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Mathias O. Senge* and Stuart A. MacGowan

*School of Chemistry
SFI Tetrapyrrole Laboratory
Trinity College Dublin
Dublin 2
Ireland*

and

*Medicinal Chemistry
Institute of Molecular Medicine
Trinity Centre for Health Sciences
Trinity College Dublin
St James's Hospital
Dublin 8
Ireland*

E-mail: sengem@tcd.ie

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Abbreviations:

BChl	bacteriochlorophyll
BPheo	bacteriopheophytin
Chl	chlorophyll
Chlide	chlorophyllide
ET	electron transfer
NSD	normal structural decomposition
OEC	2,3,7,8,12,13,17,18-octaethylchlorinato
Pheo	pheophytin
RR	resonance Raman
$\Delta 24$	deviation of the 24 macrocycle atoms in porphyrins from their least-squares plane [$\text{\AA}$]
$\Delta 26$	deviation of the 26 macrocycle atoms in phytychlorin derivatives from their least-squares plane [$\text{\AA}$]
ΔC_a	deviation of the C_a atoms from the 4N-plane [$\text{\AA}$]
ΔC_b	deviation of the C_b atoms from the 4N-plane [$\text{\AA}$]
ΔC_m	deviation of the C_m atoms from the 4N-plane [$\text{\AA}$]

I. Introduction

Chlorophylls are often termed the “pigments of life” and are the primary photosynthetic pigments in nature. They are green colored macrocyclic pigments and the term *chlorophyll*, coined by Berzelius in 1838, is derived from Greek roots and indicates the green of leaves.¹ Chlorophylls and the related bacteriochlorophylls are the ubiquitous pigments of photosynthetic organisms. As such they share common structural principles and functions. They are responsible for the primary biochemical energy generation in nature through action as reaction center and accessory pigments and give the only indications of life on earth visible from outer space.

Chlorophylls have been studied for over two centuries and, while much of their basic chemistry was established almost 100 years ago,² real breakthroughs in their exact biochemical function were only made in the last decades by X-ray crystallographic analysis of both reaction center³ and antenna complexes.⁴ Until the middle of the last century most studies were concerned with the basic structural chemistry of chlorophylls. This was followed by the elucidation of the basic anabolic pathways of Chl in higher plants, photophysical studies on their function in photosynthesis, and more recently their catabolism.^{5,6} Parallel to studies on Chl a/b from Higher Plants, the last decades have seen many efforts to elucidate the structure, function and biosynthesis of photosynthetic pigments from unicellular organisms and photosynthetic bacteria.⁷ In applied research chlorophylls are mainly used in solar energy conversion projects or as photosensitizers in photodynamic cancer therapy.^{8,9} Industrially, phytochlorin and rhodochlorin derivatives have found some use as food additives and anti-odor compounds, often in form of simple plant extracts.¹⁰ The best summaries of all chemistry pertinent to chlorophylls are still the monographs by Willstätter and Stoll² and Scheer.¹¹

Here we will focus on the structural chemistry of isolated Chl derivatives, i.e. small molecule analyses of compounds closely related to chlorophyllides, pheophorbides, phytochlorins and similar compounds.

II. Basic Structure and Reactivity of Chlorophylls

Chls are heteroaromatic compounds, the aromatic character of the underlying tetrapyrrole system and the reactivity of the functional groups in the side chains governing their chemistry. Three different classes of tetrapyrroles, differentiated by their oxidation level, occur in nature (Fig. 1): porphyrins (**1**, e.g., hemes), chlorins (**2**, e.g., Chls), and bacteriochlorins (**3**, e.g., BChls). As a cyclic tetrapyrrole with a fused five-membered ring, the overall reactivity of Chl is that of a standard phytochlorin **8**. Such compounds are capable of coordinating almost any known metal with their nitrogen atoms. Together with the conformational flexibility of the macrocycle and the variability of their side chains, this accounts for their unique role in photosynthesis.¹²

Figure 1 Basic tetrapyrrole structures and reactivity of chlorophyll.

Throughout this contribution the recommendations of the IUPAC commission on the nomenclature of tetrapyrroles¹³ have been followed as much as possible. In this system, the 24 macrocycle atoms are numbered from 1 to 24 (see formula **5** in Figure 2). Four different types of atoms are present in the porphyrin system: the four pyrrole nitrogen atoms, the methine bridge carbons (which are named *meso* carbons or C_m), and the α - and β -pyrrole carbons, named C_a and C_b , respectively. The latter abbreviations will be later used for the description of geometrical parameters and conformational properties. The practical use of this nomenclature is limited, and its actual use varies with the background of the researchers. Especially in the biological sciences a "derivative nomenclature" is often used. For the bacteriochlorophylls (BChls) a more practical nomenclature has been suggested.^{14,15}

The best known pigment is Chl a **5** (Fig. 2) which occurs in all organisms that carry out oxygenic photosynthesis. In higher plants it is accompanied in a 3:1 ratio by Chl b **7**, where the 7-methyl group has been replaced by a formyl group. Both compounds typically consist as the ester of the tetrapyrrole moiety with a C-20 terpenoid alcohol, phytol. Most compounds are magnesium chelates, but the free base of Chl a, Pheo a **6**, is also active in electron transfer and *in vivo* zinc(II) complexes have been suggested as well.^{16,17,18}

However, many other similar photosynthetic pigments occur in nature.⁸ All share either a phytychlorin **8** or 7,8-dihydrophytychlorin framework and so far over one hundred related pigments have been isolated. For example, such compounds include Chl d **9** from *Rhodophytes*, the Bchls c **10**, d, and e [which are chlorins **2** (dihydroporphyrins) and show significant variability in their peripheral groups]^{19,20} from *Chlorobiaceae* and *Chloroflexaceae*, and Bchl a **11** and b (true bacteriochlorins **3**, i.e. tetrahydroporphyrins) found in *Rhodospirillales*. Other natural pigments are Chl c, Bchl g and many of these with different esterified isoprenoid alcohols. Chemically related chlorins have also been found in many oxidoreductases, marine sponges, tunicates, and in *Bonella viridis*. A deep-sea dragon fish (*Malacosteus niger*) even utilizes a Chl derivative as a visual pigment.²¹ Most of these are believed to be derived from Chl and then processed by the plant or animal.

Figure 2 Naturally occurring Chls and related systems. Small numbers in the Chl a formula indicate the IUPAC numbering scheme. R groups may vary in different organism or at different developmental stages.

The chemistry of Chls is governed by the aromatic character of the underlying tetrapyrrole moiety and the reactivity of the functional groups in the side chains. As a cyclic tetrapyrrole with a fused five-membered ring, the overall reactivity of Chls is that of a standard heteroaromatic compound. The extended aromatic system, however, which is capable of coordinating almost any known metal with its core nitrogen atoms, together with the variability of its conformation and its side chains, is responsible for its unique role in photosynthesis. The basic aromatic system is susceptible mainly to electrophilic reactions, e.g. halogenations, with a preference for reaction at C20, the *meso* position closest to the reduced pyrrole ring. The C7-C8 double bond in phytychlorin (next to R¹) is not part of the aromatic delocalization pathway and thus is a convenient handle for modification of the Chl macrocycle via addition and oxidation reactions. The side chain substituents undergo standard transformations, e.g. the C3 vinyl group undergoes addition and oxidation reactions, the ester groups at C17³ and C13² can be saponified or transesterified, and the reactivity of ring E is generally governed by enolization and subsequent reactions of the β -keto ester system. The latter includes the so-called allomerization reactions, i.e. oxidative degradation reactions involving oxidations, hydroxylation, ring-opening or decarboxylations of the isocyclic pentanone ring. The book by Scheer¹¹ and a review by Hynninen²² therein remain the most comprehensive treatises on Chl chemistry and function, while a comprehensive review on side chain transformation has recently been given by Pavlov and Ponomarev.²³ In recent years⁷ the group of Tamika has made significant breakthroughs in chemical transformations of chlorophylls (see chapter by Tamiaki and Kunieda in this book). [Editor: reference chapter by **Hitoshi Tamiaki and Michio Kunieda** in this volume]

III. New chlorophylls

Only few truly new Chl derivatives have been identified *in vivo* in the last decade, esp. in the biological sciences. A new Chl c pigment **12** has been isolated from the phytoplankton *Emiliania huxleyi* and characterized both chromatographically and spectroscopically.²⁴ Also, the new chlorophylls petasiphyll-a **13**²⁵ and phellophyll-a **14**²⁶ have been isolated from the leaves of *Petasites formosanus* Kitamura and *Phellodendron amurense* var. *wilsonii*, respectively. The HPLC analysis of divinyl Chl a and b and some novel Chl c has been reviewed.²⁷ Several new Chl a related compounds have been isolated as antioxidants from the edible parts of the short-necked clam *R. philippinarum* and other bivalve molluscs (and their attached diatoms).²⁸ An X-ray crystal structure is available for chlorophyllonic acid a methyl ester **15**²⁹ and stereoselective syntheses of Chl a related chlorins, including some of those isolated from the above species, have been developed.³⁰

In the BChl d series new homologs have been detected in natural populations of green photosynthetic bacteria through HPLC analysis. The structure of the esterifying alcohols were confirmed chemically and via GC-MS.^{31,32}

IV. Biological Relevance of Tetrapyrrole Conformations

One aspect of tetrapyrroles that has received some attention in recent years concerned the conformation of the underlying macrocycle. A critical factor for all biological functions is the close interplay between bound cofactors and the respective apoprotein. In most cases the isolated pigments show physicochemical properties quite distinct from those found in intact pigment-protein complexes *in vivo*. The protein functions as a medium, as a scaffold for the spatial arrangement of the cofactors, it mediates the interaction with other components in a supramolecular biological system, and it acts as a ligand with effects on the configuration and conformation of the cofactors and overwhelming evidence has accumulated for the conformational flexibility of the cofactors *in vivo*.³³

Numerous synthetic, structural and spectroscopic studies have established that macrocycle conformation can control the physicochemical properties of the tetrapyrrole to a significant extent.^{12,34,35,36,37,38} For example, it has been shown that increasing nonplanarity with its destabilization of the π -system leads to bathochromically shifted absorption bands, easier oxidation, lower fluorescence yields, larger Stokes shifts, shorter lifetimes of the lowest excited states and faster intersystem crossing and internal conversion. In natural systems it can be assumed that manipulation of the macrocycle conformation via steric interactions with the surrounding protein side chain in pigment-protein complexes and/or via axial coordination of the central metal can be used to fine-tune the physicochemical properties of the macrocycle. This presents an intriguing rationale for explaining the often

diverse (physico)chemical reactivity of the same chromophore in different protein environments.

A similar rationale can be applied to the (B)Chls. Again, an extended aromatic system such as the one of Chl or BChl must be conformationally flexible and the presence of the reduced pyrrole ring in chlorins and bacteriochlorins should lead to even more conformational flexibility than is observed in porphyrins. For porphyrins the advent of the routine application of X-ray diffraction and vibrational spectroscopy to structural studies has enabled a deeper understanding of the importance of this phenomenon for the functional properties of tetrapyrroles. Despite their biological relevance structural studies on hydroporphyrins are scarce. This is mainly a result of their limited synthetic accessibility, lower chemical stability compared to porphyrins, and problems in obtaining single crystals of suitable quality for crystallographic analyses. A discussion of the available data is the main focus of the present contribution.

