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Supplementary Material Available: Tables of thermal parameters for the two polymorphs of 2,3-dichloroquinizarin (3A and 3B) (2 pages); listings of observed and calculated structure factors for the two polymorphs of 2,3-dichloroquinizarin (**3A** and **3B**) (11 pages). Ordering information is given on any current masthead page.

Ascorbic Acid Photoreductions of Zinc(II) Chlorophyll Derivatives: Access to Metal-Free Isobacteriochlorins

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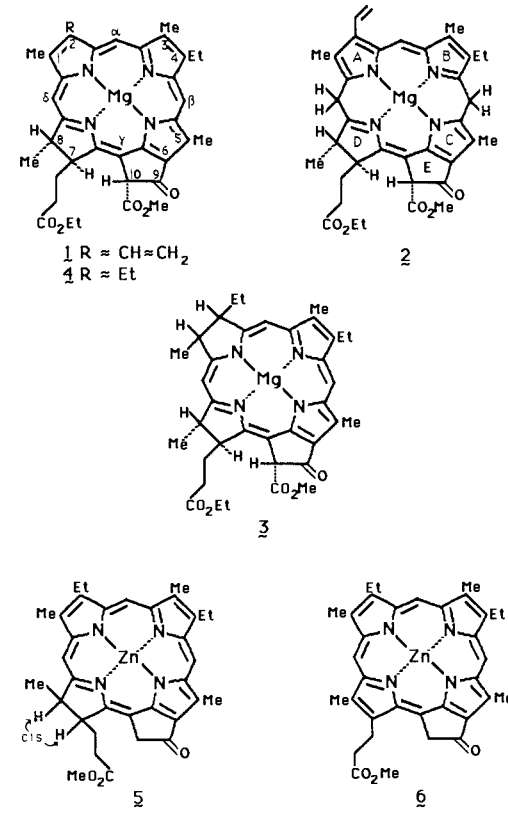
Abstract: The products and resultant stereochemistry of the ascorbic acid/organic base photoreduction of zinc(II) chlorins were investigated. In the pheophorbide series the reaction is shown to give a *cis*-isobacteriochlorin **15** with a vinyl group external to the newly reduced ring. It is further demonstrated that under the basic reaction conditions this vinyl group is prone to double-bond migration toward the ring to give a stable ethylideneisobacteriochlorin **10**. The biological implications of formation of the ethylidene moiety in this fashion are discussed. In addition, substituents were found to have a pronounced effect on the regiochemical selectivity of the reaction, as demonstrated by reduction of two rhodochlorin derivatives of methyl pheophorbide *a*. Demetalation of appropriate zinc(II) complexes yields the metal-free isobacteriochlorins **11**, **13**, and **15a**.

The ascorbic acid photoreduction of metalloporphyrins (to give chlorins) and metallochlorins (to give isobacteriochlorins) and the associated mechanistic pathways have been extensively investigated.[1-6] Originally, the interest in this area was focused on the possible relationship of this chemical reduction route to the biosynthetic formation of chlorophyll *a* from protochlorophyll. Early investigations[3,4] examined the roles of the organic base (e.g., pyridine) and the activator (ethanol or water), which were both necessary to afford reduction, and suggested that the base and ascorbate complexed to form the active reductant, which then reacted with the photoexcited metalloporphyrin or metallochlorin. The Lewis acid, which was also necessary, acts as a proton source. The product of chlorophyll *a*/ascorbic acid photoreduction, characterized by its unusual optical spectrum, is a pink compound (λ_{max} 525 nm), the formation of which can be reversed by oxygen or dehydroascorbic acid.

The structure of the ethyl chlorophyllide *a* (**1**, Chart I) photoreduction product was originally proposed to be the porphodimethene **2** by Krasnovski in 1948[5] and later confirmed by Scheer and Katz,[6] who monitored the photoreduction of chlorophyll *a* in pyridine-d_5 and hydrogen sulfide by proton NMR spectroscopy. However, prior to this structural determination, Seely demonstrated[7] that under specific conditions, photoreduction of **1** gives a stable tetrahydroporphyrin, which results from the rearrangement of the porphodimethene under light or dark conditions. The structural evidence in this report was based on a series of spectrophotometric experiments by Seely, who cleverly deduced the correct ring structure of the stable tetrahydroporphyrin.

Chart I



Primarily on the basis of interpretation of the blue-shifted band (626 nm) and on oxidation studies of the reduced products, Seely proposed the tetrahydroporphyrin **3** as the end product of the ascorbate photoreduction. The reduced product, upon oxidation with different quinone oxidants, gave optical spectra similar to those of mesochlorophyllide *a* (**4**).[7] Thus it was postulated that the vinyl group was in some way reduced during the course of

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(2) Seely, G. R.; Folkmanis, A. *J. Am. Chem. Soc.* **1964**, *86*, 2763-2770.
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(7) Seely, G. R. *J. Am. Chem. Soc.* **1966**, *88*, 3417-3422.

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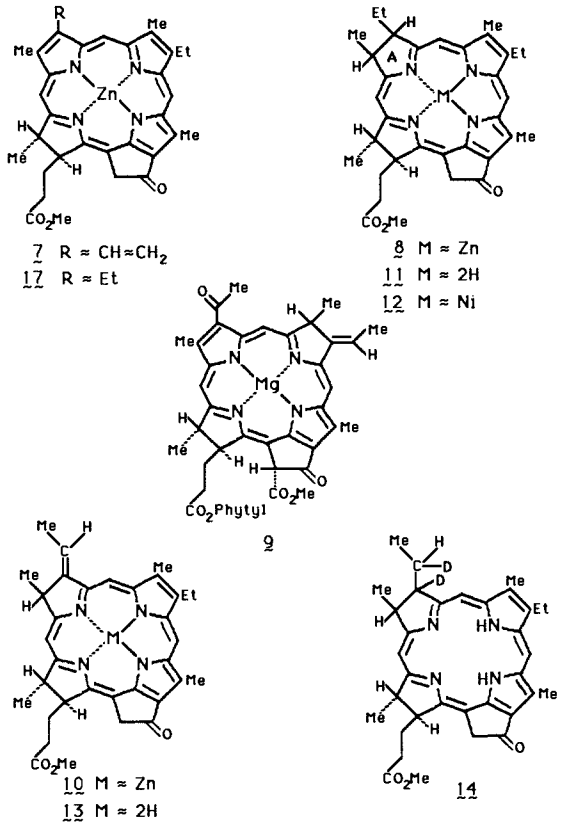
Chart II



the reaction. Since at the time this work was done there was no real biological interest in isobacteriochlorin (iBC) type tetrahydroporphyrins, no further significant investigations into the synthetic utility of this reaction were made.

The stereochemistry introduced into the newly reduced ring by the photoreduction of several zinc(II) porphyrins was investigated by Wolf and Scheer.[8,9] They found that the configuration of zinc(II) methyl mesopyropheophorbide *a* (**5**) obtained from the ascorbate photoreduction of zinc(II) phylloerythrin methyl ester (**6**) was cis and not trans as found in the pheophorbide from which **5** was derived, thereby developing a method for trans to cis isomerization of pheophorbides. It was further demonstrated that the stereochemistry of the newly reduced ring was in no way determined by the substitution pattern of the nearby 10-position. In addition, these authors found[10] a high degree of deuteriation (>90%) of the β and δ meso positions when the photoreduction was carried out in deuteriated solvents, as further evidence of the intermediate porphodimethene.

