mg), mp 231−232 °C. λ_{max}: 373 nm (ϵ 22 200), 430 (84 500), 446 (68 400), 476 (98 200), 652 (22 100), 680 (26 200), 712 (23 000), 746 (87 000). ^{1}H NMR (δ): 10.03 and 9.91 (each s, 1H), 8.91 (s, 2H), 4.28 (t, 2H), 3.91 (q, 2H), 3.73, 3.46, 3.42, 3.01 (each s, 3H), 3.20 (t, 2H), 2.12−2.95 (m, 4H), 2.12 (q, 2H), 2.03, 2.00 (each s, 3H), 1.73 (t, 3H), 0.90 (t, 3H), −2.80 and −2.90 (each s, 1H). HRMS: Calcd for $C_{36}H_{42}N_4O_4$: 658.2647. Found: 658.2631. Anal. Calcd for $C_{36}H_{36}N_4O_4S_2$: C, 65.62; H, 6.43; N, 8.50. Found: C, 65.26; H, 6.57, N, 8.14.

3,8,13,17-Tetrakis[2-(methoxycarbonyl)ethyl]-2,8,12,18-tetramethyl-7-oxochlorin (27). Coproporphyrin II tetramethyl ester **9** (150 mg) was reacted with OsO_4 (300 mg) as described above. The resulting diol **23** was not characterized

but was subjected to pinacol−pinacolone rearrangement following the general procedure to afford the title compound in 68% yield (104 mg), mp 172−175 °C. λ_{max}: 404 nm (ϵ 183 400), 508 (15 500), 546 (17 800), 584 (12 300), 640 (37 000). ^{1}H NMR (δ): 9.87, 9.85, 9.77, 9.13 (each s, 1H), 4.38, 4.33, 4.20 (each t, 2H), 3.73, 3.66, 3.65, 3.57, 3.57, 3.43, 3.29, (each s, 3H), 3.25−3.04 (m, 8H), 2.09 (s, 3H), 2.10, 1.48 (each m, 1H), −2.96, −3.02 (each s, 1H). HRMS: Calcd for $C_{40}H_{46}N_4O_9$: 726.3258. Found: 726.3251. Anal. Calcd for $C_{40}H_{46}N_4O_9$: C, 66.10; H, 6.38; N, 7.71. Found: C, 66.31; H, 6.28; N, 7.58.

3,8,13,18-Tetrakis[2-(methoxycarbonyl)ethyl]-2,8,12,18-tetramethyl-7,17-dioxobacteriochlorin (30a) (Mixture of *cis* and *trans* Isomers). Coproporphyrin II tetramethylester **9** (120 mg) was reacted with excess OsO_4 (240 mg), and the intermediate tetrahydroxybacteriochlorin was purified, but not characterized, and was immediately reacted with H_2SO_4. After the standard purification, the title compound was obtained in 62% yield (77 mg), mp 229−230 °C. λ_{max}: 408 nm (ϵ 189 800), 484 (9000), 510 (12 100), 552 (14 400), 620 (10 100), 650 (11 500), 684 (90 000). ^{1}H NMR (δ): 9.69, 9.10 (each s, 2H), 4.31 (t, 4H), 3.77, 3.53, 3.33 (each s, 6H), 3.22, 3.04 (each t, 2H), 2.12, 1.54 (each m, 2H), 2.05 (s, 6H), - 2.78 (s, 2H).). ^{13}C NMR: (no evidence of *cis*/*trans* isomerism) δ, ppm, 209.0, 173.0, 172.9, 162.5, 146.0, 136.7, 136.0, 134.7, 133.1, 94.6, 93.7, 53.1, 51.8, 51.3, 36.6, 33.1, 28.9, 23.2, 21.4, 11.4. HRMS: Calcd for $C_{40}H_{46}N_4O_{10}$: 742.3207. Found: 742.3222. Anal. Calcd for $C_{40}H_{46}N_4O_{10}$: C, 64.68; H, 6.24; N, 7.46. Found: C, 64.44; H, 6.19; N, 7.46.

3,8,13,18-Tetrakis[2-(methoxycarbonyl)ethyl]-2,8,12,18-tetramethyl-7,17-dithionobacteriochlorin (31a) (Mixture of *cis* and *trans* Isomers). The foregoing dioxobacteriochlorin **30a** (30 mg) was converted into the dithiono analogue by following the method discussed for the preparation of related bacteriochlorin **29a**; the title compound was isolated in 70% yield (22 mg), mp 283−286 °C. λ_{max}: 428 (ϵ 97 300), 446 (78 200), 476 (96 800), 656 (23 800), 680 (29 000), 713 (21 000), 746 (101 100). ^{1}H NMR (δ): 9.97, 8.92 (each s, 2H), 4.22 (t, 4H,), 3.67, 3.38, 3.21 (each s, 6H), 3.00 (m, 4H), 3.18 (m, 4H), 3.21, 2.90 (m, 4H), 2.00 (m, 4H), 2.02 (s, 6H), −1.79 (s, 2H). HRMS: Calcd for $C_{40}H_{46}N_4O_8S_2$: 774.2757. Found: 774.2753.