V. Conformational Analysis of Porphyrins

A comparative analysis of the structural chemistry of tetrapyrroles requires an analytical framework that allows both qualitative and quantitative comparisons. Even a qualitative look at some representative porphyrin conformations indicates that the macrocycle can adopt quite diverse conformations (Fig. 3). The currently used classification system³⁹ was suggested by Scheidt and Lee⁴⁰ and expanded by Shelnutt et al.⁴¹ The two out-of-plane distortions modes most easily identified are the saddle-shaped and ruffled conformation [named *sad* ("bending" in Fig. 3) and *ruf* ("twisting" in Fig. 3) by Scheidt and Lee]. A typical example for the latter is found in metalloporphyrins with small metal ions, such as Ni(II), where metal-nitrogen bond shortening is observed due to ring distortion.⁴² The ruffled distortion involves a twisting about the metal-nitrogen bond and is characterized by alternating displacement of the C_m positions above and below the mean plane. A well known example is the S_4 -ruffled modification of (2,3,7,8,12,13,17,18-octaethylporphyrinato)nickel(II).⁴³ The saddle distortion involves the alternate displacement of the pyrrole rings above and below the mean plane while the C_m positions remain more or less in plane. Typical examples for this are highly nonplanar, dodecasubstituted porphyrins, e.g. 2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetraphenylporphyrins.^{35,44} Other types of in-plane distortion are *wave* distortion⁴⁵ and *doming*. The latter is frequently found in five-coordinated complexes, where the axial ligand causes an out-of-plane displacement of the central metal or in metalloporphyrins involving large central metal ions like Tl(III).⁴⁶ While these four symmetric distortion modes offer a convenient system of classification for different porphyrin conformations, often deformations occur that do not directly correspond to any of these distortions. In most cases, the conformation of a given macrocycle can be described as a combination of any of these distortion types and includes often significant in-plane distortions (e.g., "stretching in Fig. 3). A detailed description of distortion modes and their energy levels has been given by Jentzen et al.⁴⁷

Figure 3 Illustration of different porphyrin conformations.

An analysis of the tetrapyrrole conformation requires determination of specific geometrical parameters and special visual illustrations. This goes beyond the usual analysis of bond lengths and angles. The conformation of a given macrocycle is best described by the displacement parameters of the macrocycle atoms from a mean plane (typically the 4N- or 24-macrocycle atom plane is used here). For example, the deviation of the 24-macrocycle atoms from their least-squares-plane ($\Delta 24$) has often been used as a measure for the overall degree of distortion or nonplanarity. As illustrated in Fig. 3, the displacements of the C_m and C_b atoms are of notable importance. If axial ligands are present, analysis of the porphyrin core conformation requires determination of the ligand tilt angle (φ_{ax}) and of the dihedral angle of the axial ligand plane and the N_{op} - N_{op} axis (ϕ).⁴⁰ Steric strain often affects not only out-of-plane displacements but the core conformation as well. Here the core size ($\otimes$) is defined as the average vector length from the pyrrole nitrogen atoms to the geometrical center of the 4N-plane, while the core elongation parameter (Ξ) gives the average difference between the lengths of the vectors between a nitrogen atom and its two neighboring N-atoms.

Two different graphical representations are used to illustrate the conformation of individual tetrapyrroles. One involves a linear display of the skeletal deviations from the 4N-plane in which the macrocycle deviations (to scale) are plotted against a positional parameter (not to scale) when "moving" around the ring system and looking across the 4N- or 24-macrocycle atom plane.^{38,39} The other involves plotting the individual displacement parameters for each distortion mode and illustrates the mix and interplay of the various distortions. This is based on the normal structural decomposition method (NSD) introduced by Shelnut.^{47,48} This method analyses all out-of-plane and in-plane distortion modes based on experimental or calculated positional atomic data. An example for the use of these different graphical representations is given in Fig. 4 using 5-*tert*-butylporphyrin **16**.⁴⁹ Naturally, use of these analyses for Chl and phytychlorin derivatives requires modification for the isocyclic ring V, e.g., use of a $\Delta 26$ instead of a $\Delta 24$ parameter.¹²

a)

c)

b)

Figure 4 Illustration of a conformational analysis: a) View of the molecular structure of **16** in the crystal. Hydrogen atoms have been omitted for clarity; thermal ellipsoids give 50 % occupancy. b) Skeletal deviation plot with respect to the plane of the 24 macrocycle atoms; ◆ denotes the *tert*-butyl substituted *meso* carbon; x-axis not to scale; sequence of pyrrole rings follows the IUPAC nomenclature from left to right (N21, N22, N23, N24). c) Graphical representation of the displacements along the lowest-frequency coordinates that best simulate the structure **16**. Adapted from reference 49.

VI. Chlorophyll Complexes in Photosynthesis

As for the porphyrins,⁴⁵ evidence supporting the importance of the chromophore conformation for the biological function has also been established in the past for various chlorophyll protein complexes.⁵⁰ For example, the first crystal structure of such a light harvesting complex, the antenna BChl a protein from *Prosthecochloris aestuarii*, exhibited a significant range of conformations for the seven bound BChl a molecules.^{51,52,53} The different absorption bands of the individual BChl molecules in this complex were shown to reflect the conformational differences observed in the protein crystal structure.⁵⁴

An even more intriguing example is the crystal structure of the LH2 complex from *Rhodospseudomonas acidophila*, one of the most beautiful examples of the special structural engineering used by nature to adapt photosynthetic pigments for light harvesting and storage. Nine B800 BChl and 18 B850 bacteriochlorophyll molecules are each arranged in cyclic arrays and an analysis of the BChl molecules revealed that three different conformational

types of BChl a are present.⁵⁵ The B800 BChl and the α B850 chromophores were shown to exhibit a $\Delta 26$ of 0.08 to 0.09 Å. In contrast, the β B850 chromophores were significantly more distorted with a $\Delta 26$ of 0.15 Å. This was taken as an indication for an influence of the conformation on the spectral properties.^{56,57,58}

Similarly, the bacterial photosynthetic reaction center pigments exhibit conformational flexibility. Overall the arrangement of the cofactors is roughly C_2 -symmetric with numerous pigment-protein interactions, which are responsible for the geometrical arrangement of the chromophores. The special pair is characterized by an overlap of the pyrrole rings I. Intriguingly the photochemistry is "asymmetric". Only the L side is photochemically active, although the arrangement of the cofactors (but not the apoproteins) is similar.^{59,60,61,62} The symmetry is already broken at the special pair with selective charge-transfer reactivity towards the L side and it has been suggested that the L side molecule has a less distorted macrocycle than the M side chromophore.^{63,64} While other explanations have been brought forward,⁶⁵ there is structural evidence for multiple conformations in protein structures from site-directed mutants.⁶⁶ Resonance Raman and other vibrational techniques have been used to investigate this situation and have provided supporting information for structural flexibility of the chromophores.^{67,68,69,70} This has been reviewed before³⁵ and an update will be given elsewhere.⁷¹

RR spectral changes have been observed in PSI after exposure to high light intensities, indicating the extent of photodamage to the Chl a pigments and providing insight into the mechanisms of photoprotection.⁷² In a comparative RR and fluorescence line narrowing study of isolated Chl a, b and d, specific modes have been assigned to specific parts of the molecule, and the effect of the Mg coordination state has been described.⁷³ A shift, caused by the photo-oxidation of P700, has been observed in the UVRR spectra of the nearby tryptophan and has potential as a probe for electron transfer in the ETC.⁷⁴ Reviews of recent applications and findings of RR spectroscopy regarding pigments photosynthetic complexes⁷⁵ and of the application of RR and FTIR to Chls in proteins⁷⁶ are available.

Over the past decade, there have been 117 crystal structures of photosynthetic related proteins, containing either (bacterio)chlorophylls or pheophytins, deposited in the PDB. This is a great many more than the 20 deposited in the preceding 10 years and this is a result of the efforts of the crystallographers who have persevered with the challenges associated with the crystallization and X-ray analysis of integral membrane proteins. The culmination of the work on this type of protein crystallization⁷⁷ and the subsequent measurement and analysis of diffraction data⁷⁸ has been reviewed, the latter containing brief descriptions of the structural determination of some photosynthetic pigment-protein complexes. The resolutions of the structures varies from 9.5 Å to 1.3 Å (PDB IDs: 1VCR and 3EOJ, respectively) and thus varying degrees of information are obtainable; proteins have been isolated from plants, algae, dinoflagellates, green bacteria and purple bacteria, totaling 19 distinct species. The structures include super-complexes of entire photosystems; high-resolution studies of individual subunits; wild type and mutated proteins; for reaction centers, charge-neutral and -separated states and structures reconstituted with extrinsic cofactors, all of which bear information regarding the role and nature of the (bacterio)chlorophylls and related cofactors. The following brief summary presents an overview of the up to date findings regarding the structures of PSI, PSII and available structures isolated from *Chlorobaculum tepidum*, and especially describes the structural information regarding the (bacterio)chlorophylls and related cofactors.

The crystal structure of the integrated PSI super-complex has been determined for the pea plant, *Pisum sativum* (PDB IDs: 2WSC, 2WSE and 2WSF⁷⁹; 2O01⁸⁰; 1QZV⁸¹), to a maximum resolution of 3.3 Å, and for the thermophilic cyanobacterium *Synechococcus elongatus* (PDB ID: 1JB0⁸²) at 2.5 Å. The 2.5 Å structure provides an atomic model picture

of PSI. Thus, the positions and orientations of the 96 Chl_a molecules (90 antenna cofactors and six as part of the ETC) were determined as were the Q_x and Q_y transition dipolar moments. In addition, the ring substituents were modeled for 48 of them. The pigments are coordinated directly or through water molecules to the side chains of subunits PsaA and PsaB for the ETC and 79 of the antenna Chl *a* cofactors, whilst the rest are borne by other subunits except for one that is bound by the phosphodiester group of lipid (III). The side chain donors are predominantly histidine imidazoles; however some of the antenna pigments are bound by the oxygen atoms of other residues, peptides or waters. Of course there are countless hydrophobic interactions also and, in most cases (notably this excludes the second pair of Chl *a* molecules in the ETC), significant H-bonding. The 3.3 Å structure of plant PSI (PDB ID: 2WSC⁷⁹) provides the best model from this source to date. Plant PSI consists of 18 protein subunits and 191 photochemical cofactors, of which 173 are chlorophylls (145 of the Q_x and Q_y transition dipolar moments were determined), and shows both the core and LHCI units. The PSI core is made up of 12 subunits with the majority of pigments, including those of the ETC, bound by the symmetry related dimer PsaA and PsaB. Ten of the 12 core subunits are closely related to the cyanobacterial PSI; the remaining two are involved with the LHCI and LHCII complexes, unique to plants. The LHCI peripheral antenna complex consists of four subunits: Lhca-1, -2, -3 and -4, each consisting of 15, 14, 17 and 15 chls respectively. The Chls that constitute the P700 pair appear to be identically positioned to those of the cyanobacterial system and the binding sites of the second and third pairs of the ETC are strictly conserved between the two. In contrast, however, plant PSI contains a number of gap Chls between the core complex and LHCI that mediate excitation energy transfer, and possibly affect binding, between them.⁷⁹⁻⁸¹

The crystal structure of cyanobacterial photosystem II from *Thermosynechococcus elongatus* (PDB IDs: 3BZ1 and 3BZ2⁸³; 2AXT⁸⁴) revealed each monomer as consisting of 20 protein subunits including: RCs D1 and D2; antennas CP47 and CP43 and a heme containing cytochrome b-559. The new model⁸³ (2.9 Å) allowed assignment of the phytol chains of all chl_a and of two present Pheo molecules, many of these participating in the hydrophobic binding interactions of other chls. The orientations of the chlorin rings were confirmed as had been reported earlier,⁸⁴ except for one that had to be flipped 180°.

The structure of the FMO protein from *Chlorobaculum tepidum* at 2.2 Å resolution that was reported in 2003 (PDB ID: 1M50)⁸⁵ has recently been re-refined (PDB ID: 3ENI) resulting in an improved R-value of 0.166 (obs.). Each monomer subunit of the trimer envelopes seven Bchls with two sheets, formed by a series of β strands, in what has been termed a “taco shell” arrangement. The positions of the seven Bchls were found to be similar to those of the closely related FMO protein of *Prosthecochloris aestuarii* (PDB ID: 3EOJ, 1.3 Å) with many of the observed differences accounted for by differing degrees of nonplanarity of the cofactors, rather than translational or rotational displacements. These conformational differences are considered the likely origin of the observed spectral differences between the two proteins.⁸⁵ The reader is referred to the relevant references for complete coverage.