In light of the recent interest in iBCs (sirohydrochlorin,[11] heme d_1,[12] as an intermediate in formation of factor F430[13] models), we felt it would be useful to reinvestigate the photoreduction reaction.[14] At the same time we also wished to extend the applicability of the recently published work[15,16] involving synthesis

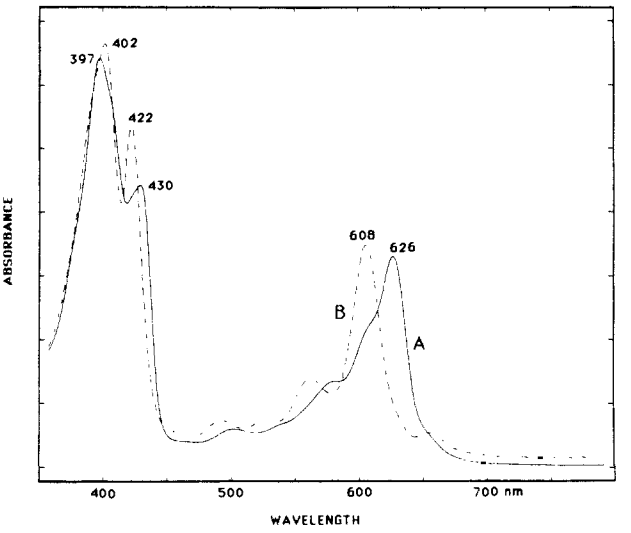


Figure 1. Optical spectra of (A) the photoreduction product **10** (in pyridine) from the reaction in pyridine and (B) the photoreduction product **15** (in pyridine) from the reaction in benzene.

of nickel(II) iBCs from nickel(II) chlorophyll derivatives, particularly with regard to preparation of metal-free iBCs (which were not accessible via the nickel route). Our intent was to fully characterize the products of this photoreduction and to determine if this reaction may provide a plausible method for synthesis of unsymmetrical iBCs, bearing in mind the recent interest that has developed in the iBC system. We also planned to explore the synthetic utility of this reduction with several other zinc chlorins in order to investigate what role substituents may play in the photoreduction.

Results and Discussion

Beginning with spectrophotometric-scale (5–10 μM) experiments, we looked at the photoreduction of zinc(II) methyl pyropheophorbide *a* (**7**, Chart II) using various irradiation wavelength regimes by employing glass filters. A 300-W tungsten–halogen projection lamp was directed through a glass filter and into the solution in either an optical glass cuvette or Pyrex flask. The distance from the light source to the reaction flask was approximately 6 in. Filters cutting out all light below 630, 600, 560, and 470 nm, as well as unfiltered light, were employed. We found no wavelength dependence of the final product distribution (two reduced products).

Under the above conditions with unfiltered light, reduction of a stirred solution of 20 mg of **7** with excess DABCO and ascorbic acid in 8% ethanol/pyridine (50 mL) was complete [<10% residual chlorin (spectrophotometry)] in approximately 1 h. The reaction was amenable to preparative scales (100–200 mg), and it was found convenient to perform irradiations overnight in the presence of excess DABCO and ascorbic acid under fluorescent white light. As observed by Seely[7] our reduced product had a long-wavelength absorption (Figure 1A) at 626 nm with a shoulder around 608 nm; it was obtained in about 55% yield after chromatography.

The high-field NMR spectrum (Table I) of this 626-nm product (in $CHCl_3$ and pyridine-d_5) was inconsistent with the expected product,[7] zinc(II) 2-ethylisobacteriochlorin (ZnEiBC) (**8**). However, the meso proton chemical shifts (8.38, 7.56, and 6.56 ppm) confirmed that ring A had been reduced. Furthermore, a one-proton multiplet at 6.80 ppm was coupled to a three-proton doublet (J = 7.1 Hz) at 2.15 ppm. The 6.80 ppm multiplet was also weakly coupled (J = 1–2 Hz) to a one-proton quartet at 4.55 ppm, which in turn was coupled (J = 7.3 Hz) to a set of doublets (three protons total) at 1.61 and 1.54 ppm. This $CH_3/CH/CH/CH_3$ spin system is indicative of, and consistent with, an

(8) Wolf, H.; Scheer, H. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 866.
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(14) For a preliminary report of part of this work, see: Smith, K. M.; Simpson, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 6834–6835.
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Table I. 360-MHz Proton NMR Shifts (ppm, in $CDCl_3$[a]) of **7** and Derived Isobacteriochlorins

	7	10	15	8	13	15a	11
α	9.52	8.37	8.32	8.48	8.39	8.38	8.30
				8.44			8.15
β	9.26	7.56	7.02	7.11	7.61	7.12	7.12
				7.10			7.00
δ	8.32	6.56	6.46	6.52	6.61	6.56	6.52
				6.49			6.45
2a-H	8.01	6.78	6.08		6.82	6.18	
2b,b'-H	6.07		5.33			5.48	
1-H		4.55	4.00	3.75	4.50	4.03	3.65
2-H			4.51	3.94		4.56	3.94
10-CH_2(AB q)	5.08	4.40	4.35	4.40	4.40	4.38	4.33
8-H	4.36	3.62	3.70	3.60	3.64	3.85	3.53 or 3.47
7-H	4.17	3.49	3.43	3.46	3.64	3.65	3.65
7-OMe	3.53	3.56	3.54	3.60	3.64	3.65	3.65
4-CH_2	3.71	3.26	3.20	3.25	3.29	3.25	3.20
5-Me	3.66	3.16	3.11	3.17	3.13	3.11	3.10
				3.13			3.15
3-Me	3.22	2.75	2.60	2.69	2.76	2.69	2.68
				2.67			2.62
2-CH_2				2.27			2.00
				2.10			1.90
				1.83			
7-CH_2CH_2	2.54	2.25	2.23	2.27	2.40	2.18	2.40
	2.45	2.05	2.08	2.10			2.15
	2.24		2.00	1.83			
	1.90						
2a-Me		2.13 (d) J = 7.1 Hz		1.10	2.16 (d), J = 5.2 Hz		1.20
				0.95			1.05
1-Me	3.30	1.61	1.46	1.56	1.67	1.65	1.50
				1.54			
8-Me	1.68	1.55	1.38	1.38	1.57	1.55	1.50
4a-Me	1.67	1.45	1.39	1.38	1.48	1.45	1.50

[a] Zinc complexes run with pyridine-d_5 in $CDCl_3$; all spectra were recorded at 25 °C.

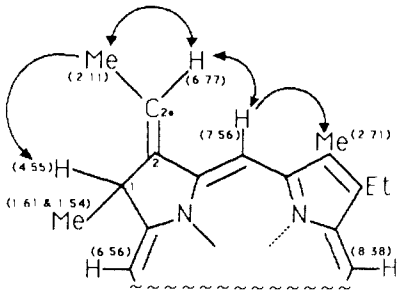


Figure 2. Network of nuclear Overhauser enhancement connectivities for compound **10**.

ethylidene structure similar to that of bacteriochlorophyll *b* (BChl-*b*) (**9**). Thus it appeared that the major reduction product was a zinc(II) ethylideneisobacteriochlorin (ZnEdiBC) (**10**). A minor (also reduced) product was observed in the NMR spectra and in the low-field region could be distinguished from the major product, but no structural information from this was evident.

Nuclear Overhauser enhancement (NOE) experiments confirmed the presence of the ethylidene moiety and were also used to determine the configuration of the ethylidene double bond. When the 6.80 ppm multiplet was irradiated, a positive enhancement was observed for the meso proton (α) at 7.56 ppm. Irradiation of this meso proton in turn showed enhancement of the multiplet at 6.80 ppm as well as a methyl group at 2.71 ppm. The 6.80 ppm multiplet was thus assigned as the 2a-H, the meso proton at 7.56 ppm as the α, and the 2.71 ppm resonance as the 3-Me. Irradiation at the methyl doublet (2a-CH_3) at 2.11 ppm showed no enhancement at any meso protons but showed a small enhancement for the 1-H at 4.55 ppm. The network of these NOE connectivities is summarized in Figure 2. Thus the methyl group of the ethylidene is directed over the reduced pyrrole ring and the hydrogen is directed toward the meso bridge. This *E* configuration is the same as found for BChl-*b*.[17]

(17) Risch, N. *J. Chem. Res.* (*S*) **1981**, 116–117.