Methyl 7-Ethyl-8-oxomesopyropheophorbide-a (61) (Isomeric Pair). Methyl dihydroxymesopyropheophorbide-a **54** (60 mg) was treated with concentrated H_2SO_4 following the general procedure. The crude product was purified on silica gel plates and was crystallized from CH_2Cl_2/hexane to give 40 mg (69%), mp >300 °C. λ_{max}: 416 nm (ϵ 43 500), 506 (10 600), 536 (9800), 604 (9700), 658 (19 600), 712 (9500). ^{1}H-NMR (δ): 9.19, 8.78, 8.50 (each s, 1H), 5.30 (m, 2H), 4.40, 4.25 (each m, 1H), 3.83 (q 2H), 3.66, 3.60 (s, 6H), 3.28 (s, 3H, 2-Me), 2.60 (q, 2H), 2.60 and 2.23 (each m, 2H), 1.91 (d, 3H), 1.71 (d, 3H), 1.69 (t, 3H), 0.47 (t, 3H), −0.10, −1.68 (each s, 1H). HRMS Calcd for $C_{34}H_{38}N_4O_4$: 566.2888. Found: 566.2890.

Methyl 8-Deethyl-3-devinyl-7-ethyl-3-formyl-8-oxochlorin e_6 Trimethyl Ester (66) and Methyl 7-Demethyl-3-devinyl-8-methyl-3-formyl-7-oxochlorin e_6 Trimethyl Ester (67). The formyl-*cis*-7,8-dihydroxybacteriochlorin e_6 **60** was stirred with H_2SO_4, and after the standard workup the oxo derivative was isolated as a 3:2 mixture of **66** and **67** in a combined yield of 64%. This mixture was not separated. Mp 240−246 °C. λ_{max}: 365 nm (ϵ 78 600), 538 (29 700), 758 (56 700). ^{1}H NMR (δ): 11.27 (s, 2H), 9.47, 8.91, 8.60 (each s, 1H, minor isomer), 9.47, 8.84 and 8.65 (each s, 1H, major isomer), 5.18 (q, 4H), 4.26 (m, 4H) 4.40 (m, 2H), 4.20 (m, 2H), 4.22, 3.75, 3.68, 3.77, 3.55 (each s, 3H, minor), 4.22, 3.76, 3.67, 3.59 and 3.72 (each s, 3H, major), 2.00−2.58 (m, 8H), 2.34 (s, 3H, major), 2.22 (s, 3H, minor), 1.57−1.62 (m, 12H), 0.69 (t, 3H, minor), 0.52 (t, 3H, major), −0.64, −0.78 (each s, 1H, major), −0.89, −1.01 (each s, 1H, minor). HRMS Calcd for $C_{36}H_{40}N_4O_8$: 656.2840. Found: 656.2856.

3-Acetyl-7-isobutyl-8-oxobacteriopheophorbide-d (64) (Mixture of *cis* and *trans* Isomers). *cis*-Diol **57** [60 mg, obtained by reacting **50** (100 mg) with OsO_4 (100 mg)] was converted into the title compounds in 68% yield (53 mg) upon stirring with H_2SO_4 as described in the general procedure. Mp 182−185 °C. ^{1}H NMR (δ): 9.84, 8.93, 8.82 (each s, 1H), 5.24 (m, 2H), 4.52 (q, 1H), 4.34 (d, 1H), 4.08 (q, 2H), 3.64, 3.61, 3.32 (each s, 3H), 2.55−2.80 (m, 4H), 2.20−2.40 (m, 2H); 1.94 (t, 3H), 1.89, 1.87 (s, 3H total), 1.81 (d, 3H), 1.20−1.35 (m, 1H), 0.38−0.51 (four d, 6H total, *cis*/*trans* isomers), −0.62, −2.00 (each s, 1H). ^{13}C NMR (δ): 209.1, 199.0, 195.0, 173.3, 169.0, 163.0 (split, *cis*/*trans* isomers), 161.5, 148.1, 147.2 (split), 139.5, 137.2, 135.2 (split), 134.9, 133.7, 131.3, 108.7, 98.5, 97.0, 95.4, 53.1, 52.3, 51.7, 49.2, 48.1, 47.6 (split), 33.5, 30.8, 29.9, 26.3 (split), 25.7, 24.1, 24.0 (split), 23.4, 20.6, 16.7, 13.1. HRMS Calcd for $C_{37}H_{42}N_4O_5$: 622.3149. Found: 622.3029.