VII. Structural Analysis of Chlorophyll Derivatives

A. Chlorophyll Derivatives

In a sense the title of this contribution is a misnomer as no isolated chlorophyll molecule has ever been characterized by X-ray crystallography. This is due to the amphiphilic character of the molecule with the hydrophilic tetrapyrrole moiety and the hydrophobic phytol chain. Thus, crystallization of an isolated Chl presented a challenge akin to that of the crystallization

of membrane proteins, e.g. the photosynthetic reaction center.^{86,87} None of the early reports on structural investigations of chlorophylls lead to a single crystal X-ray study.^{87,88} Microscopic and electron diffraction studies of microcrystals showed a dependency of the habit on the central metal,^{89,90} Transmission electron microscopy often indicated hexagonal crystal forms.⁹¹ Liquid crystals of Chl derivatives have found some interest, but are outside the scope of this contribution.⁹²

The following gives an overview of the available single crystal X-ray structures. The ones most closely related to chlorophylls and pheophorbides are compiled with their CCDC deposition numbers in Table 1.

<Insert Table 1 from end here>

1. Metallopheophorbides

The first small molecule study of a Chl derivative to be analyzed was initiated in 1937 by Ketelaar, who reported the unit cell data of ethyl Chlide a.⁹³ The first three dimensional structural analysis of this compound **17** was then reported in 1975 concomitantly by Kratky and Dunitz⁹⁴ and Strouse and coworkers.⁹⁵ Both structure determinations gave almost identical results and the molecular structure in the crystal is shown in Fig. 5. The compound crystallized as the aquo complex with a penta-coordinated magnesium center. At the same time the structure of the closely related Chl b derivative **18** was also reported.

Figure 5 View of the molecular structure of the aquo complex of **17** (left, AECLPA01⁹⁴) and **18** (right, ECPHBH⁹⁶) in the crystal. Hydrogen atoms have been omitted for clarity. Adapted from references 94 and 96.

As expected, the structure of methyl Chlide a **19** is almost identical to that of the ethyl ester.⁹⁷ Removal of the 13² ester group to yield the pyro-Chlide derivative **20** did not alter the conformation either.⁹⁸ All structures of the magnesium chelates have in common the penta-coordinated metal center (with Mg-O_{ax} ~2.03 Å), nonequivalent but typical Mg-N bond lengths (~2.03–2.18 Å). The shorter bonds are to N21 and N23, and the longest is found for Mg-N24, i.e. involving the reduced pyrrole ring. All compounds exhibited an almost planar macrocycle conformation. The $\Delta 26$ values for all these derivatives are close and range from 0.04 to 0.062 Å (see Table 1). Note, that the crystal packing in all these structures is very similar.

A very similar structure was found for the related Cd complex **22**. Formally, this is a BChl d derivative where infinite polymeric chains are formed through conjugation of the 3-hydroxymethyl group to the cadmium center.⁹⁹ The core and macrocycle conformations are very similar to those of the magnesium complexes described above. A number of related metal complexes have been studied as well, all of them with a penta-coordinated metal center.

The (chloro)iron(III) complex of phytychlorin methyl ester **23** crystallized with two independent molecules mainly distinguished by the orientation of the axial ligand. The macrocycles show significant deviations from planarity larger than those observed in corresponding magnesium(II) complexes although the overall type of conformation is similar to the Mg complexes.¹⁰¹ The core of the macrocycle is characterized by the five-coordinated iron(III) center which is ligated by the four pyrrole nitrogen atoms and a chloride atom in the axial position. The axial Fe-Cl bond lengths are 2.230(4) and 2.226(4) Å in the two independent molecules, respectively. The Fe-Cl vector is not orthogonal to the molecular plane, the Cl-Fe-N angles range from 97.8 to 107.2(3)°. The averaged bond lengths for the Fe-N_{pyrrole} bonds are 2.045(8) Å in molecule 1 and 2.026(8) Å in molecule 2, respectively. Again, the Fe-N bonds to the reduced pyrrole ring are considerably longer with 2.157(8) Å in molecule 1 and 2.135(9) Å in molecule 2. In general, the core geometry of the present iron(III) chlorin is similar to those found in other iron(III) hydroporphyrins and to those of other high-spin iron(III) porphyrins.³¹

Zinc(II) complexes are expected to be very similar to those of magnesium. However, only very few (phytychlorinato)zinc(II) derivatives have been structurally characterized. One example is compound **24**, which was crystallized both as the ethyl formate and chloroform solvate.¹⁰¹ For the latter it was shown that the compound formed polymeric structures with the zinc center coordinating to the N-OH group. This is not too surprising, zinc(II) likes to form pentacoordinated complexes and in the presence of an intramolecular donor group polymeric or dimeric structures will result. While this has been amply demonstrated for porphyrins a typical example for chlorins involves compounds **26** and **27**.¹⁰² Here, **26** forms typical polymeric structures while **27** is monomeric in the crystal.

Two structures of nickel(II) pheophorbides have been reported. The structure of the pyropheophorbide a derivative **21** exhibits a ruffled core conformation, clearly the result of the Ni-N bond contraction (Fig. 6). The severe deformations make it problematic to use Ni-derivatives as model compounds in spectroscopic studies on chlorophylls. A related study investigated the steric influence of the 20-methyl substituent in nickel(II) phytychlorins.¹⁰³ The structure of a Ni(II) 20-methylphytychlorin methyl ester **25** exhibited a highly ruffled conformation with a local increase in distortion in the vicinity of the 20-substituent when compared to the reference compound without the meso methyl group. This was indicated by larger C_m displacements and a smaller $C_a-C_{20m}-C_a$ angle (120.5°) compared to the phytychlorin without the methyl group (123.8°). Such compounds are related to naturally occurring BChl c and d and the results indicate that the larger distortion in the 20-methyl derivative might account for the 10 nm bathochromic shift in the absorption maxima of the BChl c compared to d.

Figure 6 View of the molecular structure of the nickel pyropheophorbide **21** (HAHBAT¹⁰⁴) in the crystal. Hydrogen atoms have been omitted for clarity.

The various conformational distortions in the different metal complexes of phytychlorins are clearly shown in Fig. 7. The magnesium derivative exhibits an almost planar macrocycle while a related zinc(II) derivative shows larger out-of-plane displacements mostly involving out-of-plane tilting of the pyrrole rings. These are slightly more pronounced in the iron(III)chloro derivative. In contrast the nickel(II) derivative shows a different conformation more nonplanar than the other ones. Here the largest out-of-plane

displacements are observed for the C_m carbon atoms and a rotation of the pyrrole rings about their β - β axes indicating a ruf distortion.

Figure 7 View of the skeletal deviations from the $\Delta 26$ plane in metallophorbides. The sequence of meso carbon atoms is C20, C5, C10, C15, C20 from left to right; x-axis is not to scale. a) **20** MPCHL10,⁹⁸ b) **24** CELRIU,¹⁰¹ c) **23** YINCAZ,¹⁰⁰ d) **21** HAHBAT.¹⁰⁴

2. Pheophorbides

The first structure of a Pheo a derivative was reported by Calvin and coworkers in 1972. They elucidate the structure of methyl pheophorbide a **28**.¹⁰⁵ Overall, the structure exhibited a planar macrocycle with only minimal deviations from planarity. The structure identified the basic characteristics of a chlorophyll derivative, i.e. the characteristic zig-zag conformation of the cyclopentanone ring, differences between the reduced pyrrole ring and the others and conjugation of the vinyl group with the aromatic system. Likewise, methyl mesopyropheophorbide a (methyl phytychlorin) **30**¹⁰⁶ exhibits a planar macrocycle. Only recently, the structure of a pheophorbide b **29** was reported.¹⁰⁷ The four five-membered pyrrole rings are nearly coplanar. Interestingly, for the two N-H units the formation of intramolecular N-H...N hydrogen bonds [$N\cdots N = 2.713(5)$ – $3.033(6)$ Å] was reported.

One of the most fundamental studies involved the analysis of several natural Bphea derivatives. These include the structures of **31** and **32**¹⁰⁸ and of **33**.¹⁰⁹ Note that these structures differ only in the substituents at C8 and C12, i.e. belong to the homologous series of BChl d compounds found in nature. A comparative analysis of the structures of these compounds¹¹⁰ isolated from *Chlorobium vibrioforme* revealed a series of dimeric and higher aggregates (involving the hydroxyethyl group and the ester carbonyl oxygen atom) that showed significant conformational variations for the same BPhea skeleton depending on the aggregation. Deviation of individual atoms from the N4 plane reached up to 0.5 Å.¹¹⁰ This clearly established the conformational flexibility of the basic phytychlorin macrocycle. Fig. 8 illustrates the different conformations observed in chemically closely related macrocycles. While many conformational differences involve ring V the degree of out-of-plane distortion and the type of distortion clearly varies.

Figure 8 View of the skeletal deviations from the $\Delta 26$ plane in free base pheophorbides. The sequence of *meso* carbon atoms is C20, C5, C10, C15, C20 from left to right; x-axis is not to scale. a) **28** MPOPHA,¹⁰⁵ b) **30** ROFVUE,¹⁰⁷ c) **31** (only one of the 2 independent molecules shown) BIPBIL,¹⁰⁸ d) **32** (only one of the 2 independent molecules shown) BIPBOR,¹⁰⁸ e) **33** BIXREF01,¹⁰⁹ f) **35** BAVSUM01.¹¹¹

A related structure of a closely related synthetic derivative is that of the 3-acetyl-8-ethyl)-bacteriopheophorbide d **34**¹¹² which exhibits structural features similar to the other Bpheo compounds. Note, that the zinc(II) complex of the corresponding porphyrin structure of **32** was reported as well and found to hydrogen-bonded dimers with extended π - π interactions without the expected ligation of the Zn by the 3-(1-hydroxyethyl) group.¹¹³

A few bacteriopheophorbide structures, i.e. bacteriochlorin-type tetrahydroporphyrins are available for comparison. One example is that of methyl BPheo a **35**.^{114,111} Both a solvated¹¹¹ and unsolvated¹¹⁵ form have been reported. The molecule exhibits a planar macrocycle very similar to that of the respective chlorins (dihydroporphyrins) of the Pheo series in both structures. Thus, at least in a structural sense there are only minor conformational differences between the Chl and BChl pigments based on the limited analytical data.

The different conformations observed here and in the metallo derivatives described above can be compared in more detail using Shelnutt's NSD analysis (*vide supra*).

Figure 9 NSD analysis of selected pheophorbide derivatives. Top panel gives out-of-plane distortions, lower panel in-plane distortions. a) **28** MPOPHA,¹⁰⁵ b) **20** MPCHLM10,⁹⁸ c) **23** YINCAZ,¹⁰⁰ d) **21** HAHBAT.¹⁰⁴

One of the striking features of the comparative analysis shown in Figure 9, apparent from the in plane illustrations above, is the large negative in plane *bre* deformation (-0.2914Å) observed for **21** (HAHBAT) which can be attributed as a direct consequence of coordination to Ni(II) by comparison to MPOPHA which is identical in all respects other than coordination to Mg(II). This structure also exhibits a high degree of ruffling, as is mentioned earlier, for the same reason. However, it can also be seen from the NSD that there are significant contributions from the other distortion modes *ruf*, *dom*, *wav(x)* and *pro* (all more or less >1Å), that would be less apparent from other conformational analyses due to the overwhelming ruffling. The in plane *rot* mode contribution remains similar to the others whereas the *trn(y)* contribution is greater. The rest of the in plane distortions are all considerably less.