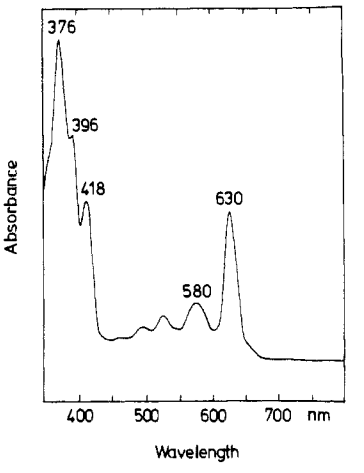
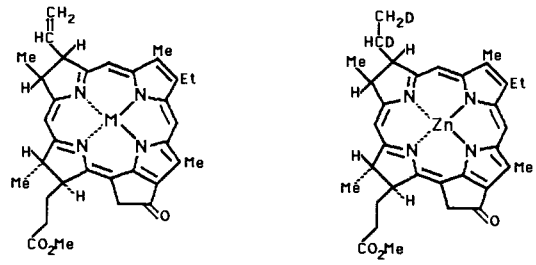


Figure 3. Optical spectrum (in dichloromethane) of the free base iBC **11**.

Under low temperatures (ice bath) and excluding oxygen ZnEdiBC (**10**) could be demetalated to the free base EdiBC (**13**), which was characterized by NMR spectroscopy (consistent with the zinc complex **10**) and its unique visible absorption spectrum. As with **10**, the visible spectrum of **13** had a shoulder on the long-wavelength absorption and appeared to be a mixture of at least two components. However, when catalytically reduced with hydrogen (or deuterium) over Pd/C, both **10** and **13** gave just one iBC (spectrophotometry). Reduction of **13** (or **10** followed by demetalation) gave 2-ethylisobacteriochlorin (EiBC) (**11**), which, when remetalated with nickel(II) acetate, gave Ni-iBC **12**, which was spectroscopically identical with the Ni-iBC obtained from Raney nickel reduction of Ni(II) methyl pyropheophorbide *a* reported earlier,[15] thus confirming the structures of **8**, **10**, **11**, and **13**.

EiBC (**11**), like EdiBC (**13**), appeared reddish blue in solution. The absorption spectrum (Figure 3) of **11** was similar to that of octaethylisobacteriochlorin[18] in that the Soret absorption (375–425

Chart III



15 M = Zn
15a M = 2H

16

nm) was split into three bands. However, the two lowest energy absorptions (584 and 630 nm) were reversed in intensity. We feel that this may be due to the presence of the strongly electron-withdrawing 9-keto group. This appears to be the first such iBC reported. The NMR spectrum (Table I) of EiBC also displayed unusual characteristics. The meso protons at room temperature in chloroform appeared as very broad singlets, while the remaining signals were much sharper. Above room temperature, at 50 °C the broad meso protons (8.28, 8.15, β-meso; 7.10, 7.00, α-meso; 6.49, 6.44, 6.41, δ-meso) sharpened considerably. At temperatures below 0 °C all peaks broadened even further until a coalescence was reached just above −55 °C, where new resonances began to appear for the meso protons. At −55 °C, the signals (compared with those observed at 25 and 50 °C) appeared to be split into two sets of signals for each meso proton. This splitting was symmetrical with respect to the signals observed at higher temperatures. The most likely explanation for this observation is that the doubling of peaks and peak broadening may be due to N–H tautomerism, which is slow on the NMR time scale. Such effects have previously been observed in chlorins[19,20] and in porphyrins[21] which showed similar coalescence temperatures. Alternately, it may be that at 25 and 50 °C the signals observed for the meso protons are an average signal for at least two very different conformations. At temperatures near −55 °C equilibration between these conformations is slowed to the point where they can be observed by NMR.

Catalytic reduction of **13** (or **10** followed by demetalation) with deuterium gave **14**, a compound with an NMR spectrum identical with that of **11** except for the marked decrease in intensity of the signals for the 2-H (3.92 ppm) and the 2-CH_2 (2.00 and 1.90 ppm) region. The fact that the 2-H signal was not completely absent in the spectrum is explained by the 608-nm side product, which does not contain an ethylidene group. Interestingly, oxidation of either **10** or **13** with 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ) gives methyl pheophorbide *a* (or the zinc complex (**7**)) as the only recoverable product. This result strongly suggested that the 608-nm side product contains a remote vinyl group on ring B, and in no case is there an ethyl group in the 2-position of any of the photoreduced products.

With the ethylidene compound characterized as the 626-nm photoreduction product and with the results of the catalytic hydrogenation and DDQ oxidations, it seemed logical that the 608-nm shoulder (Figure 1A) be zinc(II) 2-vinyl-iBC (ZnViBC) (**15**, Chart III). The NMR spectrum of **10** suggested this may be the minor product, particularly in the low-field region of the meso and vinyl protons. However, the high-field region was not sufficiently resolved to make assignments, and since the minor 608-nm product contributed only 15% of the mixture, no conclusions could be drawn about this side product from this spectrum. Furthermore, because the vinyl group in **15** would not be conjugated with the macrocycle, **15** is indistinguishable from compound **18** by either spectrophotometry or chromatography; thus further

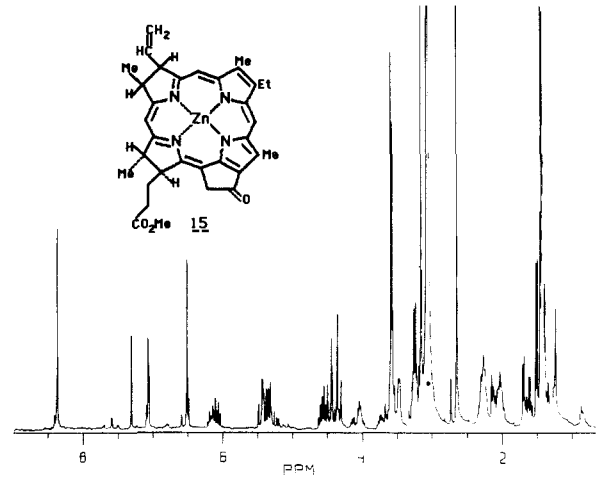


Figure 4. 360-MHz proton NMR spectrum (in $CDCl_3$ with pyridine-d_5) of zinc(II) 2-vinyl-iBC (**15**) obtained from the photoreduction in benzene. The asterisk indicates H_2O.

investigation was necessary to show that **15** is indeed a reduction product. Postulating structure **15** as the minor photoreduction product led us to the suggestion that **15** may be the actual photoreduction product, which, under basic reaction conditions, may undergo vinyl double-bond migration to give the ethylidene product **10**.