3-(1-Hydroxyethyl)-7,8-*cis*-dihydroxybacteriopheophorbide-d (58) (Mixture of Four Isomers). Acetylbacteriopheophorbide **57** (120 mg) was dissolved in dichloromethane (25 mL) and stirred at <5 °C. Sodium borohydride (100 mg) dissolved in cold methanol (10 mL) was added, and the reaction mixture was stirred under a nitrogen atmosphere for 15 min (monitored by TLC). After the standard workup, the crude reaction chromatographed as three bands; the least polar band (minor amount <5%) was identified as the starting material, the middle band (major amount) was characterized as the title compound, and the most polar band, which was in minor quantity (not characterized) was possibly a diol mixture obtained by reduction of both the acetyl group and the isocyclic keto group. The major band was crystallized from CH_2Cl_2/hexane in to afford 67 mg (70%), mp 170−172 °C. λ_{max}: 363 nm (ϵ 97 400), 536 (31 800), 652 (12 600), and 746 (56 300). ^{1}H NMR (δ): Due to the presence of four isomers, the NMR spectrum was complicated. The meso region was well resolved. The meso ^{1}H assignment and $CH(OH)CH_3$ assignments were as follows: 8.75, 8.65, 8.60, 8.55 (each s, 1H), 8.42, 8.38, 8.00, 7.95 (each s, 2H), 6.16 (m, 2H). Anal. Calcd for $C_{37}H_{46}N_4O_6$: C, 69.14; H, 7.21; N, 8.72. Found: 69.24; H, 7.13 and N, 8.59.

***cis*-3-Acetyl-12-hydroxydeuterochlorin-IX Methyl Ester 13,13-γ-Spirolactone (43).** 12,13-Dihydroxychlorin **34** (100 mg, 0.163 mmol) in dry methanol (25 mL) was refluxed with anhydrous sodium acetate (1.2 g) for 30 min. The solution after cooling was washed with water and then extracted with dichloromethane. The product was then purified on silica gel plates (elution with 5% methanol/dichloromethane) to yield the lactone (60 mg, 64%) after crystallization from dichloromethane/*n*-hexane. It had mp 246−248 °C. λ_{max}: 410 nm (ϵ 169 700), 506 (14 000), 540 (11 800), 578 (9100), 632 (28 900). ^{1}H-NMR (δ): 10.50 (s 1H), 9.66 (s, 1H), 9.05, 8.96 (each s, 1H), 8.66 (s, 1H), 4.05 (t, 2H), 3.99 (s, 1H), 3.69, 3.58, 3.28 (each s, 3H), 3.58 (s, 3H), 3.38−3.80 (m, 4H), 3.22 (3H, s), 3.06 (m, 2H), 1.87 (s, 3H), −2.37, −2.46 (each br s, 1H). HRMS: Calcd for $C_{33}H_{34}N_4O_6$: 582.24781. Found: 582.249773 (39%, M^+), 520.247587 (100%). IR: ν (KBr) 1777, 1716, 1639 cm^{-1}. Anal. Calcd for $C_{33}H_{34}N_4O_6$: C, 68.01; H, 5.89; N, 9.62. Found: C, 67.99; H, 5.85; N, 9.51.

***cis*-8-Acetyl-18-hydroxydeuterochlorin-IX Methyl Ester 17,17-γ-Spirolactone (41).** The same procedure as above was followed for the synthesis of the lactochlorin from **32**, to give the product in 64% yield, mp 250−252 °C. λ_{max}: 412 nm (ϵ 166 000), 506 (12 400), 546 (11 800), 578 (9200), 634 (32 500). ^{1}H-NMR (δ): 10.54 (s, 1H), 9.71 (s, 1H), 9.13, 9.06 (each s, 1H), 8.88 (s, 1H), 4.18 (t, 2H), 3.93 (s, 1H), 3.67 (s, 3H), 3.53 (s, 3H), 3.49 (s, 6H), 3.36−3.79 (m, 4H), 3.19 (s, 3H), 3.11 (m, 2H), 1.88 (s, 3H,), −2.50, −2.46 (each br s, 1H). HRMS: Calcd for $C_{33}H_{34}N_4O_6$: 582.24781. Found: 582.244540 (30%, M^+), 520.247072 (100%). Anal. Calcd for $C_{33}H_{34}N_4O_6$: C, 68.01; H, 5.89; N, 9.62. Found: C, 67.86; H, 5.83; N, 9.55.