It should be noted that for accurate determination of the magnitude of the in plane distortions, the chosen reference is of great importance. In this case it is the D_{4h} Cu(P) and thus the distortions are comparative to this. For comparative analysis though, this is obviously not a major issue. Also note that the absolute sign of the out of plane distortions is not as significant, because this is determined by the orientation of the macrocycle during analysis, as their within structure phase relationship.

3. Phytychlorins and Related Compounds

Some other phytychlorin-type structures have also been reported. For example, the purpurin **36** and the fused derivative **37** both exhibit planar macrocycles.¹¹⁶ A similar conformation was found for the simple phytychlorin which forms weak π -stacked aggregates in the crystal **38**.¹¹⁷

A few other structures of derivatives derived from phytychlorins have been reported which confirm the conclusions made above. Most of these are chlorin e_6 or rhodochlorin derivatives. Typically, these compounds show a higher degree of flexibility and one might expect significant deviations from planarity in the "southern half" of the molecule as a result of the presence of the *meso* substituent in position 15. However, many of these compounds exhibit a more or less planar macrocycle. This is clearly shown in the structure of **39**,¹¹⁸ which has a $\Delta 24$ of 0.058 Å and the *meso* carbons are displaced from this plane by only 0.02, 0.02, 0.05 and 0.09 Å for C5, C10, C15, and C20, respectively. The respective copper(II) complex **40** and **41** indicate the flexibility of these systems.¹¹⁹ One compound crystallized with two, the other with four independent molecules, all with relatively different conformations.

For the sake of organization the structure of **15** the natural compound chlorophyllonic acid a methyl ester should also be listed here (Fig. 10).²⁹ Overall, the macrocycle is relatively planar with $\Delta 24 = 0.08$ Å and the C_m displacements reach only 0.05 Å.

Figure 10. View of the molecular structure of the aquo complex of **15** (KUBDUB) in the crystal. Hydrogen atoms have been omitted for clarity. Adapted from reference 29.

Other examples are the aspartyl-chlorin e_6 **42**,¹²⁰ and the seleno compound **43**.¹²¹ A dimeric structure consisting of a chlorin e_6 derivative with an appended etioporphyrin unit was reported as well.¹²² Rhodochlorin XV dimethyl ester **44** presents an interesting case as two different crystal forms were found.¹²³ They form different crystal packing arrangements and overall both show only small deviations from $\Delta 24$. Still, the molecular structures of both forms are slightly different indicating the impact of crystal packing and the flexibility of the system. In the triclinic form the β -pyrrole atoms of ring IV deviate by approximately 0.4 Å from the plane of the N atoms, while in the orthorhombic form ring I is located 0.2 Å above, and ring IV 0.15 Å below the plane.

4. Dimers and Other Reaction Center Models

Based on the structural principles outlined above, many attempts have been made to obtain synthetic compounds that mimic the spatial arrangements of the two chromophores in the photosynthetic reaction center, i.e. the "special pair". Typically this involved the preparation of some kind of covalently or noncovalently linked bistetrapyrrole. Due to the difficult chemistry involved many groups have shied away from preparing such compounds with hydroporphyrins. However, a few such examples have been reported.

One of the first structures reported by Senge et al. was that of the ethyl bridged dimer **45**.¹²⁴ The compound was obtained in solvated and unsolvated forms, both of which show a similar conformation in the chlorin rings. Notably, due to the presence of a flexible linker group the two macrocycles in both forms form a twisted quasi cofacial arrangement. The twist angles of the two macrocycle planes are 54.4° and 57.3°, respectively. This arrangement is clearly shown in Fig. 11.

45

46 Z, M = Ni(II)

47 Z, M = Cu(II)

48 E, M = Ni(II)

49 E, M = Cu(II)

50

51

Figure 11 View of the molecular structure of the bischlorin **45** (JURJUB). Hydrogen atoms have been omitted for clarity. Adapted from reference 124.

Interesting results were also obtained for the ethene-bridged OEC compounds. These compounds can be prepared as either the *trans*- or *cis*-configured dimers.¹²⁵ The *cis* compounds, e.g. **46**, have a cofacial arrangement of the two macrocycles with significant π -overlap which can be modulated depending on the central metals (Fig. 12). For example, **47** has a molecular structure more akin to that shown in Fig 11 with an interchlorin angle of 131.8° .¹²⁶ Even for the *trans*-configured dimers different arrangements for the macrocycles were found. The *meso* compound **48** has an almost orthogonal arrangement of the two macrocycles which form an angle of 88.8° between them. The *rac* compound **49** shows a much more coplanar arrangement with an angle of 16.2° between the two chlorin planes. A similar structure was also found for the bis nickel(II) complex of a *trans*-configured octaethylporphyrin octaethylchlorin dimer.¹²⁶ McMurry reactions were also used to fuse phytychlorin derivatives. For example, **50** was obtained in the *trans* configuration. The chlorin macrocycles show $\Delta 2\sigma$ deviations of 0.10-0.15 Å and the two chlorin planes are almost in plane with each other ($\angle 5.7^\circ$).¹²⁷ A similar arrangement ($\angle 4.1^\circ$), albeit with larger macrocycle distortions due to the metal center was found in the bischlorin e_6 derivative **51**.

Figure 12 Side view of the molecular structure of the bischlorin **46** (TOGDEY). Hydrogen atoms have been omitted for clarity. Adapted from reference 125.

Cofacial systems can also be prepared through weaker interactions. Thus, the zinc(II) complex of anhydro-mesorhodochlorin methyl ester **52** forms a cofacial π -stacked dimer through coordination of the zinc(II) center with the cyclohexanone oxygen atom.¹²⁸ Other examples for synthetic bischlorins which are structurally distinct from phytychlorins are **53**,¹²⁹ which has a cofacial coplanar structure. The related nickel(II) compound **54**, which carries four *meso* phenyl residues, still has a cofacial structure but the two macrocycles from a more opened angle.¹³⁰

Based on phytychlorins derived from Chl *a*, Smith and coworkers presented the only example of completely conjugated and planar bischlorins **55**.¹³¹ Fig. 13 clearly shows the overall planar structure and thus the conjugation through the two chromophore units.

Figure 13 View of the molecular structure of the bisphytychlorin **55** (NAHJAH). Hydrogen atoms have been omitted for clarity. Adapted from reference 131.

B. Synthetic Hydroporphyrins

There are about a 100 "nonphytyochlorin" or "non-chlorin e₆" type crystal structures. These do give additional information on the conformation and core structure of chlorins. However, their relevance to chlorophyll derivatives is of more theoretical interest. Thus, only a brief overview and survey of related synthetic hydroporphyrin structures will be given here so that the reader can quickly gain access to the literature. A detailed conformational analysis is currently in progress and will be reported in due course.

1. Chlorins

The most accesible chlorins are those derived from 5,10,15,20-tetraphenyl- and 2,3,7,8,12,13,17,18-octaethylporphyrins. Historically, these include some of the earliest structural reports on hydroporphyrins. In the tetraphenylchlorin series a typical example is the structure of pyridine adduct of (5,10,15,20-tetraphenylchlorinato)zinc(II) **56** which was derived through reduction of the related porphyrin.¹³² Another examples is a hexacoordinated iron(II) species.¹³³

Many similar systems were obtained through β -addition reactions. 2,3-Dialkylated derivatives such as **57**¹³⁴ and **58**¹³⁵ were described by Senge and coworkers. The free base was characterized both as the unsolvated form and the methylene chloride solvate with almost identical structural features. The respective zinc(II) complex was crystallized as the methanol adduct. Other examples are **59**,¹³⁶ **60**¹³⁷ and related species¹³⁸ derived from carbene reactions, **61**¹³⁷ and **62**,¹³⁹ derived from the respective 2,3-dioxospecies, such as the basic framework in **63**.¹⁴⁰ Compound **64**, derived from **63** was crystallized in unsolvated and solvated forms while a related 7-oxo-8,8-bis(2-chloroethoxy) free base was characterized as well,¹⁴⁰ Related structures are those of the free base and nickel(II) complex of 2-aza-3-oxo-5,10,15,20-tetraphenylchlorin.¹⁴¹ Examples with less residues at the periphery are **65**,¹⁴² **66**,¹⁴³ and **67**.¹⁴⁴

Another example is the structure of *N*22-methyl-5,10,15,20-tetra(4-methylphenyl)chlorin, which has a very nonplanar conformation due to congestion in the porphyrin core.¹⁴⁵ A number of *meso* alkylchlorins include (5,10,15,20-tetramethylchlorinato)nickel(II) which exhibited a typical Ni-induced *ruf* distortion,^{146,147}

One way to stabilize hydroporphyrins against oxidation to the respective porphyrins is substitution of the β -hydrogen atoms with nonhydrogen atoms. Most successful have been derivatives with geminal alkyl residues at the reduced pyrrole ring. A relatively large number of such compounds has been structurally characterized; for example, **68**¹⁴⁸ and **69**.¹⁴⁹ An interesting compound is the intramolecularly cyclized chlorin **70**.¹⁵⁰ Despite the cyclization the molecule is still relatively planar, an indication of the flexibility of the reduced pyrrole ring to accommodate steric strain. Note that **71** is a natural compound derivative, anhydrobonellin methyl ester. These are physiologically active chlorins from the marine echurian *Bonella viridis*. The structure shows only moderate distortions. The $\Delta 24$ value is 0.12 Å and maximum C_m displacements are 0.2 Å while maximum C_b displacements are 0.55 Å in the vicinity of the fused ring.

Related synthetic compounds are the 13²,17³-cyclopheophorbide enol (not shown) for which no coordinates are available¹⁵¹ and the phytoporphyrin derivative **71**, which has a planar macrocycle.¹⁵² Other examples are those of compounds derived from pinacol

rearrangements, such as the iron complexes **72**¹⁵³ and **73**,¹⁵⁴ and the nickel complex **74**,^{155,156} β -Dihydroxy compounds have been characterized as well. Examples include **75**,¹⁵⁷ and the related 2,3-dihydroxy etiochlorin I.¹⁵⁸

2. Bacteriochlorins and Isobacteriochlorins

In contrast to the chlorins, few tetrahydroporphyrin structures have been reported. This is mainly due to the increasing instability of bacteriochlorins and isobacteriochlorins versus chlorins.

For simple *meso* substituted hydroporphyrins, the structure of 5,10,15,20-tetrabutylbacteriochlorin has been reported, which has a completely planar macrocycle.¹⁵⁹ The pyridine adduct of the zinc(II) complex of tetraphenylbacteriochlorin shows the typical feature of a five coordinated zinc tetrapyrrole.¹⁶⁰ Other examples include the carbene adduct **76**,¹³⁶ the pyridyl derivative **77**, which formed dimeric structures in the crystal through coordination of the zinc to the nitrogen atom of the pyridyl residues.¹⁶¹ For β -substituted systems the structure of **78** is typical for a nickel complex,¹⁶² Similar to the chlorins several bacteriochlorins with geminal dialkyl groups have been characterized. A representative tetrapyrrole is **79**.¹⁶³

The most simple isobacteriochlorin structures were derived from octaethylporphyrin. Classic examples are the structures of several different isomers of nickel(II) complex **80** and the related free bases.¹⁶⁴ Most isobacteriochlorin structures include a geminal dialkyl group for stabilization as well. Examples are **81**,¹⁶⁵ **82**,¹⁶⁶ **83**,¹⁶⁷ **84**,^{168,169} **85**,^{169,170} Others are those with an exocyclic double bond, e.g. **86**,¹⁷¹ An example for a compound derived from Pheo a is the nickel(II) complex of anhydromesorhodoisobacteriochlorin methyl ester **87**, with a typical *ruf* core conformation.¹⁷²

3. Special cases

Benzochlorins are a special class of hydroporphyrins where the reduced ring is constructed through an intramolecular annelation reaction. While the fused aromatic ring introduces some steric strain it also counteracts to some extent the conformational flexibility found in other hydroporphyrins by making the aromatic system more rigid. A typical example with some resemblance to phytychlorins is the structure of **88**, where the overall macrocycle is almost planar due to the fused ring systems.¹⁷³ A simpler system is that of free base octaethylbenzo[*at*]porphyrin which shows only small deviations from planarity with $\Delta 24 = 0.05 \text{ \AA}$ and maximum C_b displacements reaching $0.21 \text{ \AA}$.¹⁴⁸ The corresponding Ni(II) complex is much more distorted and shows a $\Delta 24$ value of $0.26 \text{ \AA}$. The macrocycle shows an asymmetric ruffled conformation with C_m displacements ranging from 0.28 to $0.51 \text{ \AA}$.¹⁷⁴

Although the concept of the conformational flexibility of porphyrins is now well established, few studies have been performed on specifically designed hydroporphyrins. The first examples are the classic studies on hexahydroporphyrins by Eschenmoser and coworkers.³⁹ These included compounds such as **89**¹⁷⁵ and **90**.¹⁵⁶ Synthetically, most chlorins with peripheral steric interactions are either derived from phytylchlorins *via* subsequent modifications, e.g. ring V ring-opening reactions or from rhodochlorins. Some simple nona- and decasubstituted chlorins are accessible *via* substitution reactions on octaethylchlorin.