By controlling reaction conditions, namely reaction time, we found reduced product mixtures (**15** and **10**) enriched in the 608-nm product **15**. Carefully monitoring the reaction spectrophotometrically clearly showed that the 608-nm product accumulated prior to extensive formation of the 626-nm (**10**) product. Quenching the reaction at an early point in the photoreduction gave low yields of reduced products but enriched in **15** (up to 60% of the total mixture). While separation of the mixture of reduced products from reactants was routine, the separation of the two reduced products themselves was only possible by reversed-phase high-performance liquid chromatography (HPLC). The separation was best achieved on the free base mixture (but still possible with the zinc(II) complex) obtained by briefly treating the zinc complex with trifluoroacetic acid. Milligram quantities of free base **13** and **15a** were obtained for NMR analysis by multiple analytical HPLC injections, giving sufficient material (3–5 mg) for NMR decoupling experiments of EdiBC (**13**) and routine NMR (1 mg) of ViBC (**15a**). As with compound **11**, both **13** and **15a** exhibited broad meso protons and somewhat broadened methyl and methylene proton signals at room temperature. The NMR shifts of both of these compounds (Table I) were entirely consistent with the proposed structures, and the need for separation of **15** or **15a** on a preparative scale was negated in a subsequent reaction.

To deter ethylidene formation the reaction was carried out in an ethanol/benzene medium instead of ethanol/pyridine. By changing the solvent and reducing the amount of excess DABCO, we obtained ZnViBC (**15**) with only a very small amount (<5%) of ZnEdiBC (**10**) present in the mixture. Figure 1B shows the absorption spectrum in pyridine of this purified product and Figure 4 (and Table I) the NMR spectrum in $CDCl_3$ and pyridine-d_5. Isolation of this product in good yields (60% on 20-mg scale) allowed us to examine the NMR by decoupling without the need for tedious separation. Decoupling beginning with the 2a-H vinyl proton (6.10 ppm) was consistent with the proposed structure. Catalytic reduction of **15** with D_2 and Pd/C to give **16** confirmed the presence of the vinyl group in the reduced product **15** and gave absolute assignments for the 2-ethyl group of the ZnEiBC (**8**).

Apart from the reduced products isolated from the photoreduction, two other products consistent with the scheme of the reduction were also characterized from the reductions in pyridine. One product, identified by NMR spectroscopy and spectrophotometry, was zinc(II) methyl mesopyropheophorbide *a* (**17**); the other product was the free base of this same compound. It seems logical that **17** is formed by a vinyl migration of the ZnEdiBC

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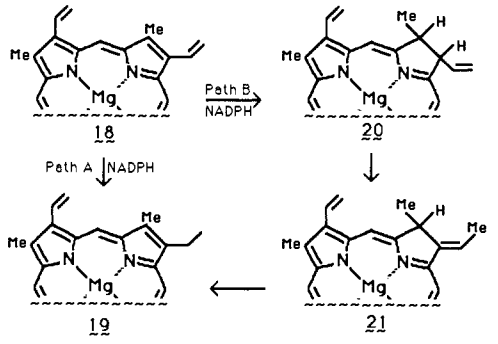
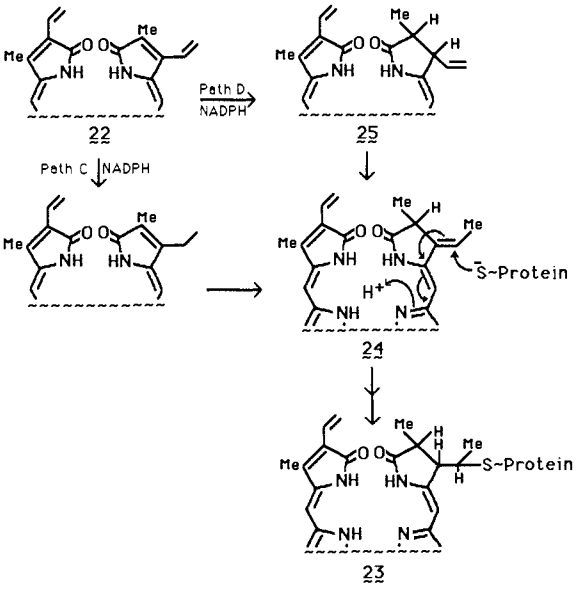
Scheme I. Possible Pathways for Biosynthetic Reduction of the 4-Vinyl Group in Chlorophyll *a* Precursors



Scheme II. Possible Pathways for Attachment of Protein Residues in Biliprotein Biosynthesis



(**10**). In fact, with prolonged irradiation or stirring in the dark, large amounts of this chlorin could be obtained. Although it was easily separated by chromatography from the ViBC/EdiBC mixture, its formation made it impossible to obtain the EdiBC product uncontaminated by ViBC in a greater ratio than 85/15 without HPLC separation. Thus formation of ZnEdiBC as the sole reduced product by prolonged base treatment was impossible.

Isolation of pure ZnViBC (**15**) also permitted an investigation of the stereochemical pathway followed in the photoreduction. As mentioned previously, the NMR spectra of this product indicated a mixture of at least two diastereomers. Separation of these diasteromers by reversed-phase HPLC proved fruitless in the case of the zinc complex **15** as well with the free base. Therefore, the 2-vinyl group was reduced and separation of the resulting ZnEiBC (**8**) and the free base **11** was investigated. In this case some separation of the free base compound was achieved but the resolution was poor and separation of quantities sufficient for NMR studies would be quite tedious. To circumvent this problem we inserted nickel(II) into EiBC (**11**) since it was already known that the cis isomers would be separable.[15]

The nickel(II) EiBC (NiEiBC) (**12**) obtained indirectly via the photoreduction was found by HPLC and NMR to be a mixture of four isomers. The reduction pathway appeared to favor the two diastereomeric cis isomers, which constituted 80% of the product and were identified by co-injection with authentic *cis*-NiEiBC (obtained from the Raney nickel reduction).[15] The two other isomers were tentatively assigned as trans isomers and together consisted of 20% of the product. One of the two trans isomers was separable by HPLC from the cis isomers while the other isomer had the same retention time as the more polar cis isomer. The NMR spectra of the nickel(II) complex also showed four isomers as indicated by four different signals for both the α and β meso protons. The chemical shifts of the two more intense signals of each of the α and β protons were identical with the signals of the cis isomers of NiEiBC (**12**) obtained from the Raney Ni reduction.

In this same manner the stereochemistry of the NiEiBC obtained by catalytic hydrogenation of ZnEdiBC (**10**) was investigated. Surprisingly, it was found, both by HPLC and by NMR spectroscopy, that this iBC was predominantly the trans isomers. The ratio of trans/cis product was approximately 70/30. This is surprising in that it infers that catalytic reduction of the ethylidene compound occurred from the more hindered face of the molecule.

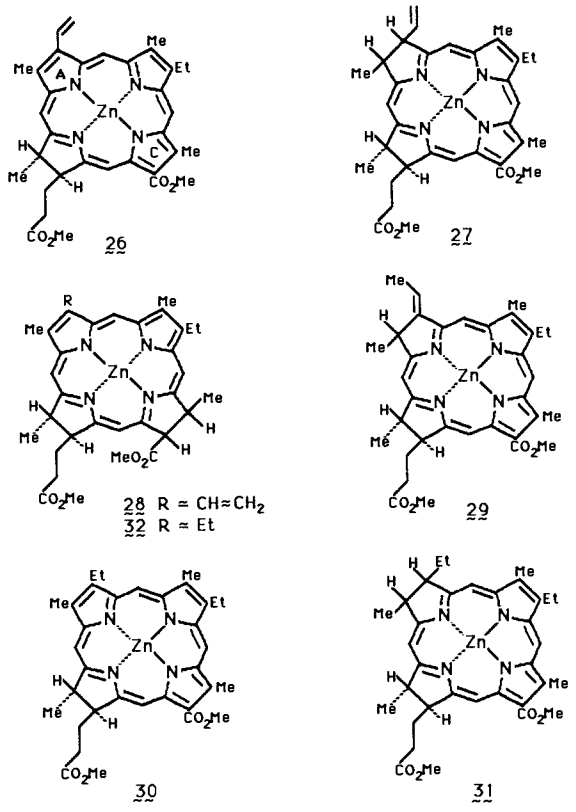
Both of these reduced compounds, the ethylidene- and the 2-vinyl-iBC, appeared to suffer little or no decomposition on silica gel, allowing for their separation from other reaction products. As crystalline solids they appear to be stable indefinitely. However, when handled excessively, problems with oxidation or rearrangement to chlorins were noted, particularly during the long periods required for reversed-phase HPLC separation of the free bases.