***trans*-3-Acetyl-12-hydroxydeuterochlorin-IX Methyl Ester 13,13-γ-Spirolactone (44).** A mixture of *cis*-lactone **43** (8 mg), chloroform (15 mL), methanol (1 mL), and silica gel was stirred as a suspension overnight in the dark. The silica gel was filtered off, and then the solvent was removed from the eluates. The product was crystallized from dichloromethane/*n*-hexane to yield the *trans*-lactone (6 mg, 75%), mp 254−256 °C. λ_{max}: 410 nm (ϵ 169 700), 506 (14 000), 540 (11 800), 578 (9100), 632 (28 900). ^{1}H-NMR (δ): 10.548 (s, 1H), 9.82 (s, 1H), 9.08, 9.02 (each s, 1H), 8.69 (s, 1H), 4.15 (t, 2H), 3.92 (s, 1H), 3.75, 3.57, 3.45 (each s, 3H), 3.61 (s, 3H), 3.40−3.80 (m, 4H), 3.24 (s, 3H), 3.10 (m, 2H), 1.89 (s, 3H), −2.28 (br s, 2H). HRMS Calcd for $C_{33}H_{34}N_4O_6$: 582.2478. Found: 582.2481. Anal. Calcd for $C_{33}H_{34}N_4O_6$: C, 68.01; H, 5.89; N, 9.62. Found: C, 67.63; H, 5.93; N, 9.29.

***trans*-8-Acetyl-18-hydroxydeuterochlorin-IX Methyl Ester 17,17-γ-Spirolactone (42).** The same procedure as above was followed for the synthesis of *trans*-spirolactone from **41**. The product had mp 242−244 °C. λ_{max}: 412 nm (ϵ 166 700), 506 (12 500), 546 (12 100), 582 (9500), 634 (32 900). ^{1}H-NMR (δ): 10.57 (s, 1H), 9.75 (s, 1H), 9.14, 9.07 (each s, 1H), 8.92 (s, 1H), 4.23 (t, 2H), 3.90 (s, 1H), 3.70 (s, 3H), 3.52 (s, 3H), 3.51 (s, 6H), 3.39−3.80 (m, 4H), 3.20 (s, 3H), 3.10 (m, 2H), 1.88 (s, 3H, s), −2.41 (br s, 2H). HRMS: Calcd for $C_{33}H_{34}N_4O_6$: 582.2478. Found: 582.2468. Anal. Calcd for $C_{33}H_{34}N_4O_6$: C, 68.01; H, 5.89; N, 9.62. Found: C, 68.04; H, 5.93; N, 9.21.

3,8-Diacetyl-12-demethyl-13-methyl-12-oxodeuteroporphyrin IX Dimethyl Ester (39) and 3,8-Diacetyl-13-de[2-(methoxycarbonyl)ethyl]-12-[2-(methoxycarbonyl)ethyl]-13-oxodeuteroporphyrin IX Monomethyl Ester (40). 3,8-Diacetyl-12,13-*cis*-dihydroxydeuteroporphyrin IX dimethyl ester **38** (50 mg) was treated with H_2SO_4 (10 mL), and after the standard workup the title compounds were isolated as a mixture and were not separated. ^{1}H NMR (δ): 10.80, 9.92, 9.90, 9.60 (each s, 1H, major isomer), 9.75, 10.18, 9.68, 9.12 (each s, 1H, minor isomer); other peaks for major and minor isomers were difficult to distinguish. HRMS: Calcd for $C_{34}H_{38}N_4O_7$: 614.2735. Found: 614.2825.

8-Acetyl-17-de[2-(methoxycarbonyl)ethyl]-18-[2-(methoxycarbonyl)ethyl]-17-oxodeuterochlorin-IX Monomethyl Ester (33). To 8-acetyl-17,18-dihydroxydeuterochlorin IX dimethyl ester **32** (90 mg) was added concd H_2SO_4 (25 mL). The general procedure was followed to give, after crystallization from dichloromethane/*n*-hexane, 32 mg (36%) of the title compound, mp 172−174 °C. λ_{max}: 414 nm (ϵ 182 400), 516 (12 100), 564 (19 200), 582 (16 200), 638 (24 500). ^{1}H-NMR (δ): 10.72, 9.94, 9.73, 9.14 (each s, 1H), 9.08 (s 1H), 4.33 (t, 2H), 3.79 (s, 3H), 3.74, 3.29 (each s, 3H), 3.64, 3.62 (each s, 3H), 3.25 (s, 3H), 3.06 (t, 2H), 1.26 (t, 2H), 0.88 (t, 2H,), −2.81, −2.91 (each s, 1H). HRMS: Calcd for $C_{34}H_{36}N_4O_6$: 596.26346. Found: 596.262705 (100%, M^+). Anal. Calcd for $C_{34}H_{36}N_4O_6$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.33; H, 6.20; N, 9.29.

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