Only a few studies have tried to address the question of the conformational flexibility in hydroporphyrins directly by the synthesis of appropriate compounds; this is the case for compounds closely related to nonplanar porphyrins. One such study was published by Kalisch and Senge and described the structural analysis of tetraphenylchlorin derivatives with an increasing number of β -ethyl groups,¹⁷⁶ and thus an increasing number of *peri*-interactions.¹⁷⁷ Typical compounds are those of the free bases **91**, **92**, and **93** and similar ones. Studies on the free bases and zinc(II) complexes clearly identified the impact of the number and regiochemical arrangement of the substituents on the conformation.

89

90

91

92

93

94 M = 2H, R = Me
95 M = Cu, R = CHO

96 M = Ni(II), X = Br
97 M = 2H, X = H

Other systems with both *meso* and β -substituents are **94**,¹⁴⁸ **95**,¹²⁶ **96** and **97**.¹⁷⁸ The available structural data of such "highly substituted chlorins" shows a large variability in the conformation of even closely related compounds. Due to the larger conformational flexibility of chlorins the effects of individual substituents on the conformation are difficult to establish

although larger displacements of substituted *meso* carbons are frequently observed in metallochlorins. Overall, and only to a rough approximation, it appears that chlorins have a tendency towards more *ruf* distortion.

Several other compounds, which technically can be termed chlorins have been structurally characterized. These include Osuka's fused systems,^{179,180} iron(III) salt derivatives,^{181,133} Smith's β,β -fused pyrroloporphyrins,¹⁸² bis(isoxazolo)bacteriochlorins,¹⁸³ purpurins^{184,185} and related compounds.¹⁸⁶ However, these compounds are structurally too distinct from chlorophyll derivatives to be relevant here.

VIII. Outlook

With regard to future structural studies, much attention has recently been given to the self-assembly of porphyrins related to the BChl c and d¹⁸⁷ and this is currently extended to the hydroporphyrins.^{188,189} Indeed, a recent paper by Wasielewski and coworkers using small- and wide-angle X-ray scattering in solution reveals that Chl trefoils self-assemble in the presence of 1,4-diazabicyclo[2.2.2]octane to yield supramolecular cyclic trimers.¹⁹⁰ Recent results indicate that fluorophobic effects may be used to construct ordered (B)Chl nanostructures,¹⁹¹ and similar strategies are used to construct LHC systems for photovoltaics.¹⁹² Computational advances will help to predict aggregation structures of chlorophylls,¹⁹³ Most likely any structural chemistry advances in this area will involve completely synthetic hydroporphyrins.¹⁹⁴ Recent advances made in the synthesis of unsymmetrical porphyrins will now be extended to the respective hydroporphyrins and will allow a definitive analysis of the interrelationship between substituent pattern, conformation, structure and physical properties. In terms of isolated "real" chlorophyll - or at least phytychlorin derivatives - novel structural information will only be slowly forthcoming. At present only few groups are focusing on the advancement of chlorophyll chemistry^{9,195,196,197} and none are active in the area of phytychlorin structural chemistry.

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IX. References

1. Krasnovsky, A. A. Jr. *Photosynth. Res.* **2003**, 76, 389.
2. Willstätter, R.; Stoll, A. *Untersuchungen über Chlorophyll. Methoden und Ergebnisse*; J. Springer: Berlin, 1913.
3. Deisenhofer, J.; Michel, H. *Angew. Chem., Int. Ed. Engl.* **1989**, 28, 829.
4. McDermott, G.; Prince, S. M.; Freer, A. A.; Hawthornthwaite-Lawless, A. M.; Papiz, M. Z.; Cogdell, R. J.; Isaacs, N. W. *Nature* **1998**, 374, 517.
5. Moser, S.; Müller, T.; Oberhuber, M.; Kräutler, B. *Eur. J. Org. Chem.* **2009**, 21.
6. Gossauer, A.; Engel, N. *J. Photochem. Photobiol. B: Biol.* **1996**, 32, 141.
7. Senge, M. O.; Wiehe, A.; Rypa, C. in *Chlorophylls and Bacteriochlorophylls: Biochemistry, Biophysics, Functions and Applications*, (Grimm, B.; Porra, R.; Rüdiger, W.; Scheer, H., eds.), Advances in Photosynthesis and Respiration, Vol. 25, Springer: Dordrecht, 2006, pp. 27–37.
8. Kruse, O.; Rupprecht, J.; Mussgnug, J. R.; Dismukes, G. C.; Hankamer, B. *Photochem. Photobiol. Sci.* **2005**, 4, 957.
9. Nyman, E. S.; Hynninen, P. H. *J. Photochem. Photobiol. B: Biol.* **2004**, 73, 1.

10. Senge, M. O.; Richter, J. in *Biorefineries – Industrial Processes and Products. Status Quo and Future Directions*, (Kamm, B.; Gruber, P. R.; Kamm, M., eds.), Vol. 2, Wiley-VCH Verlag: Weinheim, 2006, 325.
11. Scheer, H. *Chlorophylls*, CRC Press: Boca Raton, 1991.
12. Senge, M. O. *J. Photochem. Photobiol. B: Biol.* **1992**, 16, 3.
13. International Union of Pure and Applied Chemistry, International Union of Biochemistry; Joint Commission on Biochemical Nomenclature, *Pure Appl. Chem.* **1987**, 59, 779.
14. Smith, K. M. *Photosynth. Res.* **1994**, 41, 23.
15. Takaichi, S.; Wakao, N.; Hiraishi, A.; Itoh, S.; Shimada, *Photosynth. Res.* **1999**, 59, 255.
16. Wakao, N.; Yokoi, Isoyama, N.; Hiraishi, A.; Shimada, K.; Kobayashi, M.; Kise, H.; Iwaki, M.; Itoh, S.; Takaichi, S.; Sakurai, Y. *Plant Cell Physiol.* **1996**, 37, 889.
17. Hiraishi, A.; Shimada, K. *J. Gen. Appl. Microbiol.* **2001**, 47, 161.
18. Ikegami, I.; Nemoto, A.; Sakashita, K. *Plant Cell Physiol.* **2005**, 46, 729.
19. Smith, K. M.; Kehres, L. A.; Tabb, H. D. *J. Am. Chem. Soc.* **1980**, 102, 7149.
20. Senge, M. O. *Chem. Unserer Zeit* **1992**, 26, 86.
21. Douglas, R. H.; Partridge, J. C.; Dulai, K.; Hunt, D.; Mullineaux, C. W.; Tauber, A. Y.; Hynninen, P. H. *Nature* **1998**, 393, 423.
22. Hynninen, P. H. in *Chlorophylls*, (Scheer, H. ed.), CRC Press: Boca Raton, 1991, pp 145–209.
23. Pavlov, V. Y.; Ponomarev, G. V. *Khim. Geterosikl. Soed.* **2004**, 483; *Chem. Heterocycl. Chem.* **2004**, 40, 393.
24. Garrido, J. L.; Zapata, M.; Muniz, S. *J. Phycol.* **1995**, 31, 761.
25. Lin, C.; Li, C.; Wu, T. *Chem. Pharm. Bull.* **2004**, 52, 1151.
26. Wu, T.; Hsu, M.; Kuo, P.; Sreenivasulu, B.; Damu, A. G.; Su, C.; Li, C.; Chang, H. *J. Nat. Prod.* **2003**, 66, 1207.
27. Jeffery, S. W.; Wright, S. W.; Zapata, M. *Marine Freshw. Res.* **1999**, 50, 879.
28. Watanabe, N.; Yamamoto, K.; Ihshikawa, H.; Yagi, A.; Sakata, K.; Brinen, L. S.; Clardy, J. *J. Nat. Prod.* **1993**, 56, 305.
29. Yamamoto, K.; Sakata, K.; Watanabe, N.; Yagi, A.; Brinen, L. S.; Clardy, J. *Tetrahedron Lett.* **1992**, 33, 2587.
30. Ma, L.; Dolphin, D. *J. Org. Chem.* **1996**, 61, 2501.
31. Borrego, C. M.; Garcia-Gil, J.; Cristin, X. P.; Vila, X.; Abella, C. A. *FEMS Microbiol. Ecol.* **1998**, 26, 257.
32. Airs, R. L.; Borrego, C. M.; Garcia-Gil, J.; Keely, B. J.; *Photosyn. Res.* **2002**, 70, 221.
33. Huber, R. *Eur. J. Biochem.* **1990**, 187, 283.
34. Fajer, J. *Isr. J. Chem.* **1992**, 32, 363.
35. Senge, M. O. in *The Porphyrin Handbook*, (Kadish, K. M.; Smith, K. M.; Guillard, R., eds.), Vol. 1, Academic Press: San Diego, 2000, pp. 239.
36. Shelnutt, J. A.; Song, X. X.; Ma, J. G.; Jia, S. L.; Jentzen, W.; Medforth, C. J. *Chem. Soc. Rev.* **1998**, 27, 31.
37. Senge, M. O. *Chem. Commun.* **2006**, 243.
38. Kratky, C.; Waditschatka, R.; Angst, C.; Johansen, P. E.; Plaquevent, J. C.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1985**, 68, 1312.
39. Eschenmoser, A. *Ann. N. Y. Acad. Sci.* **1986**, 471, 108.
40. Scheidt, W. R.; Lee, Y.-J. *Struct. Bonding (Berlin)* **1987**, 64, 1.
41. Shelnutt, J. A.; Majumder, S. A.; Sparks, L. D.; Hobbs, J. D.; Medforth, C. J.; Senge, M. O.; Smith, K. M.; Miura, M.; Luo, L.; Quirke, J. M. E. *J. Raman Spectrosc.* **1992**, 23, 523.