Apart from providing a simple synthetic route to both the vinyl-iBC and the ethylidene macrocycles, the chemical ease with which the ethylidene can be synthesized may have important biosynthetic implications. For example, the obligatory reduction of the 4-vinyl group in magnesium(II) protoporphyrin IX monomethyl ester (**18**) to give a chlorophyll *a* precursor [e.g., **19** (Scheme I, path A)] has been believed to involve simple and direct vinyl to ethyl reduction; our demonstration of the vinyl–ethylidene chemistry might suggest that this reduction may indeed proceed through the chlorin **20** and the ethylidene compound **21** (path B). An even more compelling case can be put forward for biosynthesis of the phycobilins. Biliverdin IX α (**22**; Scheme II) is a known precursor of phycocyanobilin,[22] a progenitor of which is shown in structure **23**. Again, traditional wisdom would expect that, in order for the ethylidene moiety in **24** to be biosynthesized (for subsequent addition of the protein), a vinyl group must be reduced to ethyl (Scheme II, path C) followed by migration of the double bond *in a thermodynamically disfavored manner*. However, the alternative path D would require enzymically catalyzed reduction of a terminal double bond in biliverdin IX α (**22**) to give **25**, followed by the thermodynamically downhill migration of the vinyl double bond to the ethylidene position, to give **24**, from which **23** is accessed. Finally, the ethylidene function is also found in BChl-*b* (**9**), and once again it seems perfectly reasonable to suggest that this moiety is biosynthesized from the corresponding *vinylbacteriochlorin*, followed by migration of the vinyl double bond into the ethylidene site, rather than migration of the ring B double bond outward with concomitant loss in aromatic character.

We next investigated the photoreduction of zinc(II) rhodochlorin dimethyl ester (DME) (**26**, Chart IV)[23] and found it to behave similarly to the pheophorbide. In this case one would expect to get two different iBCs resulting from either reduction at ring A or reduction at ring C. The reduction of zinc(II) rhodochlorin in benzene proceeded quite rapidly to give two reduced products by spectrophotometric monitoring (long-wavelength absorptions at 596 nm and a shoulder at 606 nm). The 606-nm product, however, appeared to suffer oxidation during extraction. The absorption spectrum after workup but prior to any chromatography showed only one long-wavelength absorption (592 nm in CH_2Cl_2). The meso region in the proton NMR spectrum indicated that the product was solely (>95%) isobacteriochlorin **27** in which ring A has been reduced. This conclusion was based on the meso proton chemical shifts (δ, 6.68; α, 7.30 and 7.31; β and γ, 8.49, 8.50, and 8.62 ppm) and the upfield shift of the vinyl group protons (6.2 and 5.4 ppm). The meso protons were assigned on the basis of their expected chemical

(22) Brown, S. B.; Holroyd, A. J.; Vernon, D. I. *Biochem. J.* **1984**, *219*, 905–909. Brown, S. B.; Holroyd, A. J. *Biochem. J.* **1984**, *217*, 265–272.
(23) Smith, K. M.; Lewis, W. M. *Tetrahedron* **1981**, *37* (Suppl. 1), 399–403.

Chart IV



shifts. It is felt that the ester in the 6-position shifts the γ meso proton to a lower field than is typical for meso protons adjacent to reduced rings. This is also observed in the NMR spectra of the corresponding zinc(II) rhodochlorin DME (**26**). Thus the iBC observed has meso protons in the order from highest to lowest field strength $\delta > \alpha > \beta$ and γ. The iBC **28**, where rings C and D are reduced, would be expected to have meso protons ordered $\gamma > \beta$ and $\delta > \alpha$ from low to high field and is easily distinguished from **27**.

The photoreduction of zinc(II) rhodochlorin DME (**26**) was also investigated in a pyridine medium with the intent of forming an ethylidene-iBC **29**. After 1 h of irradiation of **26** in pyridine two reduced products were present. The minor product showed a long-wavelength absorption of 598 nm, probably the 2-vinyl-iBC **27** isolated in the reaction with benzene. The major product showed a 20-nm difference (618 nm) as would be expected for the formation of an ethylidene from the vinyl-iBC from the pheophorbide series. However, the NMR and optical spectra of the product prior to any chromatography indicated that during product isolation the ethylidene compound had rearranged to give zinc(II) 2-ethylrhodochlorin (**30**) as the major isolated product.

Although we were able to observe the ethylidene formation by spectrophotometric monitoring of the reaction, in this case we were not able to isolate the ethylidene product **29**. In a subsequent reaction the ethylidene mixture obtained was hydrogenated prior to purification of **31**. In this reaction a large amount of **30** (via vinyl migration) was also obtained, which was separated from the iBC **31**. However, because of the low overall yield of **31**, it was impossible to say if the iBC **31** originated from the ethylidene compound **29** or from the 2-vinyl-iBC **27** which was also present. Thus, no direct evidence beyond the visible absorption spectrum of the reaction products could be obtained for the ethylidene compound **29**. As with the pheophorbide photoreductions the rhodo iBCs **27** and **31** appeared to be mixtures of at least two diastereomers. However, no further stereochemical investigations of these compounds were made.

It has been reported[7] that mesochlorophyllide **4** does not undergo the photoreduction, and we confirmed this by showing that zinc mesopyropheophorbide *a* (**17**) does not undergo ascorbate photoreduction. Thus the 2-vinyl group in this case is necessary for reduction to the iBC. However, the results obtained in the reduction of zinc(II) rhodochlorin XV DME (**26**) suggest the reduction was preferentially directed to ring A over ring C. To determine if there may be a directive effect by the vinyl group (or any electron-withdrawing group), the photoreduction of zinc(II) 2-ethylrhodochlorin DME (**30**) was attempted. Unlike mesochlorophyllide, **30** was reduced to an iBC showing a long-wavelength absorption at 596 nm in pyridine. The photoreduction of this complex was noticeably slower than that of **26** but did go to near completion.

Separation of the reduced product from the small amount of starting material present was not possible as the product oxidized on TLC. Thus the product had to be characterized from the NMR spectra of the crude material. 360-MHz proton NMR spectroscopy of the crude product showed the main reduced product (>95%) to be the iBC **32**, where ring C is reduced. The meso protons follow the expected arrangement from highest to lowest field of $\gamma > \beta$ and $\delta > \alpha$. The minor component (approximately 15%) of the material appearing in the NMR spectrum was tentatively identified as unreacted zinc(II) 2-ethylrhodochlorin DME (**30**) based on the meso proton chemical shifts and a small visible band at 634 nm. From the NMR spectra it is evident that reduction was directed entirely to ring C. So, when the 2-vinyl group was present, reduction was favored in ring A. However, the ester group must direct reduction in the absence of the 2-vinyl group. These results imply that mesochlorophyllide *a* and zinc(II) mesopyropheophorbide *a* are not reduced, presumably due to steric constraints associated with the isocyclic ring rather than for electronic reasons.

Conclusion

Ascorbic acid photoreductions of various metallochlorins have provided a wealth of information in terms of the types of reduced products that can be accessed. As seen in the photoreduction of pheophorbides, this reaction provides easy access to ethylidene macrocycles that have not previously been accessible. By changing the solvent, good yields of the vinyl-iBC can also be obtained. Facile demetalation of the zinc(II) complexes affords metal-free iBCs **11**, **13**, and **15a**. These compounds may also be important for chemical and biosynthetic studies of natural products possessing the ethylidene moiety. The reduction appears to be ring specific, depending on the substituents present. This has obvious value in regiospecific formation of hydroporphyrins. The resultant cis stereochemistry obtained in the newly reduced ring of the iBC is consistent with the same found for the reduction of pheoporphyrins to *cis*-pheophorbides. Some trans isomers may result from the reduction, but it cannot be ruled out that these trans products are the result of partial racemization of the cis isomers under the basic conditions. This appears to be the obvious case for enolizable substituents such as in **32**, but it may also occur in **15**, but to a lesser extent. Further investigations are under way to determine other types of substituents (e.g., formyl and acetyl) that may show a directive effect as well. In early experiments[24] the acetyl group looks favorable. The regiospecific iBC products expected from these reactions should serve as useful intermediates in the synthesis of more complex chlorins.

Experimental Section

General. Electronic absorption spectra were measured on a Hewlett-Packard 8450A spectrophotometer using solutions in dichloromethane. Proton NMR spectra were obtained at 360 and 500 MHz on a Nicolet NT-360 and NT-500 spectrometers; the chemical shifts are reported relative to $CHCl_3$ at 7.260 ppm. The phrase "dried and evaporated" indicates drying with sodium sulfate, followed by evacuation with a Büchi rotary evaporator under house or oil pump vacuum.

Reactions were monitored by thin-layer chromatography (TLC) using cut strips (approximately 2 cm × 6 cm) of E. Merck silica gel 60 F254 precoated (0.25-mm thickness) plastic-backed sheets. Two types of packing material were employed in column chromatography: E. Merck neutral alumina (70–230 mesh) and Merck silica gel 60. The alumina was deactivated with either 6% H_2O (Brockmann Grade III) or 15% H_2O (Brockmann Grade V) before use. A 250-mL J. T. Baker column was

(24) Iakovides, P.; Smith, K. M., unpublished results.

used for flash chromatography. "Chromatotron" separations were performed on a Harrison Research Model 7924 Chromatotron equipped with an FMI pump; disk thickness, flow rate, and solvents are specified where appropriate, and in all cases the circular disks were coated with Kieselgel 60 PF254 (E. Merck). Analytical high-performance liquid chromatography (HPLC) was performed on a Waters Associates instrument equipped with a Model 6000A solvent delivery system, a Valco Model C6U injector, and a Perkin-Elmer LC55B variable-wavelength detector. The column and solvent systems used are specified where appropriate. All solvents were reagent grade and were filtered through a 0.45-μm Millipore filter before use.

General Procedure for Zinc(II) Insertion (7, 26, and 30). Zinc(II) Methyl Pyropheophorbide *a* (7). Methyl pyropheophorbide *a*[25] (160 mg) was dissolved in freshly distilled $CHCl_3$ (10 mL). A saturated solution of zinc acetate in methanol (2.0 mL) was added, and this mixture was refluxed for 10 min under nitrogen. After cooling to room temperature the contents of the flask were concentrated to approximately 5.0 mL. Excess methanol was added and the flask contents were again concentrated until a solid began to form. After cooling, the solid was collected by vacuum filtration, washed with cold methanol, and dried to give 180 mg of green solid, mp 142–145 °C (lit. mp 155–156 °C[26]). Vis: 422 nm (ϵ 82 800), 520 (2400), 558 (4000), 606 (9000), 656 (60 300). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): see Table I. **Zinc(II) Rhodochlorin Dimethyl Ester (26).** Yield 106 mg (93%). Vis (relative absorbance): 410 nm (1.00), 512 (0.0513), 556 (0.0436), 598 (0.098), 642 (0.509). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 9.63, 9.49 (s, α-, β-, and γ-meso H); 8.44 (s, δ-meso H); 8.10 (X of ABX, 2a-H); 6.10 (AB of ABX, 2b- and 2b′-H), 4.34 (m, 7- and 8-H); 4.26, 3.73, 3.55, 3.36, 3.30 (s, 1-, 3-, and 5-Me, 6a-, and 7d-OMe); 3.79 (m, 4-CH_2); 2.60–2.35 (m, 7-CH_2CH_2); 1.73 (d, 8-Me, J = 7.3 Hz); 1.69 (t, 4b-Me, J = 7.6 Hz). **Zinc(II) Mesorhodochlorin Dimethyl Ester (30).** Yield 19 mg (95%). Vis (relative absorbance): 414 (1.00), 516 (0.210), 554 (0.199), 592 (0.222), 636 (0.508).

Large-Scale Photoreduction of Zinc(II) Methyl Pyropheophorbide *a* (7). Zinc(II) methyl, pyropheophorbide a (7) (100 mg) was dissolved in a solution of 8% ethanol/pyridine (200 mL, degassed by saturating with nitrogen for 20 min). Diazabicyclo[2.2.2]octane (DABCO, Aldrich) (6 g) and ascorbic acid (4 g) were added, and the sealed flask was placed inside a Ray-o-net light drum. The drum contained 24 fluorescent lamps (20 W) and was equipped with a magnetic stirrer. The reaction was stirred for 20 h and monitored intermittently by spectrophotometry. When the reaction was complete the mixture was poured into ether (300 mL) and water (250 mL). The separated aqueous phase was further extracted with ether until extracts were clear. The combined organic layers were washed with water (4–5 times), dried, and evaporated to dryness. The reduced product was separated on a Chromatotron (3% methanol/methylene chloride) on a 1-mm silica gel plate and was crystallized from methylene chloride/*n*-hexane, giving 55 mg of a shiny blue solid. **Zinc(II) Ethylideneisobacteriochlorin (10).** Vis (relative absorbance): 388 nm (1.00), 422 (0.64), 496 (0.17), 622 (0.549). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): see Table I. Anal. Calcd for $C_{34}H_{36}N_4O_3Zn$: C, 66.50; H, 5.91; N, 9.12. Found: C, 66.19; H, 6.06; N, 9.19. **Zinc(II) methyl mesopyropheophorbide *a* (17)** was also isolated from the Chromatotron separation in small quantity. Mp 167–170 °C. Vis (relative absorbance): 420 nm (1.00), 512 (0.087), 552 (0.112), 598 (0.167), 644 (0.714). NMR (360 MHz, $CDCl_3$): 9.48 (s, β-meso H); 9.04 (s, α-meso H); 8.21 (s, δ-meso H); 5.05 (AB q, 10-CH_2); 4.30 (q, 8-H); 4.11 (m, 7-H); 3.70 (q, 4 H, 2- and 4-CH_2); 3.64 (s, 5-Me); 3.53 (s, 7-OMe); 3.21 (s, 3-Me); 3.17 (s, 1-Me); 2.50, 2.33, 2.23, 1.90 (each m, 7-CH_2CH_2); 1.66 (m, 8-Me, 2a- and 4a-Me).