42. Hoard, J. L. *Ann. N. Y. Acad. Sci.* **1973**, 206, 18.
43. Meyer, E. F. jr. *Acta Crystallogr.* **1972**, B28, 2162.
44. Barkigia, K. M.; Berber, M. D.; Fajer, J.; Medforth, C. J.; Renner, M. W.; Smith, K. M. *J. Am. Chem. Soc.* **1990**, 112, 8851.
45. Jentzen, W.; Simpson, M. C.; Hobbs, J. D.; Song, X.; Ema, T.; Nelson, N. Y.; Medforth, C. J.; Smith, K. M.; Veyrat, M.; Mazzanti, M.; Ramasseul, R.; Marchon, J.-C.; Takeuchi, T.; Goddard III, W. A.; Shelnut, J. A. *J. Am. Chem. Soc.* **1995**, 117, 11085.
46. Guillard, R.; Lecomte, C.; Kadish, K. M. *Struct. Bonding (Berlin)* **1987**, 64, 205.
47. Jentzen, W.; Song, X. Z.; Shelnut, J. A. *J. Phys. Chem. B* **1997**, 101, 1684.
48. Jentzen, W.; Ma, J.-G.; Shelnut, J. A. *Biophys. J.* **1998**, 74, 753.
49. Ryppa, C.; Senge, M. O.; Hatscher, S. S.; Kleinpeter, E.; Wacker, P.; Schilde, U.; Wiehe, A. *Chem. Eur. J.* **2005**, 11, 3427.
50. van Grondelle, R.; Dekker, J. P.; Gillbro, T.; Sundstrom, V. *Biochim. Biophys. Acta* **1994**, 1187, 1.
51. Fenna, R. E.; Matthews, B. W. *Nature* **1975**, 258, 573.
52. Matthews, B. W.; Fenna, R. E. *Acc. Chem. Res.* **1980**, 13, 309.
53. Tronrud, D. E.; Schmid, M. F.; Matthews, B. W. *J. Mol. Biol.* **1986**, 188, 443.
54. Gudowska-Nowak, E.; Newton, M. D.; Fajer, J. *J. Phys. Chem.* **1990**, 94, 5795.
55. Prince, S. M.; Papiz, M. Z.; Freer, A. A.; McDermott, G.; Hawthornthwaite-Lawless, A. M.; Cogdell, R. J.; Isaacs, N. W. *J. Mol. Biol.* **1997**, 268, 412.
56. Sauer, K.; Cogdell, R. J.; Prince, S. M.; Freer, A.; Isaacs, N. W.; Scheer, H. *Photochem. Photobiol.* **1996**, 64, 564.
57. Koepke, J.; Hu, X.; Muenke, C.; Schulten, K.; Michel, H. *Structure* **1996**, 4, 581.
58. Freer, A.; Prince, S.; Sauer, K.; Papiz, M.; Hawthornthwaite-Lawless, A.; McDermott, G.; Cogdell, R.; Isaacs, N. W. *Structure* **1996**, 4, 449.
59. Michel, H.; Epp, O.; Deisenhofer, J. *EMBO J.* **1986**, 5, 2445.
60. Budil, D. E.; Gast, P.; Chang, C.-H.; Schiffer, M.; Norris, J. R. *Ann. Rev. Phys. Chem.* **1987**, 38, 561.
61. Michel-Beyerle, M. E.; Plato, M.; Deisenhofer, J.; Michel, H.; Bixon, M.; Jortner, J. *Biochim. Biophys. Acta* **1988**, 932, 52.
62. Marcus, R. A.; Sutin, N. *Biochim. Biophys. Acta* **1988**, 811, 265.
63. Norris, J. R.; Budil, D. E.; Gast, P.; Chang, C.-H.; El-Kabbani, O.; Schiffer, M. *Biochim. Biophys. Acta* **1988**, 811, 265.
64. Plato, M.; Möbius, K.; Michel-Beyerle, M. E.; Bixon, M.; Jortner, J. *J. Am. Chem. Soc.* **1988**, 110, 7279.
65. Ivashin, N.; Källebring, B.; Larsson, S.; Hansson, Ö. *J. Phys. Chem. B* **1998**, 102, 5017.
66. Chirino, A. J.; Lous, E. J.; Huber, M.; Allen, J. P.; Schenck, C. C.; Paddock, M. L.; Feher, G.; Rees, D. C. *Biochemistry* **1994**, 33, 4584.
67. Palaniappan, V.; Martin, P. C.; Chynwat, V.; Frank, H. A.; Bocian, D. F. *J. Am. Chem. Soc.* **1993**, 115, 12035.
68. Czarnecki, K.; Chynwat, V.; Erickson, J. P.; Frank, H. A.; Bocian, D. F. *J. Am. Chem. Soc.* **1997**, 119, 2594.
69. Peloquin, J. M.; Violette, C. A.; Frank, H. A.; Bocian, D. F. *Biochemistry* **1990**, 29, 4892.
70. Senge, M. O. *Heterocycles* **2009**, 78, 1523.
71. Senge, M. O., in preparation.
72. Atanaska, A.; Silvia, A.; Stoitchkova, K.; Picorel, R. *Photochem. and Photobiol.* **2007**, 83, 1301.

73. Telfer, A.; Pascal, A. A.; Bordes, L.; Barber, J. Bruno, R.; *J. Phys. Chem. B.* **2010**, *114*, 2255.
74. Chen, J.; Shana, L.; Keough, J. M.; Barry, B. A. *J. Phys. Chem. B.* **2009**, *113*, 11367.
75. Bruno, R. *Photosyn. Res.* **2009**, *101*, 147.
76. Takumi, N.; Berthomieu, C. *Adv. Photosyn. Res.* **2005**, *22*, 367.
77. Li, M.; Chang, W. *Photosyn. Res.* **2009**, *102*, 223.
78. Allen, J. P.; Seng, C.; Larson, C. *Photosyn. Res.* **2009**, *102*, 231.
79. Amunts, A.; Toporik, H.; Borovikova, A.; Nelson, N.; *J. Biol. Chem.* **2010**, *285*, 3478.
80. Amunts, A.; Drory, O.; Nelson, N.; *Nature* **2007**, *447*, 58.
81. Ben-Shem, A.; Frolow, F.; Nelson, N.; *Nature* **2003**, *426*, 630.
82. Jordan, P.; Fromme, P.; Witt, H. T.; Klukas, O.; Saenger, W.; Kraub, N. *Nature*, **2001**, *411*, 909.
83. Guskov, A.; Kern, J.; Gabdulkhakov, A.; Broser, M.; Zouni, A.; Saenger, W. *Nature Struct. Mole. Biol.* **2009**, *16*, 334
84. Loll, B.; Kern, J.; Saenger, W.; Zouni, A.; Biesiadka, J. *Nature* **2005**, *438*, 1040.
85. Camara-Artigas, A.; Blackenship, R. E.; Allen, J. P. *Photosyn. Res.* **2003**, *75*, 49.
86. Deisenhofer, J.; Epp, O.; Miki, K.; Huber, R.; Michel, H. *Nature* **1985**, *318*, 618.
87. Jacobs, E. E.; Vatter, A. E.; Holt, A. S. *Arch. Biochem. Biophys.* **1954**, *53*, 228.
88. Donnay, G. *Arch. Biochem. Biophys.* **1959**, *80*, 80.
89. Kukhtevich, I. L.; Bilyak, A. I. *Biofizika* **1965**, *10*, 424.
90. Kukhtevich, I. L.; Bilyak, A. I. *Ukr. Khim. Zh.* **1965**, *31*, 943.
91. Gherorghe, V.; Tugulea, L.; Teodorescu, V. *Exp. Trends Phys.* **1979**, 239.
92. Grzegorzewski, B.; Mallek, J.; Manikowski, H.; Frackowiak, D. *Acta Phys. Polonica* **1988**, *A74*, 445.
93. Ketelaar, H. *Nature* **1937**, *140*, 196.
94. Kratky, C.; Dunitz, J. D. *Acta Cryst.* **1975**, *B31*, 1586.
95. Chow, H.-C.; Serlin, R.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7230.
96. Serlin, R.; Chow, H.-C.; Strouse, C. E. *J. Am. Chem. Soc.* **1975**, *97*, 7237.
97. Kratky, C.; Dunitz, J. D. *Acta Cryst.* **1977**, *B33*, 545.
98. Kratky, C.; Isenring, H. P.; Dunitz, J. D. *Acta Cryst.* **1977**, *B33*, 547.
99. de Boer, I.; Matysik, J.; Amakawa, M.; Yagai, S.; Tamiaki, H.; Holzwarth, A. R.; de Groot, H. J. M. *J. Am. Chem. Soc.* **2003**, *125*, 13374.
100. Senge, M. O.; Ruhlandt-Senge, K.; Smith, K. M. *Z. Naturforsch.* **1995**, *50b*, 139.
101. Knapp, S.; Huang, B.; Emge, T. J.; Sheng, S.; Krogh-Jespersen, K.; Potenza, J. A.; Schugar, H. J. *J. Am. Chem. Soc.* **1999**, *121*, 7977.
102. Taniguchi, M.; Ptaszek, M.; McDowell, B. E.; Boyle, P. D.; Lindsey, J. S. *Tetrahedron* **2007**, *63*, 3850.
103. Senge, M. O.; Smith, K. M. *Photochem. Photobiol.* **1994**, *60*, 139.
104. Senge, M. O.; Smith, K. M. *Photochem. Photobiol.* **1991**, *54*, 841.
105. Fischer, M. S.; Templeton, D. H.; Zalkin, A.; Calvin, M. *J. Am. Chem. Soc.* **1972**, *94*, 3613.
106. Senge, M. O.; Smith, K. M. *Z. Kristallogr.* **1992**, *199*, 239.
107. Chee, C. F.; Rahman, N. A.; Zain, S. M.; Ng, S. W. *Acta Cryst.* **2008**, *E64*, o1986.
108. Smith, K. M.; Goff, D. A.; Fajer, J.; Barkigia, K. M. *J. Am. Chem. Soc.* **1982**, *104*, 3747.
109. Smith, K. M.; Goff, D. A.; Fajer, J.; Barkigia, K. M. *J. Am. Chem. Soc.* **1983**, *105*, 1674.
110. Barkigia, K. M.; Chantranupong, L.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1988**, *110*, 7567.

111. Barkigia, K. M.; Gottfried, D. S.; Boxer, S. G.; Fajer, J. *J. Am. Chem. Soc.* **1989**, *111*, 6444.
112. Senge, M. O.; Bobe, F. W.; Huster, M. S.; Smith, K. M. *Liebigs Ann. Chem.* **1991**, 871.
113. Barkigia, K. M.; Melamed, D.; Sweet, R. M.; Smith, K. M.; Fajer, J. *Spectrochim. Acta A* **1997**, *53*, 463.
114. Barkigia, K. M.; Fajer, J.; Smith, K. M.; Williams, G. J. B. *J. Am. Chem. Soc.* **1981**, *103*, 5890.
115. Barkigia, K. M.; Gottfried, D. S. *Acta Cryst.* **1994**, *C50*, 2069.
116. Kozyrev, A. N.; Suresh, V.; Das, S.; Senge, M. O.; Shibata, M.; Dougherty, T. J.; Pandey, R. K. *Tetrahedron* **2000**, *56*, 3353.
117. Senge, M. O.; Smith, K. M. *Acta Cryst.* **1997**, *C53*, 1314.
118. Pajunen, A.; Stapelbroek-Mollmann, M. E.; Hynninen, P. H. *Acta Cryst.* **1996**, *C52*, 743.
119. Senge, M. O.; Ruhlandt-Senge, K.; Lee, S.-J. H.; Smith, K. M. *Z. Naturforsch.* **1995**, *50b*, 969.
120. Hargus, J. A.; Fronczek, F. R.; Vicente, M. G. H.; Smith, K. M. *Photochem. Photobiol.* **2007**, *83*, 1006.
121. Brantley, S. E.; Gerlach, B.; Olmstead, M. M.; Smith, K. M. *Tetrahedron Lett.* **1997**, *38*, 937.
122. Paolesse, R.; Pandey, R. K.; Forsyth, T. P.; Jaquinod, L.; Gerzevske, K. R.; Nurco, D. J.; Senge, M. O.; Licoccia, S.; Boschi, T.; Smith, K. M. *J. Am. Chem. Soc.* **1996**, *118*, 3869.
123. Senge, M. O.; Ruhlandt-Senge, K.; Smith, K. M. *Acta Cryst.* **1992**, *C48*, 1810.
124. Senge, M. O.; Hope, H.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 2* **1993**, 11.
125. Senge, M. O.; Kalisch, W. W.; Ruhlandt-Senge, K. *J. Chem. Soc., Chem. Commun.* **1996**, 2149.
126. Kalisch, W. W.; Senge, M. O.; Ruhlandt-Senge, K. *Photochem. Photobiol.* **1998**, *67*, 312.
127. Jaquinod, L.; Nurco, D. J.; Medforth, C. J.; Pandey, R. K.; Forsyth, T. P.; Olmstead, M. M.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1013.
128. Senge, M. O.; Smith, K. M. *Acta Cryst.* **1997**, *C53*, 1022.
129. Kopke, T.; Pink, M.; Zaleski, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15864.
130. Kopke, T.; Pink, M.; Zaleski, J. *Org. Biomol. Chem.* **2006**, *4*, 4059.
131. Jaquinod, L.; Senge, M. O.; Pandey, R. K.; Forsyth, T. P.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1840.
132. Spaulding, L. D.; Andrews, L. C.; Williams, G. J. B. *J. Am. Chem. Soc.* **1977**, *99*, 6918.
133. Simonneaux, G.; Kobeissi, M.; Toupet, L. *Inorg. Chem.* **2003**, *42*, 1644.
134. Senge, M. O.; Kalisch, W. W.; Bischoff, I. *Chem. Eur. J.* **2000**, *6*, 2721.
135. Sergeeva, N. N.; Shaker, Y. M.; Finnigan, E. M.; McCabe, T.; Senge, M. O. *Tetrahedron* **2007**, *63*, 12454.
136. Shea, K. M.; Jaquinod, L.; Khoury, R. G.; Smith, K. M. *Tetrahedron* **2000**, *56*, 3139.
137. Jaquinod, L.; Gros, C.; Khoury, R. G.; Smith, K. M. *Chem. Commun.* **1996**, 2581.
138. Jaquinod, L.; Gros, C.; Olmstead, M. M.; Antolovich, M.; Smith, K. M. *J. Chem. Soc., Chem. Commun.* **1996**, 1475.
139. Wojaczynski, J.; Latos-Grazynski, L.; Glowiak, T. *Inorg. Chem.* **1997**, *36*, 6299.
140. Kopke, T.; Pink, M.; Zaleski, J. M. *Synlett* **2008**, 1882.
141. Kopke, T.; Pink, M.; Zaleski, J. M. *Synlett* **2006**, 2183.