Catalytic Reduction of Reduced Products. Zinc(II) 2-Ethylisobacteriochlorin (8). Zinc(II) ethylideneisobacteriochlorin (**10**) (45 mg) was dissolved in previously degassed acetone (15 mL). Five milligrams of 10% Pd/C was added, and this mixture was hydrogenated under 1 atm of hydrogen (or deuterium) for 20 h. The catalyst was filtered off and washed with excess acetone. The combined acetone extracts were evaporated to dryness. The product was purified by preparative TLC (3% methanol/methylene chloride) and crystallized from methylene chloride/*n*-hexane, giving 30 mg of blue solid. Vis: 382 nm (ϵ 53 300), 392 (52 000), 412 (51 200), 480 (7000), 512 (6100), 556 (12 700), 600 (30 400), 646 (6100). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 8.48, 8.44 (s, β-meso H); 7.11, 7.10 (s, α-meso H); 6.52, 6.49 (s, δ-meso H); 4.40 (m, 10-CH_2); 3.94 (m, 1-H); 3.75 (m, 2-H); 3.60 (m, 8-H, 7d-OMe); 3.46 (m, 7-H); 3.25 (m, 4a-CH_2); 3.17, 3.13 (s, 5-Me); 2.69, 2.67 (s, 3-Me); 2.37–2.18, 2.16–1.92 (each m, 2a-H, 7-CH_2CH_2); 1.83 (m, 2a′-H); 1.56, 1.54, 1.38 (d, 1- and 8-Me); 1.45 (m, 1-, 8-, and 4b-Me); 1.10, 0.95 (t, m, 2b-Me). Anal. Calcd for $C_{34}H_{38}N_4O_3Zn\cdot H_2O$: C, 64.40; H, 6.36; N, 8.84. Found: C, 64.48; H, 6.16; N, 8.74. **2-Ethylisobacteriochlorin-d_2 (14).** Vis (relative absorbance): 376 nm (1.00), 395 (0.690), 418 (0.525), 500 (0.104), 532 (0.138), 582 (0.177), 630 (0.469). NMR (360 MHz, $CDCl_3$): 8.35, 8.38 (s, β-meso H); 7.10, 7.09 (s, α-meso H); 6.49, 6.51 (s, δ-meso H); 4.40 (AB q, 10-CH_2); 3.93 (q, 1-H); 3.73 (t, 2-H); 3.60 (m, 8-H, 7-OMe); 3.45 (m, 7-H); 3.25 (q, 4-CH_2); 3.15 (s, 5-Me); 2.65 (s, 3-Me impurity); 2.25, 2.15, 2.02 (each m, 7-CH_2CH_2, 2-CHD); 1.54 (d, 1-Me); 1.40 (m, 8- and 4a-Me); 0.90 (m, 2a-CH_2D). **Zinc(II) 2-Ethylisobacteriochlorin-d_2 (16).** Vis (relative absorbance): 382 nm (1.00), 393 (0.977), 412 (0.981), 480 (0.130), 514 (0.123), 554 (0.250), 598 (0.569), 648 (0.133). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 8.28, 8.15 (s, β-meso H); 7.10, 7.00 (s, α-meso H); 6.50, 6.43 (s, δ-meso H); 4.33 (AB q, 10-CH_2); 3.65 (m, 7-OMe, 1-H); 3.60, 3.52, 3.45 (each m, 7- and 8-H); 3.22 (q, 4-CH_2); 3.10, 3.05 (s, 5-Me); 2.68, 2.62 (s, 3-Me); 2.40, 2.15 (each m, 7-CH_2CH_2, 2-CHD); 1.61, 1.50 (d, m, 1-, 8-, and 4a-Me); 1.10 (t, 2a-Me).

2-Ethylisobacteriochlorin (11). Zinc(II) isobacteriochlorin (**8**) (20 mg) was dissolved in TFA (5 mL) previously cooled to 0 °C in an ice bath. The flask was capped and stirred in an ice bath for 5 min. The reaction mixture was diluted with methylene chloride (40 mL) and carefully poured into aqueous saturated $NaHCO_3$. After separation the organic layer was further washed with $NaHCO_3$ (2 × 50 mL) and water (3 × 50 mL), dried, and evaporated to dryness. The product was purified by preparative TLC (two plates, 3% THF/methylene chloride) and crystallized from methylene chloride/*n*-hexane, giving 12 mg of solid, mp 124–128 °C. Vis: 376 nm (ϵ 60 000), 396 (40 500), 418 (30 800), 500 (6400), 532 (8700), 580 (10 900), 630 (29 300). NMR (360 MHz, $CDCl_3$): see Table I.

Ethylidene- and 2-Vinylisobacteriochlorin Mixture. The same demetalation procedure as for mesoisobacteriochlorin **11** was employed using 7 mg of zinc(II) ethylideneisobacteriochlorin and zinc(II) 2-vinylisobacteriochlorin. The product was purified as above and then separated by reverse-phase HPLC with a Rainin Dynamax C_{18} column (flow rate, 9.0 mL/min; 95:5 methanol/H_2O; detected at 405 nm). **Band 1,2-Vinylisobacteriochlorin (15a).** HPLC retention time, 43 min. Vis (relative absorbance): 375 nm (1.00), 395 (0.67), 418 (0.59), 496 (0.24), 530 (0.27), 584 (0.31), 630 (0.65). NMR (360 MHz, $CDCl_3$): see Table I. **Band 2, Ethylideneisobacteriochlorin (13).** HPLC retention time, 51 min. Vis (relative absorbance): 375 nm (1.00), 428 (0.47), 512 (0.16), 548 (0.19), 600 (0.25), 652 (0.75). NMR (360 MHz, $CDCl_3$): see Table I.

Nickel(II) 2-Ethylisobacteriochlorin (12). 2-Ethylisobacteriochlorin (**11**) (10 mg) was dissolved in freshly distilled chloroform. Nickel(II) acetate (3 mL) saturated in methanol was added, and the reaction mixture was heated to reflux under nitrogen. After 16 h of refluxing, the reaction was allowed to cool to room temperature before dilution with methylene chloride. The diluted product was washed with water (to remove excess nickel acetate), dried, and evaporated to dryness. The product was purified by preparative TLC (3% THF/methylene chloride) and crystallized from methylene chloride/*n*-hexane. Mp 98–100 °C (lit. mp 106–108 °C[15]). Vis: 379 nm (ϵ 39 000), 410 (30 600), 466 (5900), 550 (10 700), 594 (31 000), 638 (3000). NMR (360 MHz, $CDCl_3$): 8.23, 8.22, 8.20, 8.19 ppm (s, β-meso H); 7.14, 7.09, 7.07, 7.03 (s, α-meso H); 6.51, 6.40 (s, δ-meso H); 4.19 (m, 10-CH_2); 3.88, 3.76 (m, 1-H); 3.64 (s, 7d-OMe); 3.51 (m, 2- and 8-H); 3.28 (t, 7-H, J = 7.0 Hz); 3.13 (m, 4a-CH_2); 2.99 (s, 5-Me); 2.59 (s, 3-Me); 2.35, 1.97 (m, 7-CH_2CH_2); 2.25, 1.77 (m, 2a-CH_2); 1.62, 1.09 (d, 1-Me); 1.39, (m, 4b-Me); 1.27 (d, 8-Me); 0.96, 0.82 (t, 2b-Me).

DDQ Oxidation of Zinc(II) Ethylideneisobacteriochlorin (10). Zinc(II) ethylideneisobacteriochlorin (**10**) (15 mg) was dissolved in methylene chloride (5 mL) and cooled to 0 °C (ice bath). DDQ (5.6 mg, 1.0 equiv) was dissolved in methylene chloride (3 mL) and added dropwise to the cooled zinc(II) ethylideneisobacteriochlorin solution. After 20 min of stirring, the flask was transferred directly to a rotavapor and evaporated to dryness. The crude product was purified by preparative TLC (2% methanol/methylene chloride) and obtained as a solid from *n*-hexane/methylene chloride, giving 5 mg of zinc(II) methyl pyropheophorbide *a* (**7**), mp 132–134 °C (lit. mp 155–156 °C[26]). Vis (relative absorbance): 424 nm (1.00), 524 (0.118), 568 (0.143), 608 (0.192), 654 (0.588). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 9.53 (s, β-meso H); 9.26 (s, α-meso H); 8.32 (s, δ-meso H); 8.00 (X of ABX, 2a-H); 6.10 (AB of ABX, 2b- and 2b′-H); 5.09 (AB q, 10-CH_2, J = 20 Hz); 4.38 (q, 8-H); 4.17 (m, 7-H); 3.72 (q, 4a-CH_2); 3.66, 3.54, 3.33, 3.22 (each s, 1-, 3-, and 5-Me, 7d-OMe); 2.40–2.29, 2.28–2.17, 1.96–1.85 (each m, 7-CH_2CH_2); 1.69 (d, 8-Me); 1.68 (t, 4b-Me).