142. Muthiah, C.; Ptaszek, M.; Nguyen, T. M.; Flack, K. M.; Lindsey, J. S. *J. Org. Chem.* **2007**, *72*, 7736.
143. Laha, J. K.; Muthiah, C.; Taniguchi, M.; Lindsey, J. S. *J. Org. Chem.* **2006**, *71*, 7049.
144. Galezowski, M.; Gryko, D. T. *J. Org. Chem.* **2006**, *71*, 5942.
145. Stolzenberg, A. M.; Simerly, S. W.; Steffey, B. D.; Haymond, G. S. *J. Am. Soc. Chem.* **1997**, *199*, 11843.
146. Ulman, A.; Gallucci, J.; Fisher, D.; Ibers, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 6852.
147. Gallucci, J. C.; Swepston, P. N.; Ibers, J. A. *Acta Cryst.* **1982**, *B38*, 2134.
148. Barkigia, K. M.; Thompson, M. A.; Fajer, J.; Pandey, R. K.; Smith, K. M.; Vicente, M. G. H. *New. J. Chem.* **1992**, *16*, 599.
149. Montforts, F.-P.; Meier, A.; Scheurich, G.; Haake, G.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1592.
150. Pelter, A.; Ballantine, J. A.; Murray-Rust, P.; Ferrito, V.; Psaila, A. F. *Tetrahedron Lett.* **1978**, 1881.
151. Karuso, P.; Bergquist, P. R.; Buckleton, J. S.; Cambie, R. C.; Clark, G. R.; Rickard, C. E. F. *Tetrahedron Lett.* **1986**, *27*, 2177.
152. Senge, M. O.; Pandey, R. K. **1999**, private communication to the CCDC, CCDC 121725.
153. Cai, S.; Belikova, E.; Yatsunyk, L. A.; Stolzenberg, A. M.; Walker, F. A. *Inorg. Chem.* **2005**, *44*, 1882.
154. Scheidt, W. R.; Duval, H. F.; Neal, T. J.; Ellison, M. K. *J. Am. Chem. Soc.* **2000**, *122*, 4651.
155. Stolzenberg, A. M.; Glazer, P. A.; Foxman, B. M. *Inorg. Chem.* **1986**, *25*, 983.
156. Connick, P. A.; Haller, K. J.; Macor, K. A. *Inorg. Chem.* **1993**, *32*, 3256.
157. Barkigia, K. M.; Chang, C. K.; Fajer, J. *J. Am. Chem. Soc.* **1991**, *113*, 7445.
158. Senge, M. O.; Hope, H.; Iakovides, P.; Smith, K. M. *Photochem. Photobiol.* **1993**, *58*, 748.
159. Senge, M. O.; Runge, S. *Acta Cryst.* **1998**, *C54*, 1917.
160. Barkigia, K. M.; Miura, M.; Thompson, M. A.; Fajer, J. *Inorg. Chem.* **1991**, *30*, 2233.
161. Vasudevan, J.; Stibrany, R. T.; Bumby, J.; Knapp, S.; Potenza, J. A.; Emge, T. J.; Schugar, H. J. *J. Am. Chem. Soc.* **1996**, *118*, 11676.
162. Waditschatka, R.; Kratky, C.; Jaun, B.; Heinzer, J.; Eschenmoser, A. *J. Chem. Soc., Chem. Commun.* **1985**, 1604.
163. Pandey, R. K.; Isaac, M.; MacDonald, I.; Medforth, C. J.; Senge, M. O.; Dougherty, T. J.; Smith, K. M. *J. Org. Chem.* **1997**, *62*, 1463.
164. Kratky, C.; Angst, C.; Johansen, J. E. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 211.
165. Cruse, W. B. T.; Harrison, P. J.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 2376.
166. Gibson, C. L.; Doyle, M. J.; Raithby, P. R.; Battersby, A. R. *J. Chem. Soc., Perkin Trans. I* **1994**, 1893.
167. Chang, C. K.; Barkigia, K. M.; Hanson, L. K.; Fajer, J. *J. Am. Chem. Soc.* **1986**, *108*, 1352.
168. Montforts, F.-P.; Romanowski, F.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 480.
169. Romanowski, F.; Mai, G.; Kusch, D.; Montforts, F.-P.; Bats, J. W. *Helv. Chim. Acta* **1996**, *79*, 1572.
170. Montforts, F.-P.; Mai, G.; Romanowski, F.; Bats, J. W. *Tetrahedron Lett.* **1992**, *33*, 765.
171. Barkigia, K. M.; Fajer, J.; Chang, C. K.; Young, R. *J. Am. Chem. Soc.* **1984**, *106*, 6457.

172. Renner, M. W.; Furenlid, L. R.; Barkigia, K. M.; Forman, A.; Shim, H.-K.; Simpson, D. J.; Smith, K. M.; Fajer, F. *J. Am. Chem. Soc.* **1991**, *113*, 6891.
173. Mettah, S.; Shibata, M.; Alderfer, J. L.; Senge, M. O.; Smith, K. M.; Rein, R.; Dougherty, T. J.; Pandey, R. K. *J. Org. Chem.* **1998**, *63*, 1646.
174. Arnold, D. P.; Gaete-Holmes, R.; Johnson, A. W.; Smith, A. R. P.; Williams, G. A. *J. Chem. Soc., Perkin Trans. I* **1978**, 1660.
175. Johansen, J. E.; Piermattie, V.; Angst, C.; Diener, E.; Kratky, C.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 261.
176. Kalisch, W. W.; Senge, M. O. *Tetrahedron Lett.* **1996**, *37*, 1183.
177. Senge, M. O.; Kalisch, W. W.; Runge, S. *Tetrahedron* **1998**, *54*, 3781.
178. Shea, K. M.; Jaquinod, L.; Khoury, R. G.; Smith, K. M. *J. Chem. Soc., Chem. Commun.* **1998**, 759.
179. Tanaka, T.; Nakamura, Y.; Osuka, A. *Chem. Eur. J.* **2008**, *14*, 204.
180. Tanaka, T.; Nakamura, Y.; Aratani, N.; Osuka, A. *Tetrahedron Lett.* **2008**, *49*, 3308.
181. Kobeissi, M.; Toupet, L.; Simonneaux, G. *Inorg. Chem.* **2001**, *40*, 4494.
182. Gros, C. P.; Jaquinod, L.; Khoury, R. G.; Olmstead, M. M.; Smith, K. M. *J. Porphyrins Phthalocyanines* **1997**, *1*, 201.
183. Li, X.; Zhuang, J.; Li, Y.; Liu, H.; Wang, S.; Zhu, D. *Tetrahedron Lett.* **2005**, *46*, 1555.
184. Forsyth, T. P.; Nurco, D. J.; Pandey, R. K.; Smith, K. M. *Tetrahedron Lett.* **1995**, *36*, 9093.
185. Rosenthal, J.; Hodgkiss, J. M.; Young, E. R.; Nocera, D. G. *J. Am. Chem. Soc.* **2006**, *128*, 10474.
186. Gunter, M. J.; Robinson, B. C.; Gulbis, J. M.; Tiekink, E. R. T. *Tetrahedron* **1991**, *47*, 7853.
187. Balaban, T. S. *Acc. Chem. Res.* **2005**, *38*, 612.
188. Wasielewski, M. R. *Acc. Chem. Res.* **2009**, *42*, 1910.
189. Huber, V.; Sengupta, S.; Würthner, F. *Chem. Eur. J.* **2008**, *14*, 7791.
190. Gunderson, V. L.; Conron, S. M. M.; Wasielewski, M. R. *Chem. Commun.* **2010**, 401.
191. Zhou, X.; Kang, S.-W.; Kumar, S.; Li, Q. *Liq. Cryst.* **2009**, *36*, 269.
192. Li, L.; Kang, S.-W.; Harden, J.; Sun, Q.; Zhou, X.; Dai, L.; Jakli, A.; Kumar, S.; Li, Q. *Liq. Cryst.* **2008**, *35*, 233.
193. Ben Fredi, A.; Ben Lakhdar, Z.; Ruiz-Lopes, M. F. *Chem. Commun.* **2008**, 718.
194. O'Neal, W. G.; Jacobi, P. A. *J. Am. Chem. Soc.* **2008**, *130*, 1102.
195. Miyatake, T.; Tamiaki, H. *J. Photobiol. Photochem. Rev.* **2005**, *6*, 89.
196. Nechaev, A. V.; Mironov, A. F. *Russ. J. Bioorg. Chem.* **2008**, *34*, 245.
197. Kozyrev, A. N.; Chen, Y. H.; Goswami, L. N.; Tabczynski, W. A.; Pandey, R. K. *J. Org. Chem.* **2006**, *71*, 1949.

Table 1. CCDC deposition numbers for small molecule single crystal structure determinations of chlorophyll related hydroporphyrins.