DDQ Oxidation of Ethylideneisobacteriochlorin (13). Ethylideneisobacteriochlorin **13** (20 mg) was dissolved in methylene chloride (5 mL) and cooled to 0 °C (ice bath). DDQ (8.3 mg, 1.0 equiv) was dissolved

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(26) Lai, J.-J. Ph.D. Dissertation, University of California, Davis, 1983, p 173.

in methylene chloride (3 mL) and added dropwise to the cooled ethylideneisobacteriochlorin solution. After 20 min of stirring, the flask was transferred directly to a rotavapor and evaporated to dryness. The crude product was purified on alumina (Brockman Grade III, eluting with 3-5% THF/methylene chloride), giving 6 mg (30% yield) of methyl pyropheophorbide *a*, mp 216-218 °C (lit. mp 217-219 °C,[25] 220-225 °C[27]). Vis (relative absorbance): 412 nm (1.00), 506 (0.0879), 538 (0.0814), 608 (0.0744), 666 (0.339). NMR (360 MHz, $CDCl_3$): 9.52 (s, β-meso H); 9.40 (s, α-meso H); 8.55 (s, δ-meso H); 8.03 (X of ABX, 2a-H); 6.25 (AB of ABX, 2b- and 2b'-H); 5.20 (AB q, 10-CH_2); 4.50 (q, 8-H); 4.33 (d, 7-H); 3.72 (q, 4-CH_2); 3.70 (s, 5-Me); 3.53 (s, 7-OMe); 3.42 (s, 3-Me); 3.25 (s, 1-Me); 2.70, 2.58, 2.30 (each m, 7-CH_2CH_2); 1.85 (d, 8-Me); 1.70 (t, 4a-Me).

Large-Scale Photoreduction in Benzene. Zinc(II) methyl pyropheophorbide (**7**) (85 mg) was dissolved in 10% ethanol/benzene (100 mL, previously saturated with nitrogen for 20 min). DABCO (1.4 g) and ascorbic acid (880 mg) were added, and the sealed Erlenmeyer flask was irradiated in a Ray-o-net light drum for a total of 18 h with intermittent monitoring of the visible spectrum. The product was poured into ether (200 mL) and water (100 mL) and separated. The organic layer was washed with water (4-5 times), dried, and evaporated to dryness. The product was purified by preparative TLC (3% methanol/methylene chloride) using two plates. Crystallization from methylene chloride/*n*-hexane gave 45 mg of blue solid. **Zinc(II) 2-Vinylisobacteriochlorin (15).** mp > 250 °C. Vis: 382 nm (ε 50 600), 394 (48 100), 412 (47 300), 484 (7000), 554 (12 100), 600 (27 800), 650 (5700). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): see Table I.

Zinc(II) 2-Vinylrhodoisobacteriochlorin (27). This reduction was done by the large-scale procedure using 22 mg of zinc(II) rhodochlorin (**26**), 700 mg of DABCO, and 400 mg of ascorbic acid in 50 mL of 10% ethanol/benzene. All the starting material had been completely consumed in 1 h, after which the reaction was worked up as in the previous reaction. Separation was achieved by preparative TLC (1.5% methanol/methylene chloride), and the product was obtained as a solid from *n*-hexane. Vis: 388 nm (ε 58 000), 402 (60 600), 518 (4900), 592 (29 100), 638 (7000). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 8.62, 8.49 (s, β- and δ-meso H); 7.31, 7.30 (s, α-meso H); 6.68 (s, δ-meso H); 6.20 (m, 2a-H); 5.40 (m, 2b- and 2b'-H); 4.68 (m, 2-H); 4.25, 4.10, 3.75, 3.63 (m, 1-, 7-, and 8-H, 6a-OMe); 3.60, 3.59 (s, 7d-OMe); 3.35 (q, 4a-CH_2); 3.27 (s, 5-Me); 2.76 (s, 3-Me); 2.25 (m, 7-CH_2CH_2, impurity?); 1.50 (m, 1- and 8-Me, 4b-Me).

Zinc(II) 2-Ethylisobacteriochlorin (32). Using the large-scale procedure 19 mg of zinc(II) mesorhodochlorin (**30**) was irradiated for 24 h with 800 mg of DABCO and 400 mg of ascorbic acid in 50 mL of 8% ethanol/pyridine. Purification of the reduced product was not possible as the product appeared to oxidize on silica gel. The crude product was obtained as a solid from *n*-hexane. Vis (relative absorbance of crude product): 395 nm (1.00), 554 (0.160), 594 (0.443), 630 (0.109) (chlorin impurity?). NMR (360 MHz, $CDCl_3$ and pyridine-d_5): 8.80, 7.704, 7.701 (s, α-, β-, and δ-meso H); 7.06, 7.01 (s, γ-meso H); 4.72 (m, 6-H); 4.62 (m, 5-H); 4.00-2.95 (m, 7- and 8-H, 1- and 3-Me, 6a- and 7d-OMe, 2a- and 4a-CH_2); 2.20 (m, 7-CH_2CH_2, impurity?); 1.80-1.50 (m, 5- and 8-Me, 2b- and 4b-Me).

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Lipid Bilayer Fibers from Diastereomeric and Enantiomeric *N*-Octylaldonamides

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Abstract: The aggregation behavior of eight diastereomeric *N*-octylaldonamides, three enantiomers (galacton, mannon, glucon), and corresponding racemates was investigated mainly by electron microscopy. Head groups with a sterically undisturbed all-anti conformation (galacton, mannon) lead to "whisker"-type aggregates, which appear as rolled up, bilayer sheets in both aqueous and 1,2-xylene gels. One pair of 1,3-syn-positioned OH groups in the all-anti conformation neighboring on the amide group, lead to extremely thin helical whiskers of high curvature in water (glucon) or 1,2-xylene (talon). If the outer OH groups are in syn positions in the all-anti chain conformations, the *N*-octylamides become highly water-soluble (allon, altron, idon) and form rolled up, bilayer sheets in 1,2-xylene (gulon). The length-to-diameter ratios in the aggregates are often higher than 10^4. The fibers are stabilized by amide hydrogen bonds and/or the hydrophobic effect. They can be conceived as models for prebiotic assemblies, which may lead to condensation biopolymers in aqueous media.

Hydrophobic bilayers with well-defined morphologies may serve (i) as structural models for biological membranes and (ii) as scaffoldings for synthetic functional systems. So far, spherical vesicles[1] and fibers[2-7] have been obtained, the latter being either ribbons or tubes. If composed of chiral molecules, the ribbons are usually twisted or helically wound.[5,6] In a first survey on relationships between molecular structures of several synthetic amphiphiles and their nonspherical aggregates, Kunitake singled out the interaction of linear and bent aromatic rigid segments as the most important elements.[2] We explained the helicity of elongated bilayers made from chiral molecules by involving spontaneous torsion of the edges[8] and traced fibrous aggregates[9]

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