#	Compound	Space group	T [K]	R	Esd's [$\text{\AA}$]	Comments	CCDC code	Ref.
<i>Chlorophyll derivatives:</i>								
15	Chlorophyllonic acid a methyl ester	$P2_1$	238	0.0468	0.011–0.03	$\Delta 24 = 0.087 \text{ \AA}$	KUBDUG	29
17	Ethyl chlorophyllide a	$P3_1$	295	–	–	Unit cell only	ZZZWCY	93
17	(H ₂ O)Ethyl chlorophyllide a•H ₂ O	$P3_1$	295	0.048	n.d.	$\Delta 26 = 0.062 \text{ \AA}$	AECLPA01	94
17	(H ₂ O)Ethyl chlorophyllide a•H ₂ O	$P3_1$	295	0.053	0.011–0.03	$\Delta 26 = 0.06 \text{ \AA}$	AECLPA10	95
18	(H ₂ O)Ethyl chlorophyllide b•H ₂ O	$P3_1$	120	0.048	n.d.	$\Delta 26 = 0.054 \text{ \AA}$	ECPHBH	96
19	(H ₂ O)Methyl chlorophyllide a•H ₂ O	$P2_1$	295	0.09	n.d.	$\Delta 26 = 0.04 \text{ \AA}$	MCLPHD10	97
20	(H ₂ O)Methyl pyrochlorophyllide a•Et ₂ O	$P2_12_12_1$	295	0.079	n.d.	$\Delta 26 = 0.042 \text{ \AA}$	MPCHLM10	98
21	(Methyl pyropheophorbido a)nickel(II)	$P4_32_12$	130	0.064	0.006–0.010	$\Delta 26 = 0.255 \text{ \AA}$	HAHBAT	104
22	Methyl (3-deethyl-3-hydroxymethyl-phytychlorinato)cadmium(II)	$P2_1$	277	n.d.	n.d.	$\Delta 26 = 0.05 \text{ \AA}$, polymeric structure, Cd•••HOCH ₂ -	UMAZAJ	99
23	Chloro(phytychlorinato methyl ester)iron(III)	$P2_1$	130	0.075	0.011–0.03	2 indep. mol.; $\Delta 26 = 0.13 \text{ \AA}$, 0.17 $\text{\AA}$	YINCAZ	100
24	(Methyl 2-devinyl-2-carboximinopyropheophorbido a)zinc(II)•CHCl ₃	$P2_12_12_1$	295	0.065	0.011–0.030	$\Delta 26 = 0.122 \text{ \AA}$, polymeric structure, Zn•••HON-	CELRIU	101
24	(Methyl 2-devinyl-2-carboximinopyropheophorbido a)zinc(II)•EtOCHO	$P2_12_12_1$	295	–	–	Unit cell only	CELSUH	101
25	(Methyl 20-methylphytychlorinato)nickel(II)	$P4_32_12$	130	0.057	0.006–0.010	$\Delta 26 = 0.325 \text{ \AA}$	YOVYAJ	103
28	Methyl pheophorbide a	$P2_1$	295	0.051	n.d.	$\Delta 26 = 0.049 \text{ \AA}$	MPOPHA	105
29	Methyl mesopyropheophorbide a	$P2_12_12_1$	295	0.055	0.011–0.030	$\Delta 26 = 0.04 \text{ \AA}$	KOVXUO	106
30	Pheophorbide b ethyl ester	$P2_1$	100	0.0635	0.006–0.010	$\Delta 26 = 0.044 \text{ \AA}$	ROFVUE	107
31	Methyl 8-iso-butyl-12-ethyl-bacteriopheophorbide d	$P1$	295	0.056	n.d.	$\Delta 26_1 = 0.076 \text{ \AA}$, $\Delta 26_2 = 0.067 \text{ \AA}$; 2 independent molecules	BIPBIL	108
32	Methyl 8,12-diethyl-bacteriopheophorbide d	$P1$	295	0.048	n.d.	$\Delta 26_1 = 0.071 \text{ \AA}$, $\Delta 26_2 = 0.067 \text{ \AA}$; 2 independent molecules	BIPBOR	108
33	Methyl 8-neopentyl-12-ethyl-bacteriopheophorbide d	$P2_12_12_1$	120	0.084	n.d.	$\Delta 26 = 0.089 \text{ \AA}$	BIXREF01	109
34	Methyl (12-acetyl-8-ethyl)-bacteriopheophorbide d	$P-1$	130	0.129	0.011–0.030	$\Delta 26 = 0.078 \text{ \AA}$	SOSZOP	112
35	Methyl bacteriopheophorbide a•C ₆ H ₆	$P1$	200	0.045	0.001–0.005	$\Delta 26 = 0.043 \text{ \AA}$	BAVSUM01	111
35	Methyl bacteriopheophorbide a	$P1$	200	0.076	0.011–0.030	$\Delta 26 = 0.038 \text{ \AA}$	WIKSEO	115
<i>Phytochlorins and related compounds:</i>								
36	Benzimidazolo(2,1-n)purpurin-18 13 ¹ -imino-13 ² -imide methyl ester	$P2_12_12$	126	0.0603	0.006–0.010	$\Delta 24 = 0.053 \text{ \AA}$	FOXTUH	116

37	Quinoxalino(2,3-n)deoxypyropheophorbide a methyl ester	$P2_12_12$	130	0.0577	0.001-0.005	$\Delta 26 = 0.066 \text{ \AA}$	FOXWIY	116
38	17-Decacarboxyethyl-13 ¹ -deoxo-17-propylphytychlorin	$P2_1$	126	0.0576	0.006-0.010	$\Delta 26_{av} = 0.031 \text{ \AA}$, 2 independent molecules	RIWNIU	117
39	3 ¹ ,3 ² -Didehydrorhodochlorin-15-acetic acid trimethyl ester	$P2_1$	193	0.0891	0.006-0.010	$\Delta 24 = 0.058 \text{ \AA}$	ZUBBIH	118
40	(3 ¹ ,3 ² -Didehydro-rhodochlorinato-15-formic acid trimethyl ester)copper(II)•CH ₂ Cl ₂	$P1$	130	0.0726	0.011-0.030	$\Delta 24_1 = 0.172 \text{ \AA}$, $\Delta 24_2 = 0.204 \text{ \AA}$, $\Delta 24_3 = 0.055 \text{ \AA}$, $\Delta 24_4 = 0.087 \text{ \AA}$; 4 independent molecules	ZAJLUR	119
41	(Rhodochlorinato-15-acetic acid trimethyl ester)copper(II)	$P2_1$	130	0.069	0.006-0.010	$\Delta 24_1 = 0.146 \text{ \AA}$, $\Delta 24_2 = 0.148 \text{ \AA}$; 2 independent molecules	ZAJLOL	119
42	15 ² -Mono-(<i>L</i>)-aspartylchlorin-e ₆ tetramethyl ester•CH ₃ OH•H ₂ O	$P2_12_12_1$	110	0.105	0.011-0.030	$\Delta 24_1 = 0.19 \text{ \AA}$; $\Delta 24_2 = 0.073 \text{ \AA}$, 2 indep. molecules	NIMHAT	120
43	Methyl 20-methoxycarbonylmethyl-18-methoxycarbonyl-13-ethyl-3,7,12,17-tetramethyl-8-[2-(<i>o</i> -nitrophenylselenido)ethyl]chlorin-2-propionic acid	$P2_12_12_1$	130	0.0696	0.011-0.030	$\Delta 24 = 0.103 \text{ \AA}$	REFYEG	121
44	Rhodochlorin XV dimethyl ester•CH ₂ Cl ₂	$P-1$	130	0.091	0.006-0.010	$\Delta 24 = 0.058 \text{ \AA}$	KUHPIM	123
44	Rhodochlorin XV dimethyl ester	$P2_12_12$	130	0.062	0.006-0.010	$\Delta 24 = 0.0502 \text{ \AA}$	KUHPIR	123
–	[1-(<i>trans</i> -3 ¹ -Chlorinato-e ₆ -trimethyl (2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrinato-5-yl)benzene]di-nickel(II)•CHCl ₃	$C2$	130	0.0582	0.011-0.030	$\Delta 24_{chlorin} = 0.313 \text{ \AA}$	ZUSTIQ	122
Reaction center model compounds:								
45	20,20'-Ethylenebis(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorin)•CH ₂ Cl ₂	$C2/c$	120	0.0725	0.006-0.010	$\Delta 24 = 0.07 \text{ \AA}$, centrosymmetric	JURJOV	124
45	20,20'-Ethylenebis(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorin)	$C2/c$	130	0.0631	0.006-0.010	$\Delta 24 = 0.11 \text{ \AA}$, centrosymmetric	JURJUB	124
46	{1,2-Bis[5-(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorinato)]nickel(II)} <i>cis</i> -ethene	$P-1$	128	0.082	0.006-0.010	$\Delta 24_1 = 0.506 \text{ \AA}$; $\Delta 24_2 = 0.568 \text{ \AA}$	TOGDEY	125
47	{1,2-Bis[5-(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorinato)]copper(II)} <i>cis</i> -ethene•CH ₂ Cl ₂	$P2_1/c$	130	0.178	0.011-0.030	$\Delta 24_1 = 0.10 \text{ \AA}$; $\Delta 24_2 = 0.142 \text{ \AA}$	TOGDIC	125
48	<i>Meso</i> {1,2-Bis(5-(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorinato))nickel(II)} <i>trans</i> -ethene•CH ₂ Cl ₂ •EtOH	$P-1$	130	0.0107	0.011-0.030	$\Delta 24_1 = 0.358 \text{ \AA}$; $\Delta 24_2 = 0.308 \text{ \AA}$	LOGXEK	126
49	<i>rac</i> {1,2-Bis(5-(<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorinato))copper(II)} <i>trans</i> -ethene	$P2_1/n$	130	0.0116	0.006-0.010	$\Delta 24_1 = 0.236 \text{ \AA}$; $\Delta 24_2 = 0.16 \text{ \AA}$	LOGXUA	126

–	5-((<i>E</i>)-1,2-((2,3,7,8,12,13,17,18-Octaethylporphyrinato-5-yl)-nickel(II))ethene)-((<i>trans</i> -2,3,7,8,12,13,17,18-octaethylchlorinato)-nickel(II))•CH ₂ Cl ₂	<i>P-1</i>	219	0.0702	0.001-0.005	2 independent molecules	LOGXIO	126
50	1,2-Bis(20-(1,7,12,18-tetramethyl-2,8-diethyl-13,15-ethano-17-(3-methylpropionate)-17,18-dihydroporphyrinato))- <i>trans</i> -ethene•H ₂ O	<i>P2₁2₁2₁</i>	130	0.0439	0.006-0.010	$\Delta 26_1 = 0.153 \text{ \AA}$; $\Delta 26_2 = 0.108 \text{ \AA}$	NACVES	127
51	1,2-Bis(1,7,12,18-tetramethyl-2,8-diethyl-13-(methylmethanoate)-15-(2-methylethanoate)-17-(3-methylpropionate)-17,18-dihydroporphyrinato)-nickel(II)- <i>trans</i> -ethene•H ₂ O	<i>P1</i>	130	0.0425	0.006-0.010	$\Delta 24_1 = 0.321 \text{ \AA}$; $\Delta 24_2 = 0.372 \text{ \AA}$	NACVAO	127
52	Bis((anhydro-mesorhodochlorinato-XV methyl ester)zinc(II))	<i>P-1</i>	126	0.0681	0.006-0.010	$\Delta 24 = 0.132 \text{ \AA}$; cofacial structure; Zn•••O=C	RESBEW	128
53	10,10',15,15',20,20'-Hexaphenyl-5,7:5',7'-bis(<i>o</i> -phenylene)-7,7'-bichlorin-8,8'-dione•Et ₂ O•CH ₂ Cl ₂	<i>C2/c</i>	130	0.0579	0.001-0.005	Cofacial structure	QOPMEO	129
54	10,10',15,15',20,20'-Hexaphenyl-5,7:5',7'-bis(<i>o</i> -phenylene)-7,7'-bichlorin-8,8'-dione•Et ₂ O•CH ₂ Cl ₂	<i>P2₁/n</i>	130	0.0715	0.006-0.010	Opened cofacial structure	TETWIZ	130
-	13 ¹ ,13 ^{1'} -Bis(13 ² -methoxyphytoporphyrin methyl ester)ylidene•CH ₂ Cl ₂	<i>P2₁</i>	128	0.0771	0.011-0.030	Planar bischromophore system	NAHHUZ	131
55	13 ¹ ,13 ^{1'} -Bis(phytoporphyrin methyl ester)ylidene	<i>P2₁</i>	128	0.0872	0.011-0.030	Planar bischromophore system	NAHJAH	131